

UNIVERSITAT DE BARCELONA

Avaluació de l'impacte dels contaminants orgànics polars en la qualitat de l'aigua urbana

Francesc Labad Roig

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TESI DOCTORAL

Avaluació de l'impacte dels contaminants orgànics polars en la qualitat de l'aigua urbana

Francesc Labad Roig



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Francesc Labad Roig

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“El dolor és temporal. El rendir-se, per sempre”
Derrick Rose

“Ganar no te hace mejor, ni perder perdedor... todos somos lo mismo”
Cupido

Per a tots aquells que no hi confiaven però, sobretot, per a mi

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Abreviacions i Acrònims

6-PPD	N-1,3-dimetilbutil-N'-(1,3-dimetilbutil)-p-fenilenediamina
AB	Absorció
ADI	Ingesta diària acceptable
AF	Factor d'avaluació
APCI	Ionització química a pressió atmosfèrica
APPI	Fotoionització a pressió atmosfèrica
BCASA	Barcelona Cicle de l'Aigua Societat Anònima
C	Carboni
C18	Octadecilsilà
C-Trap	Trampa de captura d'ions
CAS	Servei de resums químics
CCS	Secció transversal de col·lisió
CE	Electroforesi capil·lar
CO_2	Diòxid de carboni
D	Deuteri
Da	Daltons
DT	Temps de deriva
DTIMS	Espectrometria de mobilitat iònica amb tub de deriva
DWEL	Nivell equivalent d'aigua potable
DWI	Ingesta d'aigua potable
EAWAG	Institut Federal Suís de Ciència i Tecnologia Aquàtiques
EC_{50}	Concentració eficaç 50
ECHA	Agència Europea de Substàncies i Mescles Químiques
ERQ	Quocient del risc ambiental
ESI	Ionització per electrosprai
EU	Unió Europea
FAIMS	Espectrometria de mobilitat iònica de camp asimètric
FOE	Freqüència d'exposició
FTIR	Espectroscòpia d'infraroig per transformada de Fourier
GC	Cromatografia de gasos
GCB	Carboni negre grafititzat
H	Hidrogen
HILIC	Cromatografia de líquids d'interacció hidrofílica
HLB	Equilibri hidrofílic-hidrofòbic
HRMS	Espectrometria de masses d'alta resolució
HRQ	Quocient del risc humà
IM	Mobilitat Iònica
IPCC	Grup Intergovernamental d'Experts sobre el canvi climàtic
Km	Quilòmetre
L	Litre
LC	Cromatografia de líquids
LRMS	Espectrometria de masses de baixa resolució
LOD	Límit de detecció
Log D_{ow}	Logaritme decimal del coeficient de distribució octanol-aigua, depenent del pH
Log K_{oc}	Logaritme decimal del coeficient de distribució octanol-carboni orgànic
Log K_{ow}	Logaritme decimal del coeficient de distribució octanol-aigua
LOQ	Límit de quantificació
M	Mobilitat
m	metres
m/z	Relació massa-càrrega
MALDI	Desorció-ionització per làser assistida per matriu
MAPTAC	Metacrilat de trimetilamoni
ME	Efecte matriu
MMLC	Cromatografia de líquids de mode mixt
MS	Espectrometria de masses
msSPE	Extracció en fase sòlida multi capa
N	Nitrogen
N_2	Nitrogen gas
ng	Nanogram
NPLC	Cromatografia de líquids de fase normal
O	Oxigen
P	Persistència
PCP	Producte de cura personal
PET	Polietilè
PFAS	Substàncies per- i polifluoroalquilades
PFBS	Àcid perfluorobutansulfonic
PFHxS	Àcid perfluorohexansulfonic
PFOS	Àcid perfluorooctansulfonic

Abreviacions i Acrònims

PGC	Carboni grafític porós
PMT	Substància persistent, mòbil i tòxica
PNEC	Concentració predita sense efecte
pg	Picogram
Q	Quadrupol
Q(SAR)	Relació Quantitativa Estructura-Activitat
Q-TOF	Quadrupol-temps de vol
REACH	Registre, Avaluació, Autorització i Restricció de Substàncies Químiques
RFK	Factor de retenció
RPLC	Cromatografia de líquids de fase inversa
RR	Recuperació relativa
RSD	Desviació estàndard relativa
S	Sofre
SFC	Cromatografia amb fluids supercrítics
SPE	Extracció en fase sòlida
SUDS	Sistema de drenatge urbà sostenible
SVHC	Associació Suïssa de la Indústria Química
TENG	Nano generador triboelèctric
TIMS	Espectrometria de mobilitat d'ions atrapats
TrOCs	Contaminants orgànics traça
TWIMS	Espectrometria de mobilitat iònica d'ona viatgera
UBA	Agència Federal de Medi Ambient d'Alemanya
UFZ	Centre Helmholtz per a la Investigació Ambiental
UHPLC	Cromatografia de líquids d'ultra alta eficàcia
VAE	Evaporació assistida al buit
vMC	Compost molt mòbil
vPvM	Substància molt persistent i molt mòbil
WAX	Intercanvi aniònic feble
WCX	Intercanvi catiònic feble
WWTP	Estació de depuració d'aigües residuals
°C	Graus Centígrads
µg	Microgram
Σ	Sumatori

RESUM

Aquesta tesi doctoral es centra en l'estudi dels contaminants orgànics traça (TrOCs) en aigües urbanes, analitzant-ne la presència, desenvolupant metodologies analítiques i avaluant l'impacte ambiental. Els TrOCs són compostos químics com fàrmacs, pesticides, productes industrials i de cura personal que, fins i tot a concentracions baixes, poden tenir efectes nocius sobre els ecosistemes i la salut humana. Aquesta recerca posa un especial èmfasi en els compostos polars, sovint poc considerats en estudis científics, però d'alta rellevància a causa de la seva mobilitat i persistència en el medi aquós.

Un dels pilars de la tesi és el desenvolupament de metodologies analítiques avançades per identificar i quantificar TrOCs en aigües subterrànies, superficials, de pluja, d'escorrentia, de clavegueram i aigua de sortida de SUDS. S'han implementat dues tècniques extractives principals: l'extracció en fase sòlida multi adsorbent (msSPE) i l'evaporació assistida al buit (VAE). La msSPE va resultar especialment útil per compostos polars i moderadament polars, mentre que el VAE va demostrar ser molt versàtil i adequat per a compostos molt polars. Ambdues tècniques permeten concentrar els compostos d'interès i reduir interferències de la matriu aquosa, facilitant la seva detecció amb instruments d'alta resolució.

En la fase de separació i quantificació, es van utilitzar tècniques cromatogràfiques en fase inversa (C18) i també la cromatografía de líquids d'interacció hidrofílica (HILIC), combinades amb l'espectrometria de masses d'alta resolució amb l'analitzador Orbitrap i de mobilitat iònica, clau per a compostos que són difícils de retenir i separar mitjançant la cromatografia líquida. En conjunt, aquestes metodologies van permetre analitzar més de 100 TrOCs amb un ampli rang de polaritats, oferint separacions de compostos per a l'avaluació dels seus impactes. A més, al capítol 3, es van determinar 33 CCS de compostos orgànics de pes molecular baix i molt polars, molts d'ells reportats per primer cop a la literatura.

La recerca va evidenciar que l'aigua subterrània urbana de Barcelona està contaminada significativament per TrOCs, principalment a causa de la seva recàrrega per aigües residuals no tractades (43,7%) i per aigües superficials del riu Besòs (51,5%). També s'identificaren altres aportacions de recàrrega com les aigües d'escorrentia urbana (4.8 %).

A partir dels resultats obtinguts als capítols 4 y 5, aquesta tesi es proposa d'utilitzar certs TrOCs com a traçadors orgànics per identificar fonts de contaminació en aqüífers urbans. Compostos com la carbamazepina van ser útils per rastrejar la contribució de les aigües residuals, pluja i escorrentia. Aquesta aplicació permet millorar la gestió dels recursos hídrics identificant els orígens de la contaminació, per tal d'optimitzar les estratègies de mitigació.

Per altra banda, s'ha avaluat quin és el risc ambiental dels TrOCs quantificats a les aigües subterrànies urbanes. Mitjançant el coeficient de risc ecotoxicològic (ERQ), es va calcular el potencial de cada compost per danyar ecosistemes aquàtics. Els fàrmacs iopamidol i iohexol, el pesticida fipronil, el compost industrial melamina i altres, han demostrat presentar riscos ecològics. Paral·lelament, els resultats del risc per a la salut humana a través del coeficient de risc sanitari (HRQ), revelen que fàrmacs com valsartan i el seu metabòlit àcid valsartànic poden tenir un impacte significatiu en infants, fins i tot a concentracions baixes, fet que evidencia la necessitat d'establir controls rigorosos.

Els resultats subratllen la necessitat d'implementar tractaments efectius per eliminar TrOCs de les aigües urbanes en funció de les concentracions trobades i de l'ús al que es poden destinar. També es destaca la importància de monitoritzar especialment els compostos polars, mòbils i persistents, que són més difícils de capturar i eliminar en els sistemes aquàtics. Aquesta prioritat esdevé especialment rellevant en el context del canvi climàtic i l'escassetat hídrica, on l'aigua subterrània emergeix com una font crítica per garantir el subministrament d'aigua dolça.

En síntesi, la tesi proporciona eines analítiques i dades valuoses per abordar el repte global de la contaminació per TrOCs, especialment els molt polars, en aigües urbanes, combinant investigació científica i propostes pràctiques per millorar la qualitat de l'aigua i protegir la salut pública i el medi ambient.

Paraules clau: Espectrometria de masses, compostos polars, cromatografia de líquids, mobilitat iònica, aigua urbana, aigua subterrània, risc medi ambiental.

ABSTRACT

This doctoral thesis focuses on the analysis, presence, and impact of trace organic contaminants (TrOCs) in urban waters, emphasizing polar compounds often overlooked in the past. TrOCs, including pharmaceuticals, pesticides, and industrial chemicals, pose significant environmental and health risks, even at low concentrations.

The thesis develops advanced methodologies to extract and analyse TrOCs from various water sources such as groundwater, surface water, rainwater, and urban runoff. Two main extraction methods were implemented: a multi-layer solid-phase extraction (msSPE) and vacuum-assisted evaporation (VAE). These approaches improved analyte concentration and minimized matrix interference. Chromatographic techniques in both reverse and normal phases, combined with ion mobility spectrometry, were used to separate and quantify more than 100 TrOCs with diverse polarities.

The results indicate significant groundwater contamination in Barcelona, mainly due to untreated wastewater (43.7%) and surface water recharge (51.5%). Specific TrOCs were identified as high-risk, including pharmaceuticals (i.e., iopamidol and iohexol), the pesticide fipronil, and industrial compounds such as melamine. Urban runoff, characterized by its complexity and diverse pollutant sources, also contributed significantly to the contamination profile.

Key findings highlight the ecological and human health risks associated with polar TrOCs due to their high mobility and persistence in aquatic environments. The study emphasizes the importance of efficient treatment technologies to remove TrOCs from urban waters, safeguarding both environmental quality and public health. Furthermore, TrOCs were proposed as potential tracers to identify pollution sources and improve urban water management strategies.

Overall, results showed that polar TrOCs demand special attention in water monitoring and treatment, as they pose substantial challenges for detection and removal. By integrating advanced analytical techniques and emphasizing pollution source identification, the study contributes valuable insights to addressing the pressing issue of urban water contamination.

Keywords: High-resolution mass spectrometry, polar compounds, liquid chromatography, ion mobility, urban water, groundwater, environmental risk.

Capítol



1.
Introducció

INTRODUCCIÓ GENERAL

1.1 Per què l'aigua subterrània? Un recurs clau en períodes de sequera

En un món on cada gota compta, la sequera ha passat de ser una crisi estacional a esdevenir un recordatori constant que l'aigua és un dels nostres recursos més amenaçat. Aquesta tesi aborda els principals problemes actuals, l'any 2024, que afecten no només els humans, sinó també totes les espècies del planeta, amb especial atenció a l'escassetat d'aigua. Científics de tot el món han exposat les seves preocupacions: "El canvi climàtic és una amenaça real i imminent per a les espècies de tot el món. No només afecta els humans, sinó també a tots els éssers vius." comenta la primatòloga i antropòloga britànica, Jane Goodall. Per la seva banda, Mario Molina, premi Nobel de Química l'any 1995, afirma: "El canvi climàtic és un dels desafiaments més grans de la nostra era. Les solucions científiques i tecnològiques existeixen, però cal la voluntat política i social per implementar-les".

El canvi climàtic ha estat present al llarg de la història del nostre pla-

neta a causa de factors naturals com l'activitat volcànica, les variacions orbitals o els cicles solars (Alley et al., 2003; Petit et al., 1999). No obstant això, l'escalfament global actual és principalment conseqüència de l'activitat humana, iniciant-se a finals del segle XVIII amb la Revolució Industrial i l'ús massiu de combustibles fòssils, que han incrementat les emissions de CO_2 (Hansen et al., 2006; Mann and Jones, 2003). Ara que el canvi climàtic és àmpliament reconegut com una crisi humanitària, gràcies a grups com el Grup Intergovernamental d'Experts sobre el Canvi Climàtic (IPCC), es fa evident que l'augment de la temperatura global està accelerant-se de manera alarmant en els darrers anys (Figura 1.1A) (IPCC, 2022).

El principal objectiu d'aquesta tesi, fruit de més de quatre anys de recerca, és evidenciar els problemes actuals de l'aigua subterrània, especialment avaluant la contaminació química dels recursos hídrics naturals.

L'aigua total del planeta Terra és d'aproximadament 1.386 milions de quilòmetres cúbics, o gairebé $1.4 \cdot 10^{21}$ litres (NASA, 2011; USGS, 2019). D'aquesta quantitat només el 2.5 % és aigua dolça (~ 35 km3). L'aigua dolça es distribueix en diferents compartiments: aigua superficial i atmosfèrica, glaceres i casquets polars, i aigües subterrànies (USGS, 2019). Malauradament, no tota aquesta aigua es accessible per als humans. Per exemple la major part de l'aigua emmagatzemada a les glaceres i casquets polars (69 % del total d'aigua dolça) o certs aqüífers profunds no poden ser utilitzats (Richey et al., 2015). Dels 35 km^3 d'aigua dolça, només uns 10,4 km^3 són disponibles per a ús humà. D'aquests, 0,42 km^3 corresponen a aigua superficial, com llacs i rius, mentre que 10 km^2 són aigües subterrànies (USGS, 2019). Sembla doncs que hi ha suficient aigua a la Terra per a tothom, especialment d'aigua subterrània, però cal tenir en compte, com s'ha mencionat abans, que el canvi climàtic i d'altres motius com l'exponencial creixement de la població, l'agricultura intensiva, la desforestació, una mala gestió global de l'aigua i, una de molt important en aquesta tesi, la contaminació de l'aigua dolça, fa que no tota l'aigua sigui de qualitat òptima per al seu ús (Cronin et al., 2012; NASA, 2023).

D'altra banda, el creixement exponencial de la població mundial accelera la demanda d'aigua, especialment en zones àrides i, recentment,

també a les grans ciutats (Unhabitat, 2022). Aquest fet provoca desequilibris mediambientals com l'augment de l'evaporació d'aigua dolça i l'ús descontrolat d'aquest recurs (Gleick, 2003). La globalització comporta, en part, centralització, que significa, a grans trets, moviment de la població de les zones rurals cap a les zones urbanitzades (Figura 1.1B) (United Nations Department of Economic and Social Affairs, 2022). Aquest estrès hídric a les grans ciutats promou l'ús de possible aigua urbana per a ús domèstic i fins i tot per al consum humà. Com es ben sabut, l'aigua superficial i subterrània són emprades extensament per l'abastament públic arreu del món (Vörösmarty et al., 2010). No obstant això, altres fonts d'aigua no convencionals podrien ajudar a cobrir part de les necessitats actuals.

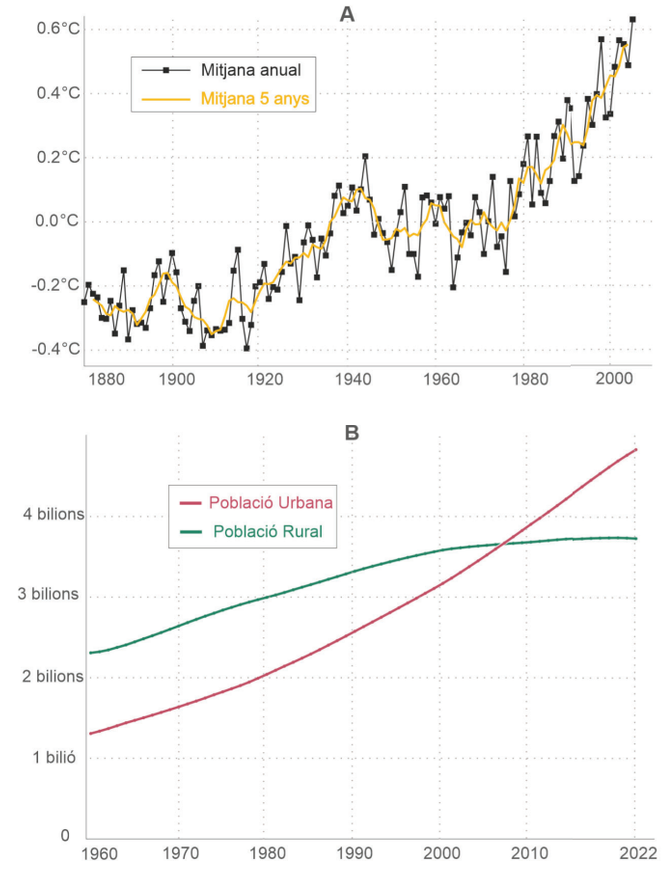


Figura 1.1. **A** Evolució de la variació de la temperatura Terrestre des de l'any 1880 fins als 2000. Adaptació de Hansen et al., (2006) **B** Evolució de la densitat poblacional mundial a zones rurals i urbanes. Adaptació de Our World in Data, (2022).

Les aigües subterrànies sota gran aglomeracions urbanes (Aigües Subterrànies Urbanes), fa poques dècades que han emergit com a una nova font de recurs hídric no convencional (Vázquez-Suñé et al., 2005). L'aigua subterrània, definida com l'aigua continguda en el terreny sota la seva superfície, és una font d'aigua convencional que pot complementar o substituir l'aigua superficial en determinats contextos (Hering, 2019). A més, les masses d'aigua subterrània són més resilients a les sequeres, oferint un valor afegit en la lluita contra el canvi climàtic (Figura 1.2). En grans zones urbanes l'ús de les aigües subterrànies s'ha anat limitant per diverses causes. La gran demanda i la necessitat de garantir la qualitat en el subministrament, ha portat a l'establiment de xarxes d'abastament públic centralitzades i molt supervisades, amb la qual cosa l'ús de les aigües subterrànies mitjançant xarxes privades de pous per part de particulars i empreses ha anat disminuint. A Barcelona, l'abastament de la ciutat es fa mitjançant aportacions d'aigües superficial (60%) i subterrànies (40%) tractats a les plants de tractament i distribuïts mitjançant la xarxa pública d'abastament. Aquest recursos no són locals, sinó que son aigües del rius Llobregat, Besòs o Ter i pous de l'àmbit Metropolità, majoritàriament fora de l'àmbit purament urbà. En els últims anys, amb la intenció d'optimitzar els recursos locals i estalviar l'ús d'aigües de la xarxa, de gran qualitat però amb un alt cost de tractament, al municipi de Barcelona s'han establert dos Plans Municipals d'aprofitament de les aigües subterrànies urbanes (Ajuntament de Barcelona, 2022). Actualment, l'aigua subterrània s'utilitza principalment per a usos no potables, com el reg de parcs, la neteja de carrers i el manteniment de fonts ornamentals (Ajuntament de Barcelona, 2022).

Coneixent la importància de l'aigua subterrània en l'actualitat i de cara al futur, resulta essencial preservar-la tant a nivell quantitatiu com qualitatiu. depèn principalment del seu estat físic i químic, que estan íntimament lligats a les fonts de recàrrega dels aqüífers. Aquestes fonts inclouen l'aigua superficial, l'aigua de pluja o escorrentia, les pèrdues de les xarxes de clavegueram i altres processos que permeten la infiltració cap als aqüífers (Healy, 2010; Vázquez-Suñé et al., 2005). Si bé aquestes fonts són responsables de la recàrrega dels aqüífers, també són el vehicle per al transport de contaminants, tant inorgànics com orgànics, cap a l'aigua subterrània (Müller et al., 2020). Històricament, els nutrients

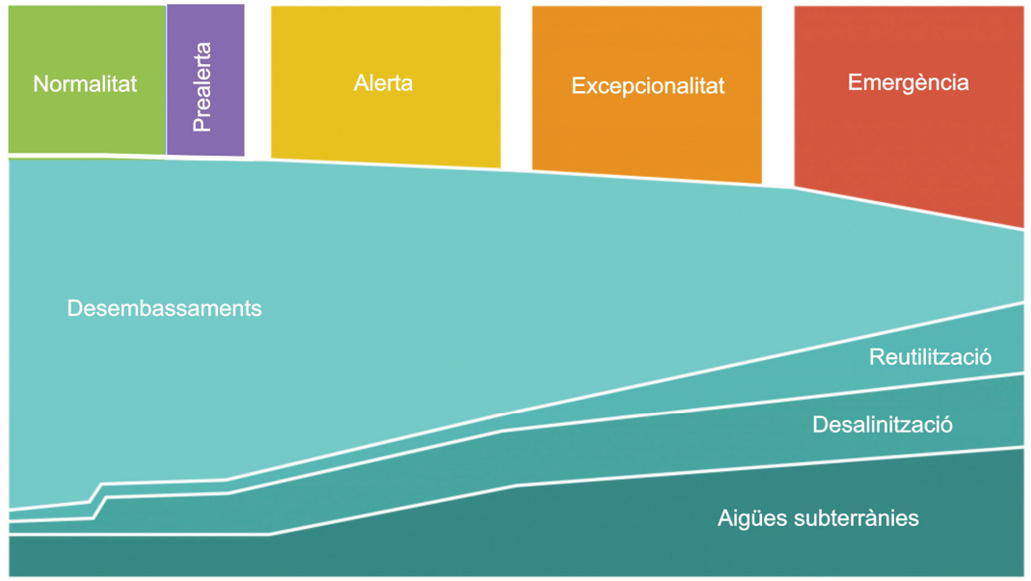


Figura 1.2. Ús dels diferents recursos hídrics de Catalunya a diferents estats d'emergència climàtica. Adaptació de CREAF, (2023).

(com els nitrats i el fòsfor) i els metalls pesants (com el plom i el crom) han estat els contaminants més monitoritzats en aigües subterrànies (Burri et al., 2019). No obstant això, en els darrers anys s'ha observat una presència significativa de contaminants orgànics traça (TrOCs, de l'anglès *Trace Organic Contaminants*), que poden causar greus impactes mediambientals i representar riscos per a la salut humana (Kumar et al., 2010; Pal et al., 2010). Aquesta família de contaminants comprèn diverses subfamílies, com ara fàrmacs, productes de cura personal, pesticides, drogues d'abús, edulcorants artificials, compostos industrials, retardants de flama i molts altres, que es detallaran a la següent secció.

1.2 Presència i fonts dels contaminants orgànics a les aigües urbanes

Què són els contaminants orgànics?

Com hem vist a la secció 1.1, tant l'aigua subterrània com les seves principals fonts de recàrrega poden contenir centenars de contaminants orgànics, aquí anomenats TrOCs. Els TrOCs són substàncies químiques

orgàniques principalment creades i usades pels humans, que acaben arribant al medi ambient i que poden causar efectes adversos als ecosistemes i a la salut humana (Pal et al., 2010). Es solen trobar a concentracions molt baixes, del ordre dels pg L-1 fins als µg L-1, i inclouen fàrmacs, productes de cura personal, herbicides, pesticides, compostos industrials, edulcorants artificials, i un llarg etc. (Kümmerer, 2009; Pal et al., 2010). Tot i estar presents a concentracions molt baixes, els TrOCs, tant individualment com amb mescla, poden ser capaços de causar efectes nocius a organismes aquàtics com peixos, crustacis o algues i terrestres com animals, plantes o humans, podent interferir amb el seu sistema endocrí, crear resistència antibiòtica, disminuir la fertilitat i capacitat reproductora, afectar al seu desenvolupament normal, etc. (Barceló and Petrovic, 2008). A més, molts TrOCs tenen la capacitat de bioacumular-se, d'altres de ser persistents al medi, d'altres de ser mòbils o també tenir més d'una característica alhora, fent que la detecció d'aquests contaminants sigui crucial per cuidar els nostres ecosistemes i per prevenir la salut humana (Deblonde et al., 2011; Sala et al., 2022; UBA, 2017). En aquesta tesi, diferents grups de TrOCs han sigut analitzats, principalment fàrmacs però incloent també compostos industrials de nova generació, edulcorants, pesticides, compostos de cura personal o compostos emprats dia a dia (com la cafeïna). Tanmateix, més enllà de les classificacions d'ús de les substàncies seleccionades per la tesi, la propietat més rellevant ha sigut la de la polaritat, analitzant compostos de polaritat moderada fins a molt polars. A les següent seccions aquesta propietat i la seva importància serà evidenciada.

Compostos més detectats a les aigües superficials, subterrànies i de pluja

Degut a la importància que suposa la contaminació de TrOCs en les aigües, s'exposaran els que més s'han trobat en aigües superficials, subterrànies, residuals i de pluja (o escorrentia) respecte les seves deteccions publicades a revisions sistemàtiques i articles més recents (Taula 1.1). Es detecten poc compostos amb un log D_{ow} per sobre de 4 a les aigües, com es pot observar a la Taula 1.1, ja que els compostos més lipofílics (o hidrofòbics) són sovint detectats a matrius com sòls, fangs o organismes vius (peixos, invertebrats, etc.) (Manjarrés-López et al., 2024). Predominen aquells amb un log D_{ow} inferiors a 3, i especialment inferiors a 2, coneguts per tenir característiques hidrofíliques, la qual cosa fa que siguin menys propensos a quedar-se retinguts a compartiments amb alta quantitat de carboni (greix, fang, sediments o sòl).

Què és el LOG D_{ow} ?

És el logaritme decimal del coeficient de distribució octanol-aigua d'un compost i, com a característica important, té en compte tant la forma neutra com ionitzada d'aquesta substància a un pH específic.

- Compostos que presentin un log D_{ow} < 0, demostren una major afinitat per l'aigua que per l'octanol (solvent orgànic de referència) i per tant seran compostos molt polars.
- Compostos amb log D_{ow} > 0 tenen una afinitat major per l'octanol, tot i que sovint fins a un valor de 3-4 es consideren polars.

Taula 1.1. Compostos (nom, nº CAS, usos i log D_{ow}) reportats a matrius urbanes d'aigua superficial, subterrània, aigües residuals i d'escorrentia incloent la concentració màxima.

Nom del compost	CAS	Usos	log D_{ow} (pH 7.4)	Matriu d'Aigua	Conc. Màxima (ng L^{-1})	Referència
17α-ethinylestradiol	57-63-6	Hormona	3.7	Sup.	57	(Zhou et al., 2019)
1H-Benzotriazol	95-14-7	Industrial	1.5	Sup.	56	(Neuwald et al., 2022)
				Sub.	1000	(Loos et al., 2010)
				Res.	221000	(Loos et al., 2013)
				Esc.	4100	(Zhang et al., 2024)
5-Methyl-1H-benzotriazol	136-85-6	Industrial	1.7	Sub.	520	(Loos et al., 2010)
				Res.	24300	(Loos et al., 2013)
				Esc.	1800	(Zhang et al., 2024)
Acefat	30560-19-1	Plaguicida	-0.5	Esc.	290	(Zhang et al., 2024)
Acesulfame	33665-90-6	Edulcorant	-2.8	Sup.	120000	(Montes et al., 2019a)
				Res.	2500000	(Loos et al., 2013)
				Esc.	3500	(Zhang et al., 2024)
Acetaminofèn	103-90-2	Fàrmac	0.4	Sup.	780	(Pal et al., 2010a)
				Sub.	17	(Bexfield et al., 2019)
				Esc.	14000	(Zhang et al., 2024)
Acridona	578-95-0	Fàrmac	3.7	Sub.	8.2	(Postigo and Barceló, 2015a)
Acyclovir	59277-89-3	Fàrmac	-1.5	Sub.	5.7	(Bexfield et al., 2019)
Amantadina	768-94-5	Fàrmac	-0.4	Sup.	48	(Montes et

Atenolol	29122-68-7	Fàrmac	-1.9	Sup.	390	(Zhou et al., 2019)
				Sub.	8.7	(Bexfield et al., 2019)
				Esc.	180	(Zhang et al., 2024)
Atorvastatina	134523-00-5	Fàrmac	1.3	Sup.	130	(Zhou et al., 2019)
				Res.	72.9	(Loos et al., 2013)
Azitromicina	83905-01-5	Fàrmac	1.4	Sub.	1600	(Sui et al., 2015)
				Esc.	1000	(Zhang et al., 2024)
Benzoylecgonina	519-09-5	Fàrmac	-0.2	Sub.	20	(Postigo and Barceló, 2015a)
Bezafibrat	41859-67-0	Fàrmac	-0.1	Sup.	15000	(Zhou et al., 2019)
				Sub.	26	(Sui et al., 2015)
				Res.	343	(Loos et al., 2013)
Bisphenol A	80-05-7	Industrial	3.6	Sub.	2300	(Loos et al., 2010)
				Esc.	13000	(Zhang et al., 2024)
Cafeïna	58-08-2	PCP	0.3	Sup.	40000	(Zhou et al., 2019)
				Sub.	680	(Bexfield et al., 2019)
				Res.	3002	(Loos et al., 2013)
				Esc.	53000	(Zhang et al., 2024)
Carbamazepina	298-46-4	Fàrmac	2.3	Sup.	12000	(Zhou et al., 2019)
				Sub.	390	(Loos et al., 2010)

				Res.	4609	(Loos et al., 2013)
				Esc.	1000	(Zhang et al., 2024)
Carisoprodol	78-44-4	Fàrmac	1.9	Sub.	58	(Bexfield et al., 2019)
Ciprofloxacina	85721-33-1	Fàrmac	-2.2	Sup.	14000	(Zhou et al., 2019)
Citalopram	59729-33-8	Fàrmac	1.3	Sup.	120	(Zhou et al., 2019)
				Sub.	7.4	(Bexfield et al., 2019)
				Res.	189	(Loos et al., 2013)
Claritromycina	81103-11-9	Fàrmac	2.4	Sup.	2400	(Zhou et al., 2019)
				Esc.	170	(Zhang et al., 2024)
Climbazole	38083-17-9	Fàrmac	3.3	Sup.	0.03	(Neuwald et al., 2022)
				Esc.	240	(Zhang et al., 2024)
Àcid clofibric	882-09-7	Fàrmac	-0.9	Sup.	250	(Pal et al., 2010a)
				Sub.	4200	(Postigo and Barceló, 2015a)
				Res.	127	(Loos et al., 2013)
Cotinina	486-56-6	PCP	0.2	Esc.	550	(Zhang et al., 2024)
Diazepam	439-14-5	Fàrmac	2.9	Sub.	100	(Sui et al., 2015)
Diclofenac	15307-86-5	Fàrmac	1.4	Sup.	19000	(Zhou et al., 2019)
				Sub.	380	(Sui et al., 2015)
				Res.	174	(Loos et al., 2013)

				Esc.	1200	(Zhang et al., 2024)
Erytromycina	114-07-8	Fàrmac	1.7	Sup.	1700	(Zhou et al., 2019)
Estriol	50-27-1	Hormona	2.7	Sup.	480	(Zhou et al., 2019)
Estrona	53-16-7	Hormona	3.4	Sup.	89	(Zhou et al., 2019)
				Sub.	4.0	(Loos et al., 2010)
ε-Caprolactam	105-60-2	Industrial	0.0	Sup.	350	(Montes et al., 2019a)
Fipronil	120068-37-3	Plaguicida	3.7	Esc.	10000	(Zhang et al., 2024)
Fipronil desulfynil	205650-65-3	Plaguicida	4.6	Esc.	1100	(Zhang et al., 2024)
Fipronil sulfide	120067-83-6	Plaguicida	5.5	Esc.	330	(Zhang et al., 2024)
Fipronil sulfona	120068-36-2	Plaguicida	4.7	Esc.	6000	(Zhang et al., 2024)
Fluconazol	86386-73-4	Fàrmac	0.7	Sub.	51	(Bexfield et al., 2019)
				Res.	598	(Loos et al., 2013)
				Esc.	160	(Zhang et al., 2024)
Gabapentina	60142-96-3	Fàrmac	-1.4	Esc.	2800	(Zhang et al., 2024)
Gemfibrozil	25812-30-0	Fàrmac	1.6	Sup.	7800	(Zhou et al., 2019)
				Res.	3619	(Loos et al., 2013)
				Esc.	750	(Sui et al., 2015)
Imidacloprid	138261-41-3	Plaguicida	-0.3	Esc.	700	(Zhang et al., 2024)
Iopamidol	60166-93-0	Fàrmac	-2.3	Sub.	1900	(Sui et al., 2015)
				Res.	6100	(Loos et al., 2013)

Ketoprofèn	22071-15-4	Fàrmac	0.1	Sup.	80	(Pal et al., 2010a)
				Sub.	2900	(Loos et al., 2010)
				Res.	1653	(Loos et al., 2013)
Lidocaïna	137-58-6	Fàrmac	1.3	Sub.	40	(Bexfield et al., 2019)
				Esc.	440	(Zhang et al., 2024)
Àcid mefenàmic	61-68-7	Fàrmac	2.0	Sup.	170	(Pal et al., 2010a)
Melamina	108-78-1	Fàrmac	-1.2	Sup.	2.1	(Neuwald et al., 2022)
				Sub.	5.9	(Neuwald et al., 2022)
Metformina	1115-70-4	Fàrmac	-3.4	Sub.	39	(Bexfield et al., 2019)
				Esc.	60000	(Zhang et al., 2024)
Metadona	76-99-3	Fàrmac	2.8	Sub.	43	(Bexfield et al., 2019)
Metopolol	37350-58-6	Fàrmac	-0.3	Sub.	360	(Sui et al., 2015)
Metrodinazol	443-48-1	Fàrmac	0.1	Esc.	160	(Zhang et al., 2024)
N-acetil-sulfametoxazol	21312-10-7	Fàrmac	-0.3	Sub.	5.5	(Postigo and Barceló, 2015a)
Àcid Naphthalè-1-sulfònic	85-47-2	Industrial	-2.7	Sup.	330	(Montes et al., 2019a)
Naproxè	22204-53-1	Fàrmac	0.5	Sup.	180	(Pal et al., 2010a)
				Sub.	150	(Sui et al., 2015)
				Res.	958	(Loos et al., 2013)
				Esc.	150	(Zhang et al., 2024)

Paraxantina	611-59-6	Fàrmac	-0.2	Sup.	1400	(Zhou et al., 2019)
Primidona	125-33-7	Fàrmac	-0.7	Sub.	140	(Sui et al., 2015)
				Esc.	3200	(Zhang et al., 2024)
Propranolol	525-66-6	Fàrmac	1.2	Sup.	590	(Zhou et al., 2019)
				Esc.	9.4	(Sui et al., 2015)
Propyphenazona	479-92-5	Fàrmac	2.1	Sup.	2000	(Zhou et al., 2019)
Sacarina	81-07-2	Edulcorant	-1.3	Sup.	7700	(Montes et al., 2019a)
				Sub.	0.11	(Neuwald et al., 2022)
Sulfadiazina	68-35-9	Fàrmac	-0.8	Sup.	19000	(Zhou et al., 2019)
				Res.	105	(Loos et al., 2013)
Sulfametoxazol	723-46-6	Fàrmac	-0.6	Sup.	12000	(Zhou et al., 2019)
				Sub.	120	(Sui et al., 2015)
				Res.	1691	(Loos et al., 2013)
				Esc.	6000	(Zhang et al., 2024)
Sulfapyridine	144-83-2	Fàrmac	0.4	Sup.	12000	(Zhou et al., 2019)
Tiametoxam	153719-23-4	Plaguicida	-0.3	Esc.	390	(Zhou et al., 2019)
Tramadol	3715-90-0	Fàrmac	0.5	Sup.	7700	(Zhou et al., 2019)
Àcid trifluorometansulfònic	1493-13-6	Industrial	-3.9	Sup.	970	(Montes et al., 2019a)
Trimetoprim	738-70-5	Fàrmac	-1.2	Sup.	210	(Pal et al., 2010a)
				Sub.	15	(Bexfield et al., 2019)

				Res.	800	(Loos et al., 2013)
				Esc.	420	(Zhang et al., 2024)
Valsartan	137862-53-4	Fàrmac	-0.9	Sup.	7500	(Zhou et al., 2019)
				Esc.	1700	(Zhang et al., 2024)
Àcid valsartànic	164265-78-5	Fàrmac	2.3	Esc.	150	(Zhang et al., 2024)
Venlafaxina	93413-69-5	Fàrmac	1.4	Sup.	580	(Zhou et al., 2019)
				Res.	548	(Loos et al., 2013)
				Esc.	110	(Zhang et al., 2024)

Sup.: Superficial; Sub.: Subterrània; Res.: Residual; Esc. Escorrentia

Vies de contaminació de les aigües subterrànies urbanes

Les aigües subterrànies rurals solen estar contaminades per compostos utilitzats en activitats agrícoles o veterinàries, com ara plaguicides o productes d'ús veterinari, les aigües subterrànies urbanes es veuen afectades principalment per compostos relacionats amb l'activitat humana i l'activitat industrial (també present en medis urbans), com fàrmacs, compostos industrials i contaminants emergents com els productes de cura personal. Aquest conjunt de compostos, coneguts com TrOCs, representa un risc important per a la qualitat dels recursos hídrics a les zones urbanes.

Tot i que l'aigua subterrània en el seu estat natural és generalment exempta de TrOCs, les diverses vies o fonts de recàrrega són responsables de transportar aquests contaminants als aqüífers. Abans d'arribar-hi, l'aigua passa per un procés d'infiltració natural a través del sòl, el qual pot actuar com una barrera mitigant. En aquest procés, l'aigua travessa la superfície del sòl fins a arribar a l'aqüífer (Figura 1.3) (Lerner, 2002). Aquesta infiltració natural contribueix a reduir la concentració de TrOCs gràcies a diversos processos com per exemple l'adsorció al sòl, però la seva eficàcia depèn de factors com la naturalesa del sòl (poro-

sitat, duresa, etc.), el cabal i la velocitat del flux d'aigua, així com les propietats físico-químiques dels contaminants implicats (Lerner, 2002; Vázquez-Suñé et al., 2010).

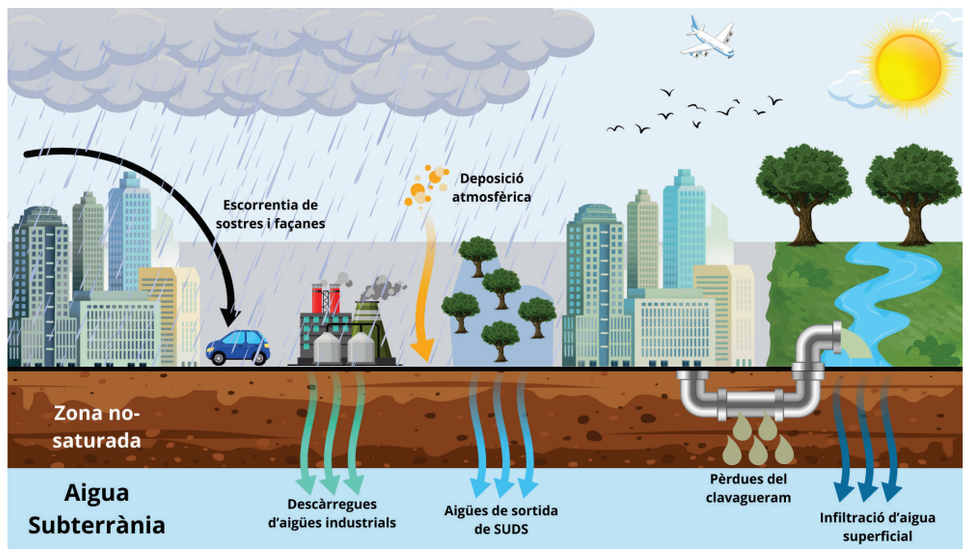


Figura 1.3. Esquema de les vies de recàrrega i contaminació dels aqüífers urbans. SUDS: de l'anglès Sustainable Urban Drainage Systems.

Els TrOCs arriben a les aigües subterrànies principalment si tenen propietats hidrofíliques que limiten la seva retenció durant el procés d'infiltració. Aquestes molècules solen ser polars o hidrofíliques (Postigo and Barceló, 2015b). Tanmateix, compostos menys polars també poden infiltrar-se en grans quantitats, especialment si estan presents de manera constant en el medi o si el sòl no és prou adsorbent (Elliott et al., 2022; Labad et al., 2023; Postigo and Barceló, 2015b). Més enllà de la arribada de TrOCs als aqüífers, també es interessant conèixer el temps de residència o persistència, ja que les aigües subterrànies tenen la capacitat d'anar acumulant aigua (si no es usada) (Peter Arp et al., 2023).

Les fonts de recàrrega als aqüífers sovint esdevenen vies de contaminació importants. Les aigües superficials com la dels rius, poden ser una important font de recàrrega i, per tant, d'entrada de contaminants que provenen d'abocaments legals i il·legals d'aigües residuals o industrials o agrícoles. Les estacions depuradores d'aigua residual (WWTP, de l'anglès *wastewater treatment plants*) estan dissenyades per eliminar parcialment patògens i contaminants inorgànics com nitrats i fosfats (Fu

and Wang, 2011). No obstant això, aquestes instal·lacions no són capaces d'eliminar completament les substàncies orgàniques presents en les aigües residuals. A més, durant els processos de tractament, es poden generar productes de transformació que poden ser més tòxics, persistents i polars que els compostos originals (Bueno et al., 2012; Schaider et al., 2017). Tot i l'aplicació de tractaments avançats, s'han trobat compostos polars en els efluents de les WWTP, demostrant la seva resistència a aquests processos (Loos et al., 2013). Per tant, les aigües superficials o rius que passen per zones urbanes constitueixen una de les principals fonts de TrOCs que potencialment poden afectar ales aqüífers urbans.

Un altre factor crític és el clavegueram urbà, que pot contaminar les aigües subterrànies a causa de fuites en la xarxa que recarreguen els aqüífers locals. Encara que no hi ha dades específiques sobre les pèrdues del clavegueram de Barcelona, es calcula que globalment entre el 3 – 5 % de l'aigua residual que circula per aquestes canonades un es perd a través de fuites, les quals s'infiltren als aqüífers (Abueltayef et al., 2023; Kingdom et al., 2006; Wolf et al., 2012). L'impacte de la recàrrega directe d'aigües residuals pot ser considerable, ja que sovint contenen concentracions elevades de fàrmacs, productes de cura personal i altres substàncies contaminants (Gros et al., 2017; Musolff et al., 2010).

Finalment, l'aigua d'escorrentia urbana, que es genera en episodis de pluja a la ciutat i que dissol i "arrossega" cap al clavegueram, els rius urbans o s'infiltra en sòls una gran diversitat de contaminants urbans. En el cas que aquestes aigües arribin a recarregar els aqüífers locals, aquests es podrien veure afectats per la contaminació aportada. L'aigua d'escorrentia urbana poden contenir una àmplia gamma de TrOCs, des de compostos volàtils i semi-volàtils presents a l'atmosfera, partícules provinents de la deposició atmosfèrica, fins a substàncies procedents de façanes, sostres i superfícies urbanes (Burant et al., 2018; Müller et al., 2020; Mutzner et al., 2023). Malgrat que la superfície urbana de ciutats com Barcelona està majoritàriament coberta per materials aparentment impermeables, l'aigua d'escorrentia pot infiltrar-se per àrees permeables, com parcs, jardins, a través del sòl o a través de les pèrdues del clavegueram (Masoner et al., 2019; Pinasseau et al., 2020). Cal afegir que a Barcelona recentment s'estan implementant Solucions Urbanes per al

Desenvolupament Sostenible (SUDS) que, d'entre altres objectius, pretenen millorar la qualitat de l'aigua d'escorrentia, mitjançant l'ús de materials filtrants entre el sòl i l'aqüífer (Carriquiry et al., 2020).

Per avaluar quantitativament l'aportació d'aigua de cada font de recàrrega i, en conseqüència, la qualitat de les aigües subterrànies, s'estan desenvolupant estudis hidrogeològics juntament amb models matemàtics que permeten simular el flux de l'aigua i el transport del contaminants en els aqüífers. Aquests models permeten monitoritzar i caracteritzar les recàrregues dels aqüífers, proporcionant informació clau per identificar les principals fonts de contaminació i prevenir possibles riscos futurs (Labad et al., 2023; Nikolenko et al., 2024; Tubau et al., 2014). Comprendre i quantificar la contribució de cada font de recàrrega és essencial per preveure els tipus de contaminants presents i establir estratègies de gestió eficaces per protegir aquests recursos vitals.

1.3 Context legislatiu de l'aigua subterrània

Legislació actual d'aigües a la Unió Europea

Diferents organitzacions han considerat uns criteris legislatius per diferent tipus de contaminants en aigües subterrànies. En aquest apartat ens centrarem amb la legislació proposada per la Unió Europea que es la que utilitza també l'estat espanyol, així com Catalunya i per tant, la ciutat de Barcelona. La primera directiva la trobem el 23 d'octubre de l'any 2000 on s'aborden diferents aspectes sobre l'estat i conservació actuals d'aigües dolces (Parlamento Europeo y del Consejo, 2000). En relació a les aigües subterrànies i compostos orgànics, aquesta directiva no menciona cap límit en concret més enllà d'abocaments d'alguns metalls com el mercuri i el cadmi, d'hexaclorociclohexà (un insecticida moderadament perillós) i de substàncies perilloses, prèviament legislades en directives anteriors (Parlamento Europeo y del Consejo, 2000). Al 2006, sortí la segona directiva on l'estat de l'aigua subterrània es té en compte. Cal mencionar que prèviament, al 2001, es va publicar i acceptar el conveni d'Estocolm sobre contaminants orgànic persistents (que s'ha anat actualitzant periòdicament), on s'inclouen diferents substàncies orgàniques perilloses pel medi ambient com alguns plaguicides i com-

postos industrials com els bifenils perclorats. Aquest conveni és un punt i apart en la conservació de la contaminació orgànica al medi ambient (UNEP, 2019). Tornant a la directiva més específica de l'aigua subterrània, aquesta inclou per primer cop els nivells de nitrats (50 mg L^{-1}) i substàncies actives dels plaguicides, inclosos metabòlits i productes de degradació a un nivell individual de 0.1 µg L^{-1} i total (sumatori) de 0.5 µg L^{-1} (Parlamento Europeo y del Consejo, 2006). Durant un espai de temps de més de 16 anys, aquesta va ser la última actualització legislativa en el marc de les aigües subterrànies, fins a finals del 2022, on es proposada una nova directiva que, a més dels nitrats i plaguicides, s'han inclòs límits en substàncies perfluoroalquíliques i polifluoroalquíliques, més conegudes com PFAS (de l'anglès *per- and polyfluoroalkyl substances*), amb un límit de 0.0044 µg L^{-1}. A més, dues substàncies farmacèutiques com la carbamazepina (límit de 0.25 µg L^{-1}), el sulfametoxazol (límit de 0.01 µg L^{-1}) i la suma de substàncies farmacèutiques, amb límit de 0.25 µg L^{-1}, van ser incloses en aquesta proposta de directiva (Parlamento Europeo y del Consejo, 2022).

Com ja veurem, en aquesta tesi alguns d'aquests límits s'han vist sobrepassats. Cal mencionar que aquesta legislació és insuficient si es vol considerar l'aigua subterrània com a principal font d'aigua potable i de consum a la ciutat, ja que els contaminants orgànics poden arribar als aqüífers a diferents nivells i amb toxicitat iguals o fins i tot més altes de les substàncies actualment regulades. De fet, els compostos més polars queden fora del àmbit legislatiu actual, els que per les seves propietats serien els contaminants que poden arribar amb més facilitat a l'aigua subterrània (Figura 1.4).

TrOCs sota vigilància en el marc de les aigües

Tot i que la legislació actual referent les aigües i en concret les aigües subterrànies ja ha estat descrita a l'apartat 1.3, no es poden ignorar les diferents llistes referents als contaminants orgànics emergents a les aigües. Diferents agències governamentals elaboren llistats per monitoritzar algunes substàncies que poden ser perilloses pel medi ambient, com la Unió Europea i l'Agència Europea de Substàncies i Mescles Químiques (ECHA) que s'encarrega de la implementació del reglament del Registre, Avaluació, Autorització i Restricció de Substàncies Químiques

(REACH) o com l'Agència Federal del medi ambient d'Alemanya (UBA). A més, altres institucions, no-governamentals, també elaboren els seus llistats com ara la Societat Química de Suïssa (SVCH), l'Institut Federal Suís de Ciència i Tecnologia Aquàtiques (EAWAG) o el Centre Helmholtz per a la Investigació Ambiental (UFZ), entre d'altres. Aquestes institucions sovint col·laboren amb entitats governamentals per l'elaboració de lleis i llistats oficials per a la limitació i/o prohibició de les substàncies prioritzades. Aquí ens centrarem principalment en dues llistes, la coneguda Watch List (Llista de Vigilància), elaborada per la Unió Europea, i la llista anomenada SVCH-ECHA, elaborada per la SVCH amb col·laboració amb la ECHA. Totes dues tenen finalitats diferents, la Watch List té un enfocament regulador per a substàncies que poden afectar únicament a l'aigua, en concret a l'aigua superficial. En aquesta tesi, la Watch List s'ha utilitzat per prioritzar contaminants a les aigües subterrànies degut a la manca de llistes per a TrOCs a aigües urbanes. D'altra banda, la llista SCVH-ECHA, té un enfocament més científic per a recopilar dades de substàncies potencialment perilloses per a tot el medi ambient, inclús a nivell humà. Podem concloure que abans d'entrar a la Watch List, que són substàncies que es poden arribar a prohibir aviat i han sigut prèviament monitoritzades amb exhaustivitat, és molt probable que una substància primer aparegui a la llista SVHC-ECHA, ja que aquesta inclou substàncies no analitzades prèviament degut a la complexitat dels anàlisis necessaris per detectar-les (ECHA, 2023; European Comission, 2022). A la Figura 1.4, es pot visualitzar el que es coneix com l'actual analytical gap (buit analític). Aquests tipus de compostos no han estat en el focus d'atenció degut a les seves característiques hidrofíliques, que dificulten el seu anàlisi. Per exemple, les columnes cromatogràfiques convencionalment més emprades no eren capaces de retindre d'aquest tipus de compostos (Figura 1.4).

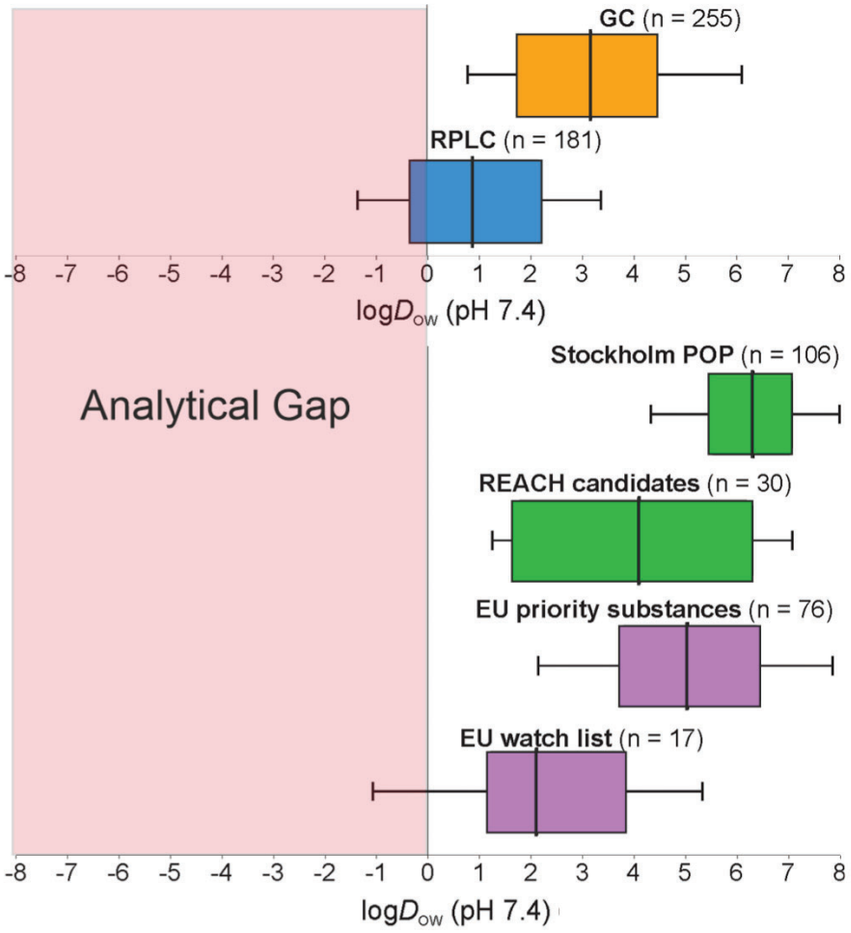


Figura 1.4. Gràfic de caixa i bigotis dels log D_{ow} dels compostos: 1) detectats emprant cromatografia de gasos (GC, de l'anglès *gas chromatography*) i per cromatografia líquida de fase inversa (RPLC, de l'anglès *reversed-phase líquid chromatography*), i 2) TrOCs inclosos a; conveni d'Estocolm, la REACH l'any 2016, la llista de substancies prioritàries segons la directiva de l'aigua i a la Watch List. Els bigotis senyalen els percentils 10 i 90. Adaptació de (Reemtsma et al., 2016).

Degut a la falta d'informació tant de toxicitat com de presència i nivells dels compostos orgànics polars, l'UBA va generar un llistat de compostos potencialment tòxics, persistent i mòbils. La persistència i la mobilitat són característiques imprescindibles per a que un compost romangui durant llargs períodes de temps a les aigües sense patir adsorcions o degradacions en aquest medi.

Una classificació dedicada a les aigües: els PMT i vPvM

Respecte als compostos persistents i mòbils, es necessari explicar la classificació suggerida per la REACH, els PMTs (de l'anglès P*ersistent Mobile and Toxic*) i els vPvM (de l'anglès *very Persistent and very Mobile*) (Peter Arp et al., 2023). Aquest grup de compostos seran mencionats recurrentment en aquesta tesi. Un compost, per complir els criteris de PMT, ha de ser persistent, mòbil i tòxic en el medi ambient. En el cas dels vPvM han de complir criteris de persistència elevada i ser altament mòbils en el medi ambient. A continuació es descriuen els criteris establerts per la REACH (només seran esmentats els criteris que involucrin una rellevància en la tesi present). Per tant, un compost serà persistent (P) quan la semivida de degradació en aigua dolça a 12 °C i pH entre 4 i 9 sigui superior a 40 dies. Per a que un compost sigui considerat molt persistent (vP) la regla anterior juntament amb una semivida de degradació superior a 60 dies, s'ha de complir. Per la part de mobilitat (M), els compostos que tinguin un log K_{OC} menor a 4.0, en l'interval de pH 4-9, seran considerats mòbils i, molt mòbils (vM) amb un log K_{OC} menor a 3.0 (Arp and Hale, 2019). Com el K_{OC}, que es el coeficient de partició entre el carboni orgànic (fase orgànica) i l'aigua (fase aquosa), per a moltes substàncies es difícil d'obtenir, el log D_{OW} (coeficient de distribució octanol-aigua dependent del pH), determinat experimentalment o estimats amb models Q(SAR), model de relacions quantitatives d'activitat-propietat espacial, es també acceptat amb els mateixos criteris.

Aquests criteris han estats proposats especialment per protegir les aigües, en especial les aigües potables i subterrànies, que sovint han caigut fora del àmbit de la legislació en relació a contaminants orgànics (UBA, 2017).

1.4 Mètodes analítics per a l'extracció i separació de TrOCs

En aquesta secció es parlarà dels diferents mètodes analítics enfocats a la extracció/preconcentració de les mostres aquoses (urbanes) de TrOCs. Primer però, s'explicarà breument els passos necessaris per desenvolupar un mètode analític, adaptat a la química analítica ambiental. Més enllà del disseny experimental, necessari per tal d'intentar solucionar un problema actual, l'extracció/preconcentració dels analits d'interès és un dels passos més crítics, ja que aquest pas permetrà que els compostos siguin aïllats de la mostra per obtenir-los en un solvent de treball (normalment metanol, acetonitril o aigua, entre d'altres). Un cop els analits han sigut aïllats, es procedeix a la seva detecció, en aquest cas la cromatografia líquida, que es capaç de separar un a un cada compost a analitzar, acoblada a un espectròmetre de masses, que es l'instrument que s'encarrega de transformar els senyals electròniques en dades interpretables.

Els TrOCs porten sent analitzats dècades en molts tipus de matrius/mostres, ja siguin sòlides com el sòl, múscul de tot tipus d'animals, aliments, etc., com gasoses (aire atmosfèric, aire d'interiors, etc.). També hi ha mostres líquides, com ara aigües de diversos tipus, orina, sang, begudes, etc. en les quals l'objectiu comú es traspassar els compostos que volem analitzar de la matriu original a un solvent de treball, reduint així la interferència de la matriu. Cal dir que depenent del tipus d'aigua i els compostos d'interès, el pas d'extracció es pot evitar o fer el que s'anomena un enriquiment, on es concentren els analits però alhora també la matriu de la mostra. Aquest pas, sigui extracció o enriquiment, sol ser essencial per a que la posterior detecció i quantificació dels compostos d'interès sigui efectiva i sensible.

Mètodes d'extracció de TrOCs en aigües

Les aigües poden provenir des de rius d'alta muntanya, on tant matèria orgànica com contaminació humana s'espera ser baixa, fins a aigües de clavegueram on els sediments, particulats i la contaminació per les aportacions de les llars i la indústria tenen una presència elevada. . Aleshores, diferents estratègies d'anàlisi s'han d'adoptar depenent el tipus

d'aigua que es tingui com a mostra. En aquest cas, ens centrarem en cinc tipus de mostres d'aigua: subterrània, superficial, d'escorrentia, de clavegueram i de pluja. Cal mencionar però, que l'extracció no només depèn del tipus de matriu sinó també dels compostos d'interès. Per tant, les característiques físico-químiques dels analits d'interès també juguen un paper clau alhora de triar o desenvolupar un mètode d'extracció. No és el mateix analitzar antibiòtics macròlids, com ara l'azitromicina o l'eritromicina, que són molècules de pes molecular elevat respecte al grup dels microcontaminants amb una alta lipofilicitat, que voler extreure, per exemple, la melamina, un compost emprat en l'industria del plàstic, que té un pes molecular petit i és molt hidrofílica. Depenent de l'aproximació de detecció aplicada al espectròmetre de masses, l'anàlisi no dirigit (*non-target analysis*), que consisteix en un cribratge de TrOCs presents a una mostra, fa que els mètodes d'extracció hagin de ser poc restrictius per a poder tenir el màxim nombre d'analits.

Aquesta tesi doctoral, s'ha centrat en fàrmacs, productes de cura personal, compostos industrials, edulcorants artificials i plaguicides. En menor mesura també vam incloure a la llista algun agent anticorrosiu, disruptor endocrí, filtre solar, etc. que seran englobats en llistats mencionat prèviament. Concretament, s'han inclòs dues seccions per descriure dos tipus d'extracció dels TrOCs, depenent de la seva polaritat, concretament del paràmetre log D_{ow}. S'utilitza per descriure la hidrofobicitat relativa d'una substància en condicions fisiològiques, tenint en compte tant les formes ionitzades com les no ionitzades del compost. En aquest estudi, els compostos amb un log $D_{ow} > 2$ seran anomenats semi-polars. D'altra banda, quan $0 \leq \log D_{ow} \leq 2$ es compleix, aquests compostos seran els polars. Per últim, els compostos molt-polars seran aquells que presentin un log $D_{ow} < 0$.

Extracció i pretractament de compostos polars i semi-polars en aigües

En aquesta secció es citen els mètodes (extraccions i pretractaments) descrits a la literatura per a TrOCs amb un log $D_{ow} > 0$ en aigües. En aquesta tesi, s'analitzen diferents tipus de famílies de contaminants, incloent fàrmacs, pesticides, productes de cura personal i compostos in-

dustrials (Fatta-Kassinos et al., 2011). En general, els TrOCs de polaritat baixa són molècules de pes molecular >300 Da, amb cadenes de carboni llargues i amb pocs grups funcionals polars (àcids carboxílics, èsters, etc.) (Weitzel et al., 2011). Diferents tipus d'extraccions son emprades per pretractar la mostra i separar contaminants orgànics amb polaritat baixa i intermèdia en tot tipus d'aigua, com ara, l'extracció líquid-líquid, l'extracció en fase sòlida (SPE, de l'anglès *solid-phase extraction*), l'extracció per adsorció en barra giratòria, l'extracció accelerada amb dissolvents, liofilització, etc. (Gonçalves et al., 2021; Gros et al., 2006; Kostopoulou and Nikolaou, 2008; Murrell and Dorman, 2021; Sadutto and Picó, 2020). Si més no, la SPE es el mètode d'extracció més emprat en els últims anys. Aquesta tècnica no només permet reduir l'efecte matriu i preconcentrar els compostos d'interès a un dissolvent de treball, si no que permet concentrar la mostra a factors de més de mil, depenent del volum inicial de mostra, cosa molt interesant per a tenir límits de detecció i quantificació (LOD i LOQ, de l'anglès *limit of detection and limit of quantification*, respectivament) molt baixos i poder detectar nivells traça dels contaminants (Badawy et al., 2022). La SPE basa el seu principi d'acció amb l'adsorció dels contaminants d'interès a un material adsorbent. Per tant, un dels factors més important quan s'escull l'SPE com a mètode de pretractament de la mostra aquosa, és triar el adsorbent més adient per als contaminants d'interès. També és important la quantitat d'adsorbent, sent les més populars entre 5 i 500 mg. Segons Badawy et al. (2022) els adsorbents, en general, tenen la capacitat de retenir fins al 5 % de la seva massa, abans de que es produeixin ruptures significatives, és a dir, que es formin canals preferents (Badawy et al., 2022). L'adsorbent més emprat per aquest tipus d'anàlisis és el HLB (de l'anglès *Hydrophilic-Lipophilic Balanced*) que consisteix bàsicament d'un copolímer anomenat poly(divinylbenzene-co-N-vinylpyrrolidone) que conté la part hidrofòbica (divinylbenzene) i la seva part hidrofílica (N-vinylpyrrolidine). El cartutx HLB es emprat per retenir tota mena de compostos des de no polars fins a polaritat moderada (Andrade-Eiroa et al., 2016; Halwatura and Aga, 2023). Tal com l'adsorbent de HLB s'engloba dins dels adsorbents de fase inversa, també hi ha altres amb funcions similars com ara l'Strata-X o el Bond Elut que difereixen de la marca comercial, i alguna funció específica. D'altra banda existeixen altres famílies d'adsorbents com els d'exclusió per mida, que enlloc d'actuar per afinitat i polaritat, funcionen per a molècules grans (Andrade-Eiroa et al., 2016). Els adsorbents d'intercanvi iònic, que tenen afinitat per molècules ionitzades tant positivament (cations) com negativament (anions) i també els adsorbents de modalitat mixta, que comparteixen propietats d'intercanviadors iònics i de fase inversa. Aquest tipus d'adsorbents són útils per a retenir compostos iònics en la matriu d'interès, a més, es pot utilitzar el pH per controlar les espècies iòniques disponibles, ja que depenent del seu pKa (logaritme negatiu de la constant de dissociació àcida que indica la tendència d'una molècula a alliberar protons en solució aquosa) i el pH, les molècules seran iòniques o neutres. Per tant, per molècules iòniques a mostres medi ambientals, els adsorbents iònics són molt eficients, com exemple, es poden trobar diferents estudis que empren aquest mode de SPE per extreure PFAS de diferents matrius (Brumovský et al., 2018).

Extracció i preconcentració de TrOCs de polaritat alta en aigües

Centrant ara l'atenció en els compostos de polaritat alta, directament relacionat amb la mobilitat (d'ara en endavant, vMC, de l'anglès *very Mobile Compounds*), la bibliografia sobre compostos amb un log D_{ow} < 0 es escassa, pels quals al moment de començar la tesi existien pocs mètodes analítics. Tot i que durant molts anys aquestes substàncies han sigut ignorades en el marc de la química analítica, aquests vMC han estat detectats en aigües de consum i de boca, provocant interès en analitzar vMC a escala global (Loos et al., 2007; Montes et al., 2017a). A més, ja que algunes d'aquestes molècules no es poden analitzar, amb metodologies tradicionals com la SPE usant adsorbents típics ni tampoc separacions amb cromatografia líquida utilitzant columnes de fase inversa. Cal mencionar que la tècnica de separació amb més èxit per separar TrOCs de polaritat mitja alta és la cromatografia liquida. En els últims anys, s'han extret i preconcentrat amb èxit diferents vMC en aigües, on trobem èmfasi amb extraccions de SPE amb adsorbents amb diferents mecanismes de retenció, evaporació de la mostra mitjançant diferent tècniques, liofilització, entre d'altres. on el punt comú es aconseguir que els vMC quedin presents al extracte. A la Taula 1.2 es detallen els mètodes d'extracció més rellevants de compostos de polaritat alta descrits ala literatura fins al moment. Començant per la SPE, Köke et al. (2018) van desenvolupar

dos mètodes d'extracció, una SPE multi-capa (msSPE, de l'anglès *multi-sorbent solid-phase extraction*) i evaporació per rota-vapor (Köke et al., 2018). El mètode amb msSPE consistia en un cartutx de 3mL omplert de tres capes d'adsorbents, WAX (de l'anglès *Weak Anion eXchange*), WCX (de l'anglès *Weak Cation eXchange*) i GCB (de l'anglès *Graphatised Carbon Black*) de dalt a baix. A més quatre diferents mescles d'eluents varen ser provades, ja que l'adsorbent de carboni pot ser interessant per a l'extracció de vMC, però com a principal inconvenient es el pas d'elució dels analits, ja que amb el carboni, es poden formar enllaços químics forts (enllaços d'hidrogen) o enllaços π amb electrons deslocalitzats o electrons lliures (Hennion´laboratoire, 2000). Tot i que s'ha mencionat abans que l'adsorbent de HLB ha estat dissenyat per captar compostos en un rang de polaritat ample, hi ha estudis demostrant la seva ineficàcia per vMC, tenint recuperacions d'entre 0 i 20 % per a un 63 % dels compostos que analitzava (Boulard et al., 2018). Això pot ser degut a la baixa eficàcia d'aquest adsorbent a crear enllaços via dipol i enllaços d'hidrogen. D'altra banda, els adsorbents d'intercanvi iònic tenen una rellevància molt elevada per l'extracció de vMC. Els compostos molt polars solen tenir grups ionitzables com ara cianurs, àcids carboxílics o sulfúrics, per això l'intercanvi iònic es efectiu per a la seva extracció. Es troben al mercat cartutxos amb intercanviadors aniònics i catiònics sols o com a multicapa addicionant un altra tipus d'adsorbent com l'HLB o Carboni. Finalment, les tècniques que més rellevància han guanyat en aquest camp són sens dubte les evaporatives (evaporació i liofilització). Tenen l'avantatge de que totes les substàncies presents en la matriu aquosa romandran en la seva forma original al extracte resultant, sempre que no siguin exposades a altes temperatures on els compostos més volàtils podrien ser evaporats o provocar la degradació o transformació d'altres substàncies. Com a aspecte desfavorable, cal mencionar que l'efecte matriu serà, normalment, més alt que amb altres tècniques com la SPE degut a que no es fa cap neteja dels components de la matriu. A més els factors de concentració i, per tant, els límits de detecció es veuran afectats, degut a que no es poden emprar alts volums de mostra per un rendiment de consum econòmic i de temps. A la Taula 1.2 es poden veure resumits els mètodes d'extracció que hi ha a la literatura actualment, on es pot veure una tendència recent cap a les tècniques evaporatives. Addicionalment, el tipus de columna emprada per a la separació i determinació dels TrOCs en un

sistema de cromatografia liquida acoblada a espectrometria de masses (LC-MS, de l'anglès *liquid chromatography mass spectometry*) (detallat a la Taula 1.2 i discutit a la següent secció).

Taula 1.2. Mètodes d'extracció i preconcentració de vMC reportats a la literatura.

Tipus d'Extracció	Matriu emprada	Tipus de Cromatografia Líquida	Referència
SPE amb carboni	Aigua subterrània Aigua superficial	Fase reversa (C18)	(Di Corcia et al., 1993)
	Aigua de boca	Fase reversa (PGC)	(Pichon et al., 1995)
SPE multi-capa (msSPE)	Aigua de depuradora de sortida	Fase reversa (C18) Fase normal (HILIC) Fluid supercrític (SFC)	(Bieber et al., 2017)
	Aigua de boca Aigua superficial Aigua de depuradora de sortida	Fase normal (HILIC)	(Köke et al., 2018)
	Aigua subterrània Aigua superficial	Fase reversa (C18) Intercanvi iònic (MMLC) Fase normal (HILIC) Fluid supercrític (SFC)	(Schulze et al., 2019)
	Aigua de boca Aigua superficial	Fase normal (HILIC) Fluid supercrític (SFC)	(Schulze et al., 2020)
SPE d'intercanvi iònic	Aigua de boca Aigua subterrània Aigua superficial Aigua residual urbana	Fase normal (HILIC)	(Daniel Zahn et al., 2016)
	Aigua de boca Aigua subterrània Aigua superficial	Intercanvi iònic (MMLC)	(Montes et al., 2017b)
	Aigua subterrània Aigua superficial Aigua de depuradora de sortida	Fase normal (HILIC)	(Boulard et al., 2018)
	Aigua de boca Aigua superficial	Fase reversa (C18) Intercanvi iònic (MMLC)	(Montes et al., 2019b)
Liofilització	Aigua subterrània Aigua superficial Aigua de depuradora de sortida	Fase normal (HILIC)	(Boulard et al., 2018)

	Aigua superficial Aigua de depuradora d'entrada i de sortida	Fase reversa (C18)	(Mechelke et al., 2019)
Evaporació	Aigua de boca Aigua superficial Aigua de depuradora de sortida	Fase normal (HILIC)	(Köke et al., 2018)
	Aigua subterrània Aigua superficial	Fase reversa (C18) Intercanvi iònic (MMLC) Fase normal (HILIC) Fluid supercrític (SFC)	(Schulze et al., 2019)
	Aigua superficial	Fase normal (HILIC)	(Zahn et al., 2019)
	Aigua de boca Aigua superficial	Fluid supercrític (SFC)	(Schulze et al., 2020)
	Aigua superficial	Fase normal (HILIC) Fluid supercrític (SFC)	(Neuwald et al., 2021)
	Aigua de boca Aigua superficial	Fase normal (HILIC)	(Kolkman et al., 2021)

PGC: Porous graphitic carbon; SFC: Supercritical fluid chromatography; HILIC: Hydrophilic interaction liquid chromatography; MMLC: Mixed mode liquid chromatography

Tipus de cromatografies líquides per l'anàlisi de compostos orgànics

Un cop els analits son preconcentrats al vial, la seva detecció es realitza mitjançant LC-MS en el que hi ha dos passos, la separació cromatogràfica i la seva posterior detecció mitjançant espectrometria de masses. Per l'anàlisi de TrOCs hi ha molts tipus d'instrumentació a l'abast, com detecció per ultraviolada, fluorescència i d'altres que no han estat emprades en aquesta tesi ja que els seus límits de detecció no són adequats per a la família de compostos analitzats a la tesi. Tampoc s'ha emprat la cromatografia de gasos, que tot i que es important sobretot per compostos no-polars i volàtils, no es la tècnica adequada per a la detecció dels compostos d'interès d'aquest estudi. Altres grups han emprat la cromatografia de fluids supercrítics i la cromatografia iònica, que seran esmentats superficialment en aquesta tesi (Figura 1.5). En canvi, la mobilitat iònica també serà tractada amb profunditat en un apartat únic d'aquesta tesi, ja que el seu ús és important en aquesta tesi. La principal tècnica d'anàlisi que serà tractada en profunditat en aquest estudi serà la cromatografia de líquids (LC, de l'anglès *líquid chromatography*) acoblada a un instrument d'espectrometria de masses (MS, de l'anglès *mass spectrometry*). Breument, la cromatografia líquida s'usa per separar els analits d'interès en el temps. És a dir, l'objectiu és que els analits tinguin un temps de retenció diferent els uns amb els altres per a que la seva posterior detecció per MS sigui més precisa. Aquesta tècnica permet evitar interferències de la matriu, supressions de la ionització entre d'altres avantatges. La LC es basa en el principi de la separació dels components d'una mescla (o extracte) a través de la interacció amb dues fases: la fase mòbil (líquida) i la fase estacionaria (sòlida), que també pot ser líquida suportada en un sòlid. Per tant, l'afinitat que tingui cada analit en cada una de les fases (estacionaria o mòbil) determinarà el temps de residència dins la columna cromatogràfica (Žuvela et al., 2019). La fase sòlida és intrínseca de la columna cromatogràfica que s'usa, mentre que la líquida pot ser qualsevol solvent compatible amb un espectròmetre de masses. Es pot classificar en sis tipus de cromatografia líquida: de fase normal, de fase inversa, HILIC, d'intercanvi iònic, cromatografia per exclusió de mida i cromatografia per afinitat. Quan es diu que s'usa fase inversa, que es la fase més emprada en la química analítica, s'està utilitzant una fase

sòlida apolar (normalment una cadena de carbonis, C18) i una fase mòbil polar, com aigua o metanol. D'altra banda, la fase normal és al contrari, fase sòlida polar (normalment sílice o alúmina) i fase mòbil apolar com hexà o toluè. La cromatografia HILIC es pot considerar una variant de la fase normal ja que comparteix les propietats de les fases tant mòbils com estacionaries. Per últim, la LC d'intercanvi iònic basa el seu principi en interaccions iòniques, per tant, la fase sòlida contindrà un adsorbent amb grups iònics, ja sigui d'intercanvi catiònic (normalment amb grups d'àcid sulfònic) o d'intercanvi aniònic (normalment amb grups d'amoni quaternari).

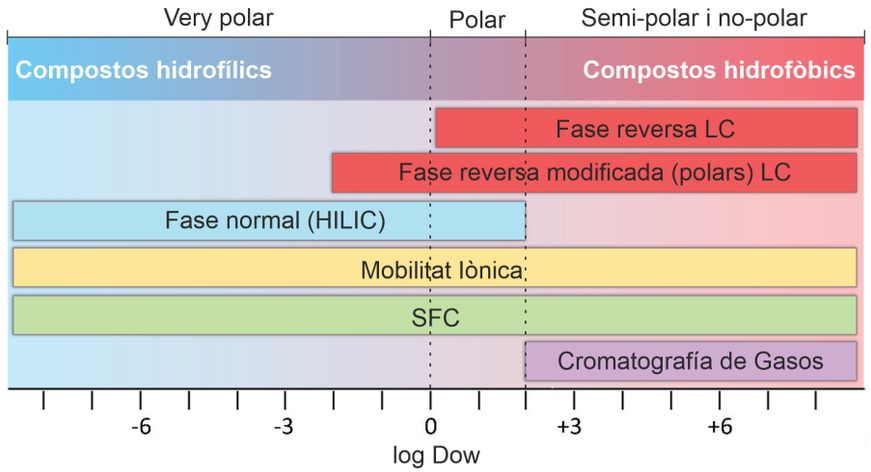


Figura 1.5. Diagrama de les diferents cromatografies (incloent mobilitat iònica) en base a la polaritat (log D_{ow}) de les substàncies separables de cada tècnica. Basat en (Bieber and Letzel, 2020).

Retenció de compostos polars i semi-polars en LC

Els compostos polars i semi-polars, retinguts (la majoria) eficientment en la fase inversa com s'ha descrit a la secció 1.4. Per tant, una cromatografia basada en una retenció mitjançant una fase inversa serà en general la fase proposada per a la retenció d'aquestes substàncies. Actualment, hi ha moltes columnes cromatogràfiques de fase inversa al mercat, algunes de modificades per millorar la retenció de compostos més polars, altres específiques per la retenció d'una família específica de compostos, etc. Es degut a la varietat de fases estacionaries modificades disponibles, més la versatilitat que permet la fase inversa per usar diferents solvents amb diferent poder eluotròpic, la que fa que la fase

inversa hagi tingut i tingui tant d'èxit amb la separació de compostos de polaritat moderada (Žuvela et al., 2019). Com es pot observar a la Figura 1.5, la fase inversa cobreix un gran espectre de polaritats, demostrant la seva amplia versatilitat amb moltes famílies de compostos orgànics com fàrmacs, pesticides o productes de cura personal.

Retenció de compostos molt polars en LC

En canvi, quan es volen analitzar en compostos molt polars (log D_{ow} < 0) la fase inversa, deixa de tenir una òptima funcionalitat (Figura 1.5). Com ja s'ha mencionat anteriorment, la fase inversa consta d'una fase estacionaria no-polar, el que fa que compostos hidrofílics no tinguin afinitat per ella i s'elueixin amb la fase mòbil (polar) sense retenir-se i per tant, sortint de la columna amb el volum mort. Per això la HILIC, juga un paper fonamental per poder separar adequadament vMC ja que al disposar d'una fase estacionària polar, els vMC poden crear interaccions amb facilitat, retenint-se a la fase estacionària i eluint-se lentament amb la fase mòbil no-polar (Labad and Pérez, 2024). Altres tipus de cromatografies per la retenció de vMC son d'intercanvi iònic o la SFC. La cromatografia iònica es ideal per retenir compostos iònics, que depenent els pKa dels analits i del pH de la fase mòbil, pot ser una opció recomanable per vMC. La SFC comparteix els principis de la LC, consta d'una fase estacionaria que pot tenir propietats tant apolars com polars i d'una fase mòbil que consta d'un fluid supercrític. El que fa tant especial la SFC precisament es la fase mòbil, que sol ser CO_2 en estat supercrític (31.1 °C i 73.8 bar) on presenta propietats (viscositat i difusivitat) d'un gas i un líquid (densitat) al mateix temps. Al usar-se CO_2, que es considerat un solvent amb característiques apolars, la fase estacionaria que s'usa amb més freqüència es polar, per tant compartint les característiques de la fase normal (Xhaferaj et al., 2020). Com a desavantatge principal es troba les instal·lacions necessàries per obtenir les condicions de fluid supercrític, fent que aquesta sigui complicada de tenir per l'elevat cost i manteniment. Recentment, han sortit al mercat columnes anomenades mixtes (MM, de l'anglès *mixed mode*) que comparteixen propietats de dos tipus de cromatografies, generalment intercanvi iònic amb fase inversa o fase normal. Aquestes columnes poden retenir i separar vMC ja que comparteixen propietats d'intercanviador iònic per retenir compostos

carregats i propietats de fase normal per retenir compostos polars neutres. La limitació principal però són els solvents de la fase mòbil, sovint incompatibles amb les dues modalitats simultàniament (Li et al., 2014; Musatadi et al., 2023). A la Taula 1.3, es mostren resumides els tipus de cromatografies disponibles per vMC amb les seves avantatges i desavantatges.

Taula 1.3. Mètodes analítics de separació per vMC amb les seves principals avantatges i desavantatges.

Tècnica	Avantatges	Desavantatges
CROMATOGRÀFIA LÍQUIDA		
RPLC	• Fàcil implementació • Compatible amb molts solvents orgànics • Rang ampli de tipus de fases estacionàries disponibles • Bona retenció de diferent tipus de compostos • Amplia bibliografia per a molècula petita	• Baixa retenció de vMC (log D_{ow} < 0)
NPLC (HILIC)	• Fàcil implementació • Compatible amb molts solvents orgànics • Adequada retenció de vMC	• Exclusiu per a compostos polars i molt polars • Sensible a canvis de pH • Limitació amb la quantitat d'aigua de la fase mòbil
MMLC	• Retenció de diferents tipus de compostos (carregats i neutres)	• Limitació de solvents • Molt sensible al pH • Poca robustesa
ALTRES CROMATOGRAFÍES		
SFC	• Retenció de tot tipus de compostos • Possibilitat de treballar en condicions similars de RP i NP al mateix temps	• Difícil implementació • Cost econòmic alt • Poca bibliografia per a molècula petita
CE	• Independent de la polaritat • Separació de tot tipus de molècules (iòniques) • Independent de fases estacionàries i mòbils • Cost econòmic baix	• Dependent de la ionitzabilitat dels analits • Baixa resolució a concentracions baixes
MOBILITAT IÒNICA		
IM (injecció directa)	• Independent de la polaritat • Separació de tot tipus de molècules • Independent de fases estacionaries i mòbils • Anàlisi molt ràpid i sensible • Capaç de separar enantiòmers	• Difícil separació de molècules de forma i mida similar • Requereix un calibratge exhaustiu diari • Poca bibliografia per a molècula petita

NPLC: Normal-Phase Liquid Chromatography; CE: Capillary Electrophoresis; IM: Ion Mobility

A la Taula 1.2 es descriuen 18 estudis que determinen compostos polars en aigües i en total, 29 columnes han estat testades per aquest propòsit. Deixant de banda els estudis del 1993 i 1995, quatre tipus de cromatografia han servit per separar amb èxit els vMC, en ordre creixent: la MMLC s'ha utilitzat un 14.8 % dels cops, seguit de la RPLC (18.5%), després la SFC (22.2%) i l'HILIC (44.5 %). Això ens dona una idea de la versatilitat que proporciona l'HILIC, ja que es de fàcil instal·lació i en base al gradient cromatogràfic, es pot aconseguir una retenció adequada.

1.5 Mètodes analítics per a la detecció i quantificació de TrOCs

Un cop hem descobert quins mètodes d'extracció i separació són els mes idonis per als TrOCs d'interès en aigües, ara cal entendre com es poden detectar i posteriorment, quantificar per a conèixer la presència i quantitat o concentració present de cada TrOC a cada mostra. Actualment, hi ha diverses tècniques dedicades a aquest propòsit com ara, la detecció amb matriu de díodes, detecció ultraviolat-visible, fluorescència, ressonància magnètica nuclear, espectroscòpia d'infraroig per transformada de Fourier, la ja esmentada MS. Tot i que hi ha diferents mètodes de detecció, la MS, es la més emprada per la detecció de TrOCs en quantitats traça.

L'Espectrometria de masses

L'Espectrometria de masses va néixer ara fa més d'un centenar d'any. Al 1912 J.J. Thompson va construir el primer espectrògraf de masses i ja cap als anys 50 van aparèixer els primers instruments comercialment disponibles. Els avenços amb la MS han sigut exponencials en el últims anys. L'MS permet identificar i quantificar molècules en base a la relació massa (m) / càrrega (z). Per tant, l'MS només és adequada per l'anàlisi de molècules carregades positivament o negativament. Per aquest motiu, tots els espectròmetres de masses estan constituïts d'una font de ionització, col·locat previ a l'entrada dels ions al espectròmetre de masses. Cal mencionar, que tots els espectròmetres de masses disposen d'un rang de *m/z* (relació massa-càrrega) operatiu, normalment entre 50 a 1000 o fins a 1200 (els més nous) i, que fora d'aquest rang, la seva operativitat és

nul·la. Posterior a la ionització es produeix de la separació dels ions que podem parlar de 4 tipus, i que depenent la tècnica, es diferenciarà entre espectrometria de masses de baixa resolució (LRMS, de l'anglès *low-resolution mass spectrometry*) i espectrometria de masses d'altra resolució (HRMS, de l'anglès *high-resolution mass spectrometry*). Finalment, l'últim pas consisteix en la detecció dels ions, que hi ha tres tipus de detectors principals: detector de multiplicador d'electrons, detector fotomultiplicador i detector de plaques de microcanals. La Figura 1.6 explica esquemàticament el procediment d'un espectròmetre de masses.

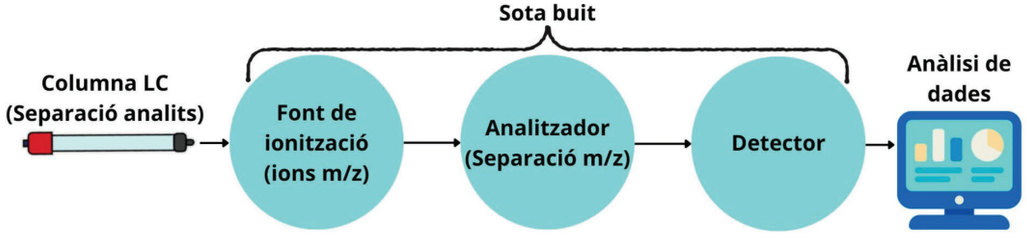


Figura 1.6. Diagrama esquemàtic del funcionament d'un espectròmetre de masses.

La ionització

Hi ha moltes tècniques de ionització disponibles avui dia, les podem classificar bàsicament en tres categories: les fortes (o clàssiques), les suaus i les d'ambient. Les que destaquen pel seu ús a la LC son les ionitzacions suaus com ara la ionització per electrosprai (ESI, de l'anglès *electrospray ionization*), la ionització química a pressió atmosfèrica (APCI, de l'anglès *atmospheric pressure chemical ionization*), la fotoionització a pressió atmosfèrica (APPI, de l'anglès *atmospheric pressure photoionization*) i la desorció/ionització làser assistida per matriu (MALDI, de l'anglès *matrix-assisted laser desorption/ionization*). Degut a la versatilitat i rendiment que proporciona l'ESI per a molècules petites, en aquesta tesi s'ha emprat només l'ESI.

L'ESI té com a objectiu convertir les molècules presents en la fase líquida (mostra/extracte) en ions en fase gasosa. Per aconseguir-ho, una alíquota del extracte (o mostra) s'introdueix en un capil·lar connectat a un alt voltatge. La combinació del flux de líquid (microfluxe) amb el camp elèctric genera la ionització de les molècules a través del conegut

con de Taylor. En aquest procés, les gotes solvatades carregades que, mitjançant l'evaporació induïda per un gas neutre (normalment N_2), es van fragmentant progressivament fins a alliberar ions individuals, que són transportats en forma gasosa cap a l'entrada del espectròmetre de masses (Konermann et al., 2012). Els principals avantatges d'aquesta tècnica de ionització són la seva compatibilitat amb l'espectròmetria de masses, el fet de ser una ionització suau (que evita la fragmentació de molècules), la seva elevada sensibilitat, i la seva gran versatilitat per molts tipus de compostos químics. D'altra banda, com aspectes negatius podem destacar la necessitat de tenir un solvent compatible i òptim per assegurar una correcta ionització i la possible competència entre els analits d'interès i els components de la matriu, que pot afectar l'eficiència de la ionització (Konermann et al., 2012).

Resolució dels espectròmetres de masses

En funció de la resolució de massa, l'espectrometria de masses es pot classificar en dues categories: LRMS i HRMS. La resolució es defineix com la capacitat de l'analitzador de masses de distingir entre dos ions amb valors de *m/z* propers. En el cas de la LRMS, la seva resolució sol situar-se entre 500 i 2000, la qual cosa permet detectar masses nominals o, en alguns casos, amb una precisió d'un decimal. En canvi, els instruments d'alta resolució poden assolir resolucions superiors a 100.000, fet que permet determinar masses exactes amb una precisió de fins a cinc decimals. Per exemple la melamina, quan es'analitza amb HRMS en mode de ionització positiva, genera un ió protonat amb *m/z* = 127.07267. Si aquest mateix compost s'analitzés mitjançant LRMS, només es podria determinar *m/z* = 127, o en el millor dels casos, *m/z* = 127.1. Aquesta diferència és crucial per a la identificació precisa de compostos, especialment quan hi ha molècules isobàriques, és a dir, compostos amb la mateixa massa nominal però estructures diferents. Tot i que la LRMS és una tècnica àmpliament utilitzada per al control de qualitat i l'anàlisi de rutina gràcies al seu cost més baix, presenta limitacions en termes de resolució i sensibilitat. Per contra, la HRMS ofereix avantatges significatius per a l'anàlisi estructural i la identificació de compostos desconeguts, permetent una major precisió en la determinació de masses i facilitant la diferenciació d'ions amb masses molt similars (Aceña et al.,

2015; López-Ruiz et al., 2019). Per acabar, parlem de LRMS amb analitzadors com el quadrupol simple (Q), el triple quadrupol (QqQ) o trampa de ions. Els analitzadors HRMS més emprats són els Q-TOF (Q-TOF, de l'anglès *quadrupole time-of-flight*), la ressonància de ciclotró d'ions de transformada de Fourier (FT-ICR, de l'anglès *Fourier Transform ion cyclotron resonance*) o l'Orbitrap, sent aquest últim amb el que s'ha treballat en aquesta tesi.

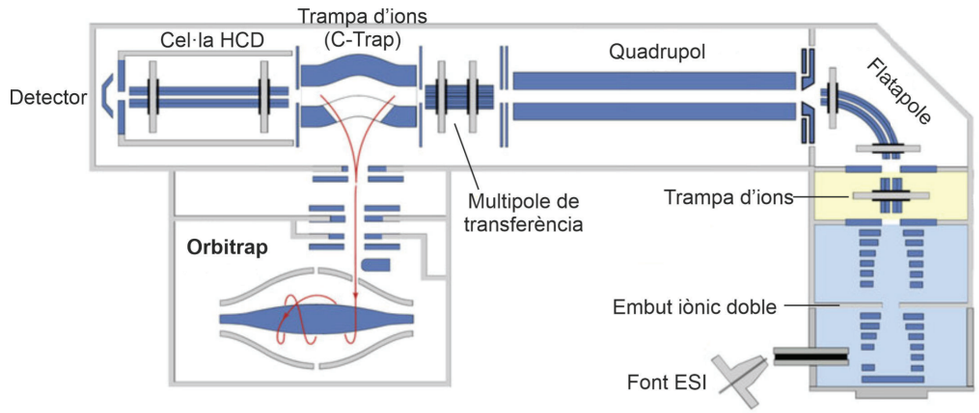


Figura 1.7. Diagrama esquemàtic de les parts d'un Orbitrap, basat en (Ben-Nissan et al., 2017). HCD: de l'anglès *Higher-energy collision dissociation.*

El QExactive Orbitrap ha estat l'instrument seleccionat en aquesta tesi, degut a que es tracta d'un HRMS permetent assolir límits de detecció baixos, necessaris per a l'anàlisi de TrOCs. A la Figura 1.7 es poden veure els seus components habituals. L'analitzador d'alta resolució és una trampa característica, anomenada Orbitrap, que consta d'un elèctrode central en forma d'espiral i un elèctrode exterior en forma de cilindre envoltant (Zubarev and Makarov, 2013). Els ions, transportats des de la font de ionització, a través de diferents camps elèctrics, passant per un quadrupol i la trampa de ions anomenada C-Trap, es mouen formant òrbites al voltant del elèctrode central i oscil·lant longitudinalment al llarg del seu eix. Les molècules son separades segons la seva *m/z*, les molècules amb un *m/z* baix formaran òrbites més petites i per tant es mouran més ràpidament que les molècules amb *m/z* grans (Zubarev and Makarov, 2013).El QExactive Orbitrap presenta diferents característiques positives com l'alta resolució, permetent la diferenciació de ions amb *m/z* propers; alta precisió de massa, crucial per la identificació inequívoca de compostos i sovint imprescindible per l'anàlisi no dirigit; estabilitat a llarg termini, el que permet no calibrar l'equip constantment. Com a característiques negatives se'n poden extreure la complexitat operativa però sobretot el temps d'adquisició, que es el seu principal inconvenient a l'hora de realitzar anàlisi amb molts analits (es necessita rapidesa per no perdre ions d'interès) i que altres instruments com els QTOF-MS són capaços de realitzar. El Q-Exactive Orbitrap-MS ha sigut l'instrument que s'ha emprat en aquesta tesi.

La Mobilitat Iònica i la seva utilitat pels TrOCs

Com a separació de TrOCs, més enllà de la LC, existeix la IM. Aquesta tècnica, desenvolupada a mitjans del segle XX, basa la separació dels ions en la seva velocitat a través d'un gas mitjançant l'acció d'un camp elèctric (Borsdorf and Eiceman, 2006). La separació doncs ve determinada per diferents factors, i) mida i forma de l'ió, ii) càrrega de l'ió, iii) pressió i temperatura del gas i iv) intensitat del camp elèctric. Considerant unes condicions constant tant del gas com del camp elèctric, així com una càrrega de 1 (ja sigui positiva o negativa i considerant que per a molècules petites es l'estat més comú), el que determinarà la velocitat, i per tant, separació dels analits serà la mida i formà de l'ió d'interès (Weitzel et al., 2011). Tot i que, recentment l'IM ha tingut el seu impacte amb l'àmbit de la molècula gran, com ara proteïnes i pèptids, degut a la capacitat de l'IM de separar isòmers conformacionals, també té la seva cabuda a l'àmbit de la molècula petita (Aly et al., 2022). L'aplicació de l'IM a la molècula petita ha estat en auge des de l'última dècada, degut a que l'evolució i millora de la resolució instrumentals dels equips ha permès una separació més eficient entre molècules de similar forma i mida, ja que les molècules petites difereixen molt menys en aquest aspecte que les grans. La forma de quantificar aquesta forma i mida característica de cada compost, ve determinada per la secció transversal de col·lisió (CCS, de l'anglès *collision cross section*) (Rainey et al., 2022). Aquests CCS però depenen del equip amb el que es mesura i de com es calibra aquest equip. Ja que hi ha fins a set tipus de IM tot i que només seran mencionats aquells més emprats amb la molècula petita. Existeixen quatre principals; la IM en tub de deriva (DTIMS, de l'anglès *drift tube ion mobility spectrometry*); la IM de camp assimetric (FAIMS, de l'anglès *field asymmetric ion mobility spectrometry*); la IM d'ions atrapats (TIMS, de l'anglès *trapped ion mobility*

spectrometry) i; la IM d'ona viatgera (TWIMS, de l'anglès *travelling wave ion mobility spectrometry*). Totes, tenen mecanismes diferenciats per separar els ions, bàsicament centrats en com aplicar el camp elèctric per aconseguir aquest objectiu. Degut això i tornant al càlcul dels CCS, es molt important conèixer l'equip amb els que es treballa i calibrar-lo en base a les bases de dades disponibles de CCS per tal d'obtenir un valor comparable i precís (Baker et al., 2023). Com a conclusió, l'IM es una tècnica que ens permet separar i identificar ions només tenint en compte el CCS del analit d'interès, sense tenir en conte altres propietat com la polaritat, tant important en la LC. La part negativa es la dificultat de separar molècules amb un *m/z* proper i el precís calibratge necessari per obtenir resultats comparables amb altres instruments d'IM i estudis.

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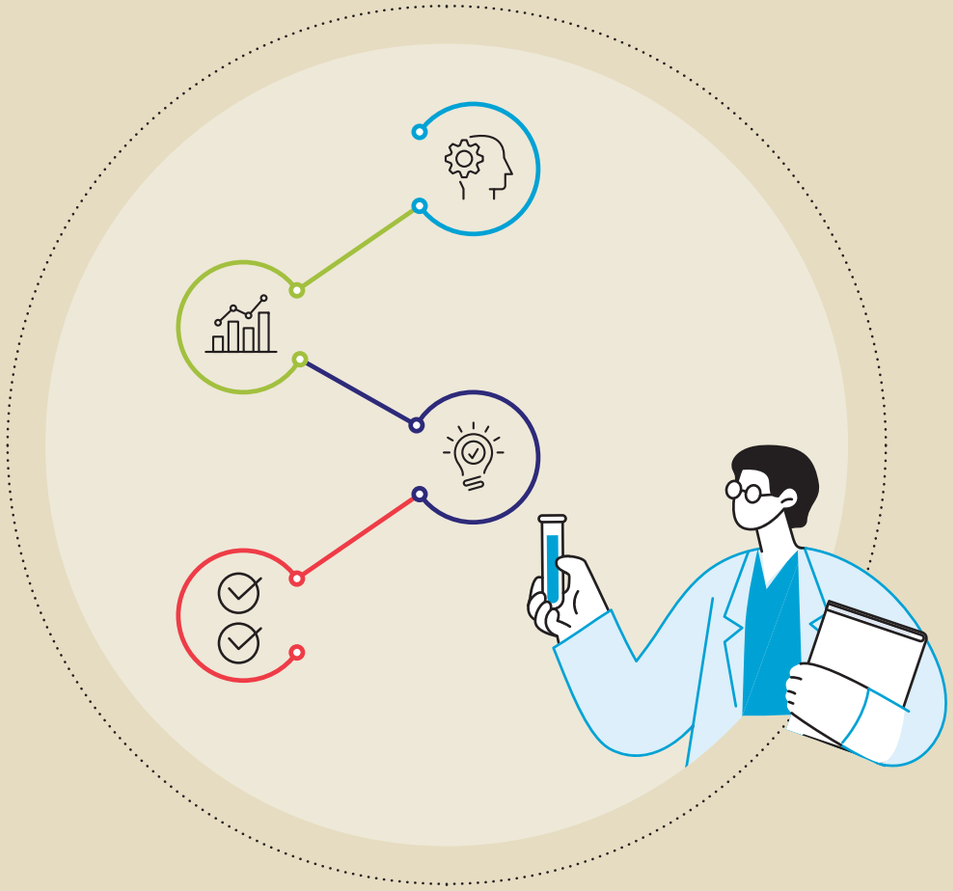
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Capítol



2.

Objectius i Estructura

2

OBJECTIUS I ESTRUCTURA DE LA TESI

2.1 Objectius

El malbaratament del recurs de l'aigua a escala mundial ha esdevingut un problema actual que, a més, s'ha vist negativament accentuat amb el canvi climàtic, provocant esdeveniments d'inundacions i de sequera que agreugen la qualitat d'aigua potable. Per tal de preservar aquest recurs cal tenir aigua d'alta qualitat, en especial a les zones urbanes on la densitat de població es elevada. Malauradament, aquestes zones solen ser on més substàncies orgàniques es fan servir. El destí final d'aquestes substàncies que s'utilitzen a la nostra vida diària són: sistemes de clavegueram, rius, superfícies urbanes, carrers, etc. Com a última instància, aquestes substàncies que inclouen fàrmacs, pesticides, compostos industrials o edulcorants artificials entre d'altres, poden arribar a les aigües subterrànies, font molt valuosa per obtenir aigua de consum de qualitat. Segons l'escenari descrit anteriorment, les hipòtesis inicials d'aquesta tesi van ser: i) determinar si l'aigua subterrània urbana presenta una qualitat suficient per a ser utilitzada en diversos usos urbans; ii) saber si els contaminants més polars, a causa de la seva major capa-

citat per infiltrar-se i arribar a les aigües subterrànies, seran els que es detectaran amb major freqüència i en concentracions més elevades i; iii) veure com aquests contaminants poden arribar principalment a través del procés de recàrrega depenent d'aportacions externes, com ara l'aigua de pluja i escorrentia, fuites del clavegueram i infiltracions procedents de rius adjacents, aportant contaminants orgànics de diferents orígens. Per tant l'objectiu principal d'aquesta tesi és **estudiar els TrOCs en les masses d'aigua urbanes per conèixer la seva presència i aportació de cada font de recàrrega a l'aigua subterrània**. D'aquest objectiu general, s'extrauen altres objectius específics:

- Desenvolupar mètodes analítics d'extracció, separació cromatogràfica de TrOCs, amb especial atenció als més hidrofílics.
- Usar la mobilitat iònica per detectar TrOCs iònics, mòbils i tòxics amb potencial de comprometre la qualitat de l'aigua.
- Avaluar la presència de TrOCs en les fonts de recàrrega d'aigua urbana subterrània, com les aigües superficials, d'escorrentia, de pluja, de clavegueram i de SUDS. Per conèixer les fonts de contaminació més importants de l'aigua subterrània mitjançant models hidrogeològics en base a paràmetres físico-químics i TrOCs.
- Identificació de TrOCs detectats únicament en les diferents matrius aquoses urbanes estudiades.
- Avaluació del risc medi ambiental que presenten els TrOCs al medi urbà, mitjançant la seva persistència, toxicitat i concentració.

2.2 Estructura de la tesi

Aquesta tesi es dividirà en 6 capítols, on s'inclouen els diferents articles científics que hi han resultat. El *Capítol 1* es correspon a la introducció general on es descriu la problemàtica actual dels recursos hídrics, entrant en profunditat amb l'aigua subterrània urbana i les seves principals fonts de recàrrega. També s'han introduït els contaminants orgànics, aquí anomenats TrOCs, i se n'ha mencionat la seva legislació en les aigües a més de la problemàtica associada a aquestes substàncies per contaminació de la mateixa i la seva subseqüent perillositat per als

organismes vius. S'ha posat en context tota la metodologia analítica necessària per a l'extracció i detecció dels TrOCs, entrant en detall amb els compostos molt polars, que presenten unes dificultats analítiques afegides. Finalment les tècniques de detecció dels TrOCs, en específic, els cromatògrafs de líquids i l'espectrometria de masses, passant per la mobilitat iònica, han estat descrites en profunditat i emprades extensivament en aquesta tesi.

El *Capítol 2* exposarà els objectius principals de la tesi acompanyat amb una breu explicació de l'estructura de la mateixa.

Els *Capítols 3*, *4* i *5* exposen els resultats de la tesi. Tots tres consten d'una breu introducció, els articles científics resultants i una petita discussió englobant tots els resultats inclosos en cada capítol.

El *Capítol 3* engloba tota la metodologia analítica desenvolupada en aquesta tesi, necessària per l'anàlisi de compostos polars i molt polars en aigua urbana, incloent dues publicacions científiques, una referida a l'extracció mitjançant tècniques evaporatives i emprant una columna HILIC i l'altre detallant l'ús de la mobilitat iònica per TrOCs molt polars.

- Publicació #1: **Labad, F.**, Pérez, S., 2024. LC-MS analysis of polar and highly polar organic pollutants in Barcelona urban groundwater using orthogonal LC separation modes. Environ. Sci. Pollut. Res. https://doi.org/10.1007/s11356-024-33471-y
- Publicació #2: **Labad, F.**, Pérez, S., Qualitative and quantiative analysis of highly-polar contaminants in Atlanta urban water. Submitted to Analytica Chimica Acta.

En el *Capítol 4* s'exposen els resultats de la presència de TrOCs en aigües urbanes, incloent aigua subterrània, aigua de pluja i aigua d'escorrentia urbana posant especial atenció als TrOCs més polars. S'han emprat dues metodologies d'extracció i separació diferents i un total de tres publicacions s'han dut a terme:

- Publicació #3: **Labad, F.**, Ginebreda, A., Criollo, R., Vázquez-Suñé, E., Pérez, S., Jurado, A., 2023. Occurrence, data-based modelling, and risk assessment of emerging contaminants in an alluvial aqui-

fer polluted by river recharge. Environ. Pollut. 316, 120504. https://doi.org/10.1016/j.envpol.2022.120504

- Publicació #4: **Labad, F.**, Santana-Viera, S., Jiaqi, X., Borrell-Diaz, X., Teixidó, M., Pérez, S., 2025. Surveillance and environmental risk of very mobile pollutants in urban stormwater and rainwater in a water-stressed city. Journal of Hazardous Materials, 486, 136959. https://doi.org/10.1016/j.jhazmat.2024.136959

- Publicació #5: Santana-Viera, S., **Labad, F.**, Pintado-Herrera, M., Montemurro, N., Teixidó, M., Lara-Martín, P., Pérez, S. Comprehensive target and suspect analysis of persistent, mobile and toxic compounds in urban stormwater. Submitted to NPJ Clean Water.

El *Capítol 5* està orientat a mostrar els resultats obtinguts en relació a les fonts de contaminació de l'aigua subterrània, com ara aigües d'escorrentia, superficial i clavegueram, amb l'aplicació de models i aportacions dels contaminants depenent del seu origen, a la ciutat de Barcelona. Un total de dues publicacions més completen la tesi:

- Publicació #6: Nikolenko, O., **Labad, F.**, Pujades, E., Scheiber, L., Pérez, S., Ginebreda, A., Jurado, A., 2024. Combination of multivariate data analysis and mixing modelling to assess tracer potential of contaminants of emerging concern in aquifers. Environ. Pollut. 341, 123020. https://doi.org/10.1016/j.envpol.2023.123020

- Publicació #7: **Labad, F.**, Jurado, A., Scheiber, L., Teixidó, M., Vázquez-Suñé, E., Pérez, S. Source Apportionment of Organic Contaminants in Urban Groundwater: Assessing Recharge Contributions. Submitted to the Journal of Hazardous Materials

L'últim, el *Capítol 6*, contindrà les conclusions de la tesi i la seva descripció. Aquestes conclusions generals estan basades amb relació a la problemàtica actual amb el recurs de l'aigua, detallada al *Capítol 1*, els objectius del *Capítol 2* i els resultats dels *Capítols 3*, *4* i *5*.

Capítol



3.

Desenvolupament de mètodes per a l'anàlisi de TrOCs polars en aigües urbanes

DESENVOLUPAMENT DE MÈTODES PER A L'ANÀLISI DE TrOCs POLARS EN AIGÜES URBANES

3

3.1 Introducció

Actualment, els compostos polars estan al punt de mira dels investigadors ja que tenen la capacitat de traspassar les barreres naturals, evitant acumular-se així a teixits orgànics com sòls, fangs o fauna. Un cop alliberats al medi ambient a través dels sistemes de sanejament domèstic, els abocaments industrials o com a conseqüència de les activitats antropogèniques diàries, com ara el trànsit vehicular i l'activitat humana en entorns urbans, poden arribar a les aigües subterrànies, comprometen la seva qualitat (UBA, 2017). La problemàtica al començament de la tesi respecte al anàlisis de TrOCs de polaritat alta era que s'havien de desenvolupar noves metodologies per poder fer el seu monitoratge tant ales aigües subterrànies com a les seves fonts de contaminació per protegir les aigües dolces del nostre planeta. La problemàtica analítica es centra en dos passos: el primer, l'extracció dels analits d'interès de la matriu, en aquesta tesi sempre serà l'aigua, i el segon, la separació cromatogràfica i detecció dels mateixos. Degut a que els TrOCs analitzats són presents al medi en concentracions molt baixes, es necessita una ex-

tracció eficient i que permeti una preconcentració dels compostos per tal de poder detectar-los, en aquesta tesi, en instruments de cromatografia de líquids acoblada a un espectròmetre de masses d'alta resolució.

Mètodes de preconcentració de mostra emprats en aquesta tesis per a l'anàlisi dels TrOCs

Tenint en compte, la gran varietat de TrOCs que s'han analitzat en aquesta tesi (~ 200 compostos), dues metodologies de tractament de mostra s'han desenvolupat i validat: una extracció basada en SPE i un enriquiment basat en l'evaporació.

Respecte a l'extracció en fase sòlida, al grup es va desenvolupar una metodologia emprant diferents adsorbents per crear un cartutx multi-adsorbent de dues capes (Fagnani et al., 2022). Aquest cartutx, fet manualment al laboratori, consistia en un cartutx de propilè buit de 6 mL, omplert per una capa superior de 200 mg d'adsorbent HLB i per una capa inferior d'una mescla de tres adsorbents, 100 mg de WAX, 100 mg de WCX i 150 mg de Bond Elut PPL, on tres frites de polietilè de 20 µm separen les capes (Figura 3.1), activats i condicionats amb 5 mL de metanol, . Un cop els 500 mL de la mostra d'aigua passaven pels cartutxos es deixaven assecar sota buit durant 2 h aproximadament, per evitar que l'aigua intersticial restant pogués eluir algun compost en el següent pas. L'elució seleccionada consistia en un total de 15 mL de solvent, amb l'objectiu d'eluir els compostos adherits als adsorbents, seguint els passos següents: i) 2*3 mL 5% amoníac en metanol:acetat d'etil (50:50, v/v); ii) 2*3mL 2% àcid fòrmic en metanol:acetat d'etil (50:50, v/v) i; iii) 3mL metanol:acetat d'etil (50:50, v/v). S'ha seleccionat una barreja de metanol i acetat d'etil com a dissolvents en funció de les seves polaritats, aconseguint així una mescla amb capacitat per arrossegar TrOCs de diferents característiques. D'altra banda, l'amoníac té l'objectiu de neutralitzar els possibles àcids (amb càrrega negativa) adherits, amb més probabilitat, al adsorbent WAX, mentre que l'àcid fòrmic ho fa per a les bases (amb càrrega positiva), fet que permet que la mescla metanol acetat d'etil, un cop neutres, eluïssin aquests compostos. Finalment, els 15 mL de solvent son evaporats sota un corrent suau de nitrogen i reconstituïts amb 0.5mL d'una mescla de solvents depenent de la separació cromatogràfica, 95:5 d'aigua:acetonitril per la columna C18 i 2:98 d'aigua:acetonitril per la columna HILIC.

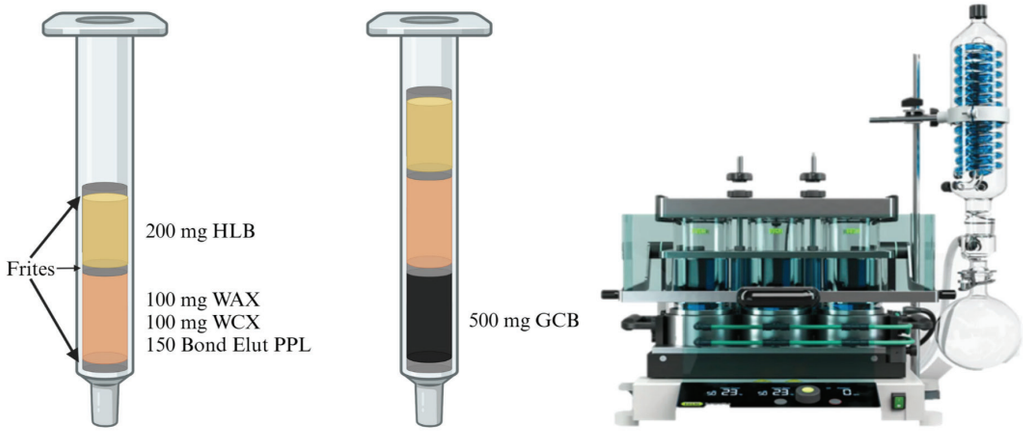


Figura 3.1. Representació gràfica dels mètodes d'extracció emprats en aquesta tesi.

El cartutx mencionat va ser emprat als estudis #1, #3, i #6, ja que ofereix una recuperació acceptable per una gran varietat de TrOCs de polaritat baixa a moderada. Tot i això, per a la majoria de compostos de polaritat més elevada, les recuperacions no complien els paràmetres de qualitat establerts (Pihlström et al., 2019).

Per aquesta raó, es va afegir una tercera capa al cartutx preparat al laboratori, pensada per retenir aquells compostos que aconseguien eluir-se sense quedar retinguts. A la Figura 3.1 es mostra que, l'adsorbent escollit va ser el GCB, on estudis previs indicaven la seva funcionalitat per complir aquest objectiu (Köke et al., 2018). Prèviament a validar la nova barreja d'adsorbents, tres diferents combinacions de solvents d'elució varen ser provats seguint la bibliografia; i) la mateixa combinació de solvents, prèviament descrita; ii) elució amb 3*5mL de metanol; iii) elució a la inversa (cartutx girat) amb metanol, per tal d'evitar que els compostos que s'hagin retingut a la part superior del adsorbent, hagin de traspassar tot el gruix del GCB, evitant una possible incompleta elució. Aquest metodologia presentava d'un alt cost econòmic per la quantitat d'adsorbents i solvents necessaris, era laboriós i requeria d'un temps considerable per a la seva correcta execució.

Paral·lelament al desenvolupament de la SPE amb carboni, i també seguint l'escassa bibliografia relativa a l'extracció de TrOCs polars en aigua, es va desenvolupar un mètode evaporatiu (Mechelke et al., 2019). Aquest mètode bàsicament consisteix en evaporar una quantitat d'aigua al buit per tal de concentrar els analits d'interès sense haver de dependre d'una extracció i d'adsorbents com la SPE. En les primeres proves, com no disponiem encara d'un sistema d'evaporació al buit, es van evaporar 10mL d'aigua sota una corrent de nitrogen usant el TurboVap (Thermo-Fisher Scientific, Alemanya). Aquest enriquiment va ser molt lent i es van necessitar més de 10 h per evaporar la mostra d'aigua totalment. Per això es va decidir comprar (descrits a l'apartat de Discussió) un equip d'evaporació equipat amb un bany d'aigua i que treballa sota buit (similar a un rota-vapor) amb capacitat per a 12 vials (Buchi Syncore Plus). A més, els vials estan dissenyats amb un apèndix de 0.3mL, per evitar l'evaporació a sequedat de les mostres Figura 3.1. Aquest mètode extractiu es anomenat d'ara en endavant evaporació assistida al buit (VAE, de l'anglès *vacuum-assisted evaporation*).

Mètodes de separació i quantificació cromatogràfica per als TrOCs d'interès

Un cop s'han preconcentrat els TrOCs d'interès a un vial cromatogràfic, es va separar aquesta mescla a un cromatògraf de líquids, concretament d'un Acquity UHPLC (de l'anglès Ultra High Performance Liquid Chromatograpy) (Waters), acoblat a un HRMS, en aquest cas, un Orbitrap Q-Exactive (Thermo). Seguint amb la gran quantitat de TrOCs seleccionat per aquesta tesi, amb les seves diferents propietats físico-químiques, és difícil assolir una separació cromatogràfica òptima per a tots els compostos en una fase estacionaria.

A l'inici de la tesi, es van arribar a provar diferents columnes cromatogràfiques amb diferents gradients per a trobar la més eficient a nivell de resolució de pics i de temps, evitant els gradients superiors a 20 min. Les columnes testejades varen ser les següents: fase-inversa Acquity HSS T3 (100 mm * 2.1 mm * 1.8 µm), HILIC BEH Amide (100 mm * 2.1 mm * 1.7 mm) ambdós de Waters i, per últim, la de mode mixt Raptor Polar X (100 mm * 2.1 mm * 2.7 µm) de Restek, que comparteix propietats d'HILIC amb intercanviador iònic (Figura 3.2).

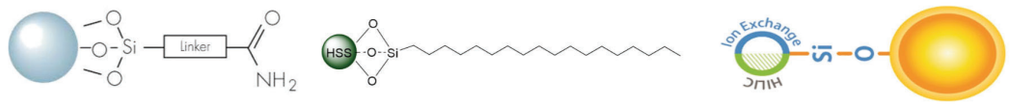


Figura 3.2. Representació gràfica del farciment de les columnes de LC emprades.

En primer lloc, cal mencionar que cada una d'aquestes tres columnes té propietats diferents i que, per tant, els compostos que es retinguin millor en cada una d'elles serà diferent. Teòricament, els compostos poc polars i de polaritat intermèdia, fins a log D_{ow} = 0, patiran una retenció adequada amb la columna HSS T3, mentre que la columna BEH Amide tindrà una utilitat major per a compostos molt polars (log D_{ow} < 0) que per a TrOCs de polaritat alta. D'altra banda, la columna Raptor Polar X, es idònia tant per retenir compostos polars, usant la seva modalitat d'HILIC, com per retenir els compostos iònics (a pH de treball) mitjançant la modalitat d'intercanvi de ions. Tot i això, el gradient cromatogràfic té un paper molt important per a que cada columna expressi el seu màxim rendiment, sempre tenint en compte les propietats dels compostos d'interès. A la secció de Discussió d'aquest mateix capítol, s'exposen els gradients amb millors resultats per a cada una d'aquestes columnes.

L'ús de la Mobilitat Iònica per a vMC

La tècnica de separació i detecció emprada en aquesta tesi va ser la IM, que basa el seu principi de separació en la mida, el diàmetre i la càrrega de cada molècula. Aquesta tècnica, em mode d'injecció directe, no depèn de la polaritat dels compostos ni tampoc d'una afinitat dels mateixos amb una fase estacionària, fent-la interessant per retenir aquelles molècules que presenten dificultats en ser correctament retingudes mitjançant l'ús de columnes cromatogràfiques. L'instrument emprat a les instal·lacions de Georgia Institute of Technology (Atlanta, Georgia, USA) va ser el Synapt G2S, el qual treballa amb TWIMS. Breument, TWIMS treballa utilitzant un tub de deriva a baixa pressió en el qual el camp elèctric s'aplica de manera localitzada en una petita regió del tub . Aquesta regió es desplaça seqüencialment al llarg del tub, generant una ona que impulsa els ions cap al detector evitant així l'ús de voltatges elevats (Shvartsburg and Smith, 2008). La Figura 3.3B representa esquemàticament el mode de treball del TWIMS. El principal inconvenient és la impossibilitat de

determinar directament les CCS, ja que aquestes s'adquireixen amb un camp elèctric constant. Degut això, l'equip s'ha de calibrar sovint emprant calibrants amb CCS coneguts que es fan servir com a referència per corregir els resultats posteriors. Els CCS són extrets majoritàriament dels DTIMS, ja que són els que empren un camp elèctric continu i, per tant, l'única variable que influeix en l'arribada dels analits són forma, grandària i càrrega (Figura 3.3A). A la secció de Discussió, s'exposen els resultats de l'aplicabilitat d'aquesta tècnica amb les molècules altament polars (petites) i seran comparades amb les columnes de LC.

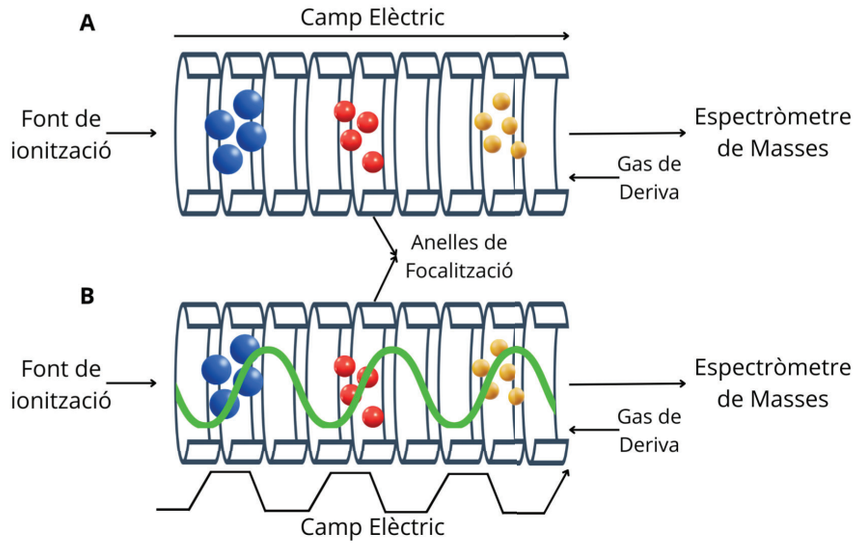


Figura 3.3. Representació gràfica del funcionament d'un IM de (A) tub de deriva (*drift-tube*) i (B) ona viatgera (*travelling-wave*).

3.2 Resultats

Aquest capítol inclou dues publicacions científiques (una ja publicada i l'altra enviada a revista) on s'inclouen els dos mètodes analítics desenvolupats durant la tesi. En un s'inclou el mètode extractiu basat en evaporació i el anàlisis mitjançant LC-HRMS usant mostres d'aigua subterrània de la ciutat de Barcelona (Espanya) i l'altra, realitzat durant l'estada doctoral al Georgia Institute of Technology, basat en la separació d'analits molt polars, emprant TWIMS, en mostres d'aigua superficial urbana de la ciutat d'Atlanta (Estats Units). Les publicacions són:

- Publicació #1: **Labad, F.**, Pérez, S., 2024. LC-MS analysis of polar and highly polar organic pollutants in Barcelona urban groundwater using orthogonal LC separation modes. Environ. Sci. Pollut. Res. 1-11. https://doi.org/10.1007/s11356-024-33471-y

- Publicació #2: **Labad, F.**, Pérez, S., 2024. Ion Mobility as a possibility to separate highly polar small molecules: Occurrence of very mobile compounds in urban surface water of Atlanta. Submitted to Analytica Chimica Acta.

PUBLICACIÓ CIENTÍFICA #1

LC-MS analysis of polar and highly polar organic pollutants in Barcelona urban groundwater using orthogonal LC separation modes

Labad, F., Pérez, S.

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ENVIRONMENTAL CHEMISTRY FOR A POLLUTION FREE SOCIETY

LC–MS analysis of polar and highly polar organic pollutants in Barcelona urban groundwater using orthogonal LC separation modes

Francesc Labad[1] · **Sandra Pérez**[1]

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Abstract
Groundwater samples may contain thousands of organic pollutants from infiltration of surface water, sewer leakages, and to a minor extent from public water supply network losses. Polar ($0 < \log D < -2.0$) and very polar substances ($\log D < -2.0$) have been largely beyond the scope of applied analytical methodologies in environmental monitoring because of challenges related to their extraction from the sample and subsequent chromatographic separation. In this study, we developed an analytical workflow for 96 pollutants covering a broad polarity range, including pharmaceuticals, industrial chemicals, and artificial sweeteners, potentially seeping through the soil in urban areas. The Besos aquifer located at the Northern-eastern edge of the city of Barcelona was chosen as a study area due to the deterioration of the quality of the aquifers over the past years and the proven presence of numerous pollutants. The methodology consisted of vacuum-assisted evaporation (VAE) followed by chromatographic separation of the sample on two columns with orthogonal retention mechanisms, namely, an HSS T3 column (modified C18) and a BEH amide column (HILIC). The analytes were detected by high-resolution mass spectrometry on a Q Exactive Orbitrap system in data-independent acquisition mode. Taking into consideration the retention as well as the peak shape, a Quality Score (QS) was assigned for each analyte to evaluate the quality of each chromatographic peak of each compound. While 67 compounds, including 19 polar and 48 moderately polar, were satisfactorily retained on an HSS T3, 29 compounds, including 14 highly polar, 14 polar, and one moderately polar, were analyzed in the BEH amide column. The optimized methodology was applied for the analysis of 89 out of 96 validated contaminants with satisfactory recoveries in samples collected from seven wells, providing low LODs (0.02 to 0.45 ng L^{-1}) and LOQs (0.06 to 1.34 ng L^{-1}). A number of highly polar and polar compounds not previously reported to occur in GW, including artificial sweeteners, pharmaceuticals, and industrial chemicals, were detected at concentrations as high as few μg L^{-1}.

Keywords Pharmaceuticals · Industrial chemicals · VAE · LC-HRMS/MS Q Exactive Orbitrap

Introduction

In southern Europe, as a result of the limited availability of surface water and the growing demand for drinking water, alternative water resources such as groundwater (GW) need to be explored. Although GW can be thought to be protected from surface impacts by pollutant adsorption and degradation processes occurring during water infiltration (Arias-Estévez et al. 2008), there is a risk of pollution from seepage of surface water, sewer leakages, and to a minor extent from public water supply networks losses (Bester et al. 2008; Osenbrück et al. 2007; Schulze et al. 2018). When urban GW is located in a deltaic zone, like the Besos River north of the Barcelona metropolitan area, an additional threat is seawater intrusion (Jurado et al. 2012 and 2014; Tubau et al. 2014; López-Serna et al. 2013; Vázquez-Suñé et al. 2010). Therefore, GW is potentially polluted with a multitude of organic xenobiotics of diverse physico-chemical properties. Whereas many non-polar compounds can be retained in the soil, compounds of high polarity are more susceptible to reaching GW (Reemtsma et al. 2006; Schulze et al.

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2019). The two major parameters quantitatively describing the polarity of an organic compound are the partition coefficient (log *P*) and the pH-dependent distribution coefficient (log *D*). They influence their mobility and ultimately GW vulnerability. Recent studies have classified compounds with log *D* 0–2 as polar and those with log $D < 0$ as very polar (Neumann and Schliebner 2019; Peter Arp and Hale 2019).

Several studies have demonstrated the presence of non-polar pollutants in GW (Grujić et al. 2009; Heberer et al. 2004; Loos et al. 2010; Wolf et al. 2012) across Europe. In two studies from German groundwater, assessing the presence of six 6 PhACs (Heberer et al. 2004) and 22 personal care products (Wolf et al. 2012), respectively, the levels ranged from non-detected to 4.2 µg L^{-1}. A Serbian study demonstrated the presence of four PhACs (azithromycin, carbamazepine, paracetamol, and trimethoprim) (Grujić et al. 2009). A pan-European study involving 23 countries investigated the presence of 59 contaminants in 164 GW samples, with the most frequently detected compounds being DEET, caffeine, PFOA, and atrazine (Loos et al. 2010). Most of the studies were focused on the occurrence of non-polar and medium-polar substances, whereas polar and very polar pollutants were largely outside the scope of the analytical methodologies applied because of challenges related to their extraction from the sample and subsequent chromatographic separation. The few studies related to polar substances in GW relate to pesticides (Köck-Schulmeyer et al. 2014), some industrial chemicals (Heberer et al. 1998; Schorr et al. 2023), and one study treating with surface water and effluent and influent wastewater, demonstrating the presence up to 27 polar chemicals (log $D -6$ to 1), combining pharmaceuticals and industrial compounds (Mechelke et al. 2019).

As far as sample enrichment is concerned, solid-phase extraction (SPE) is the most common method for the preconcentration of organic pollutants in aqueous samples (Huntscha et al. 2012; López-Serna et al. 2011; Richardson et al. 2017; Ruff et al. 2015). Nevertheless, most commercially available SPE cartridges, such as the popular hydrophilic-lipophilic balance (HLB) sorbent (Dias and Poole 2002), have been demonstrated to poorly retain polar to very-polar compounds because they were designed for extracting non to medium-polar compounds. Conversely, graphitized carbon black (GCB) with its high retention capability for polar compounds exhibits severe problems in their desorption (Schulze et al. 2019). To address selectivity issues related to the use of single sorbent, multi-sorbent SPE (msSPE) has been proposed; it consists of an SPE cartridge filled with a (layered) combination of sorbents such as HLB and ion exchange resins (di Corcia et al. 1993; Fagnani et al. 2022; Gilart et al. 2014; Köke et al. 2018; Osorio et al. 2016). For the sake of simplicity and ease of use, alternative preconcentration methods with reduced risk of analyte losses were developed including enrichment by evaporative techniques (Angeles and Aga 2020; Köke et al. 2018; Mechelke et al. 2019; Schulze et al. 2020). Vacuum-assisted evaporation (VAE) has several advantages over msSPE, such as time-saving, solvent-free sample extraction, cost-saving, and minimal sample handling.

Besides the critical sample enrichment step, poor analyte retention is commonly observed when using typical reversed-phase liquid chromatographic (RPLC) columns, which have been successfully employed in the past for multi-class organic contaminant separations (Ruff et al. 2015). Therefore, novel retention modes have been explored in recent years to enhance the retention of polar organic compounds, such as hydrophilic interaction liquid chromatography (HILIC) (Reemtsma et al. 2016; Tang et al. 2016; van Nuijs et al. 2011; Montes et al. 2019). To the best of the author's knowledge, no HILIC-based method for the analysis of highly polar substances in urban groundwaters has been previously reported in the literature.

Here, we propose an analytical procedure using two orthogonal LC columns for the quantitative determination of groundwater pollutants with different polarities; the normal phase with a polar stationary phase (used for the retention of polar to highly-polar substances) and the reversed phase, with opposite retention principle, retaining non-polar to medium-polar substances. It allowed for sensitive measurement of the target analytes in urban GW samples from a polluted area.

Materials and methods

Chemicals, reagents, and solutions

The analytes included in this work were selected based on their environmental occurrence and inclusion in watch lists (European Parliament and of the Council 2013; Peter Arp and Hale 2019). The list included 96 compounds with a wide range of polarities (from log *D*-6 to 2) of which were classified as highly polar (log $D < -2$), polar ($0 > \log D > -2$), and moderately polar compounds ($0 < \log D < 2$). Analytical reference standards used for method development were of high purity (Sigma Aldrich (St. Louis, MO, U.S.). Isotope-labeled compounds used as surrogates were purchased from Cerilliant (Sigma Aldrich), Santa Cruz Biotechnology (Dallas, TX, USA), or Toronto Research Chemicals (Toronto, ON, Canada). Chemical structures and relevant properties of the target compounds are compiled in Table S1.

For stock solution and sample preparation, LC–MS grade acetonitrile (ACN, ≥ 99.9%), methanol (MeOH, ≥ 99.9%), ethyl acetate (EtOAc, ≥ 99.9%), dimethyl sulfoxide (DMSO, ≥ 99.9%), and HPLC water were purchased from Merck (Darmstadt, Germany). Formic acid (FA, ≥ 96.0%, ACS grade), ammonium acetate, and ammonia solution

(29.0%, ACS grade) were supplied by Sigma Aldrich. LC/MS Optima™ Grade ACN, water, and ammonium fluoride for the preparation of the mobile phase were purchased from Fisher Chemical (Fisher Scientific SL, Madrid, Spain). Individual analyte stock solutions were prepared at a concentration of 1000 µg mL^{-1} in either MeOH, ACN, DMSO, or HPLC water, depending on the solubility of each compound, and stored at − 20 °C. Mixed working solutions of the analytes and the isotopically labeled compounds were prepared in MeOH at 2 µg mL^{-1} from stock solutions for method development, validation study, and calibration purposes.

Sample collection

The study area was located in the northeast of Spain, specifically, in the Besos River Delta, which includes the municipalities of Barcelona, Santa Coloma de Gramenet and Badalona, and the entire municipality of Sant Adria del Besos. In July 2020, 1-L groundwater samples from along the Besos River were collected from seven wells (Fig. 1, Table S6), in amber polyethylene terephthalate (PET) bottles, and stored at − 20 °C until analysis. Before collection, each well was pumped for 10 to 15 min to ensure a representative aliquot of the groundwater well. Sample parameters such as pH, electric conductivity, temperature, and hardness were measured in situ and are shown in Table S2. The water in the shallow aquifer is a mixture of recharged waters that come from different sources, such as river bank infiltration from the Besos River, infiltration of rain and urban runoff, losses from the supply and sewer network, and seawater, as demonstrated elsewhere (Vázquez-Suñé et al. 2010).

Sample processing

Upon arrival of the samples at the laboratory, samples were filtered under vacuum through a 0.7-µm glass microfiber filter GF/F (Whatman). Ten milliliters of filtered samples were spiked with the internal standard mixture to achieve a final concentration of 50 µg L^{-1}.

Protocol A

A 10-mL sample aliquot was concentrated using a VAE system (BÜCHI™ SyncorePlus, Switzerland) operating at 55 °C, 250 rpm orbital rotation, and a vacuum gradient to reach a final pressure of 20 mbar (Mechelke et al. 2019). The shape of the evaporation tube ensured a residual volume of 0.3 mL, which was then transferred to a 1.5 mL Eppendorf tube for centrifugation purposes (4000 rpm, 4 °C for 10 min). Then, the supernatant was transferred to an HPLC

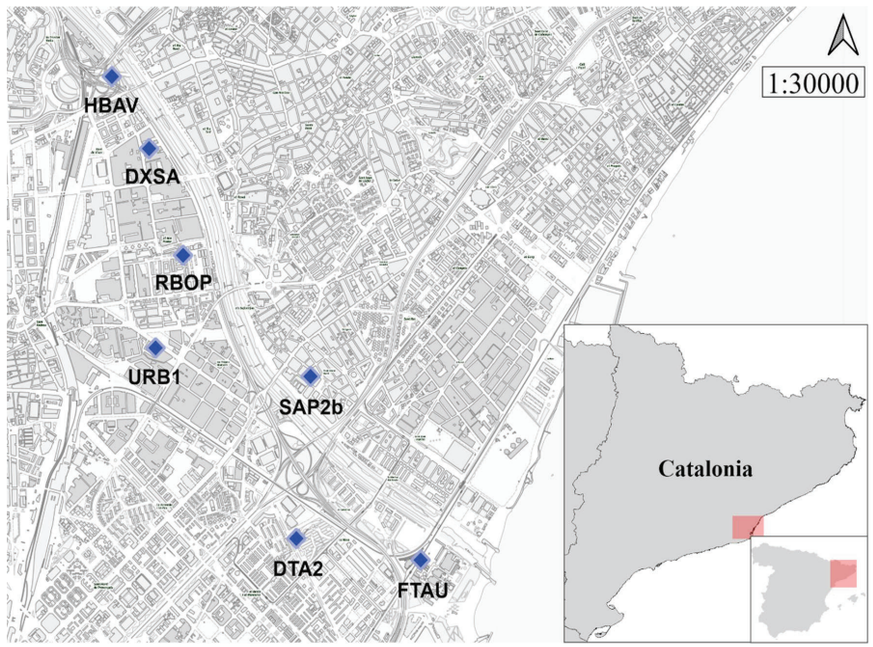


Fig. 1 Location of the seven sampled GW wells in the vicinity of Besos River

vial and evaporated under a gentle stream of N_2 using a Pierce Reacti-Therm III (Thermo-Fisher Scientific, Germany). The sample was reconstituted in 500 µL ACN/H_2O (95:5, v/v) for HILIC separation (Figure S1).

Protocol B

Following the same Protocol A enrichment process, once the VAE process ends, the residuals of 0.3 mL were transferred into an HPLC vial and 200 µL of H_2O were added before RP chromatographic separation, obtaining a final sample volume of 500 µL (Figure S1).

UPLC–Q Exactive Orbitrap-MS conditions and identification criteria

The two columns used in the study were an HSS T3 (100 × 2.1 mm, 1.8 µm particle size) and a BEH amide (100 × 2.1 mm, 1.7 µm), both from Waters (Milford, MA). The former contains a C18-modified package designed to retain nonpolar to moderately polar compounds, which generally fits with the physicochemical properties of the target analytes (New and Chan 2008). An ACQUITY UPLC system (Waters) was interfaced with a Q Exactive mass spectrometer (Thermo-Fisher Scientific, Germany) equipped with a heated electrospray ionization (HESI) probe. The system was controlled by Xcalibur 4.1 software and calibrated using a calibration solution. The LC conditions were optimized to achieve the best chromatographic separation. The flow rate for the HSS T3 column was set to 0.2 mL min^{-1}, and mobile phases and further details can be found in (Gómez-Navarro et al. 2023). For the BEH amide column, the mobile phases consisted of (A) acetonitrile/water (98:2, v/v) with 5 mM ammonium formate and (B) 5 mM ammonium formate. The injection volume was 10 µL, and the column temperature was 40 °C. The optimized elution conditions for both columns are described in Table S3. Methanol was injected every six samples to check for any possible carryover or cross-contamination. In addition, to ensure the integrity of the analysis, quality control samples (QC) were prepared by spiking extracts of GW samples with standards and IS mixture (50 µg L^{-1}) and were injected every six samples. For quantitative purposes, a 12-point calibration curve (0.05 to 300 µg L^{-1}) was constructed containing all surrogates at 50 µg L^{-1}.

The tuning methods and parameters used for the MS acquisitions were optimized. Moreover, a targeted-DIA experiment was performed to allow the acquisition of MS^2 spectra only for ions defined in an inclusion list (Table S4) where the isolation window was set to 1.5 m/z, obtaining individual m/z and RT windows of high-quality MS^2 spectra (Gómez-Navarro et al. 2023). Calibration was performed periodically in both electrospray ionization modes using two different high-purity mixtures from Thermo Fisher Scientific (Germany). The MS optimization was performed by injecting a standard solution containing all compounds at a concentration of 10 µg mL^{-1} in 100% H_2O for the HSS T3 column and H_2O/ACN (5:95, v/v) for the BEH amide.

Thermo Xcalibur software version 4.1 was used for instrument control and qualitative analysis. For quantitation of analytes in samples, data were processed using Thermo TraceFinder 5.1 software. For validation and quantification purposes, the Guidance SANTE 12682/2019 was followed (Pihlström et al. 2018).

Method validation

For both protocols, A and B, three levels (1, 50, and 200 µg L^{-1}) were used to assess the accuracy, precision, matrix effects, and limits of detection and quantification of all target analytes (Table S5 and S7). A total of 89 compounds were quantified in this study. The LOD ranged from 0.02 to 0.45 ng L^{-1}, while LOQ ranged from 0.06 to 1.34 ng L^{-1} across the selected analytes. The calibration curve as well as all validation samples was prepared in matrix-matched groundwater. Regarding validation purposes, samples were prepared in triplicate and the matrix effect was corrected with the use of internal standards.

Results and discussion

Column performance

Given the wide range of target compound polarities, two stationary phase chemistries, namely, an RP C18 (HSS T3) and a HILIC (BEH amide) were tested in order to assess the suitability concerning retention factor and peak shape. The conditions offering an adequate compromise of separation efficiency and chromatographic runtime were a flow rate was 0.2 mL min^{-1} with a total analysis time of 19 and 15 min, respectively (Table S3). The capacity factor (RFK) was calculated according to the following equation:

$$RFK = (t_r - t_0)/t_0 \quad (1)$$

where t_r is the retention time of the analyte and t_0 is the elution time of an unretained compound (Table S4). The analyte providing t_0 for the HSS T3 column was eflornithine (log D − 3.0) which was the first peak detectable without being retained in the column using the optimized gradient (t_r 0.88 min).

Comparing the two columns, there is a general trend between retention and polarity; in the HSS T3 column, low polar compounds are more retained, and in the BEH amide column is the opposite (Figure S2). For instance, using the

HSS T3 column, some of the polar compounds studied, such as melamine, zanamivir, or 5-fluorouracil, showed poor retention (RFK < 1.5), combined with the peak shape quality of some of them such as metformin (Figure S3). The BEH amide column was also tested for the separation of 96 compounds to assess selectivity differences between the two columns. While eflornithine was the compound with no retention on the HSS T3 column, pentobarbital (log D 1.90) was the first detectable peak within the optimized HILIC gradient (t_r 0.91 min) and was selected as reference compound for RFK calculations. As an example, zanamivir was poorly retained in RP conditions (RFK 0.14) as was expected due to its high polarity (log D − 6.0). Using the BEH amide column helped retain and thus analyze this highly polar compound obtaining an RFK of 13.4. Other examples not related to polarity such as methenamine (log D 0.99) were also observed. This molecule was poorly retained in the HSS T3 column (RFK 0.11), whereas using the BEH amide column its retention increased to RFK 11.29.

Looking in-depth, a group of moderately polar compounds seems to have similar behavior, in both columns (Fig. 2). There are substances of this group that share similar properties, for example, propranolol, carazolol, and tramadol (log D of 1.15, 1.14, and 0.52, respectively) molecules sharing some functional groups as all three have 1 alcohol, 1 amine, and between 1 and 2 ethers, see Table S1 for structures. Following this pattern, metoprolol (log D − 0.3) was considered a polar compound, but it follows a similar behavior to the three molecules beforementioned and it could be mainly due to metoprolol having the same functional groups. Finally, atenolol could fit also with that pattern; however, atenolol contains an amide group at the end of the chain that makes it more polar (log D 1.9) and, as a result, its retention time in the reversed-phase column decreases considerably with respect the other four compounds. Eight more compounds inside this group could not be easily classified; there are citalopram, cocaine, hyoscine, neotame, oseltamivir, paroxetine, sitagliptin, and venlafaxine. From Fig. 2, it can also be observed that, above all, three highly polar compounds are well retained in both columns but more retained when using the HSS T3 column. These compounds are iopromide, sulisobenzone (BP4), and tetracycline (log D − 2.12, − 3.47, and − 3.20, respectively), all three large molecules (MW > 300 Da) with at least one aromatic group on their structures.

Additionally, the peak shape was used as a criterion for assessing the goodness of the separation (Kruve et al. 2015). Some compounds displayed peak shapes differing from Gaussian peaks in both columns (Figure S3). Thus, in order to evaluate the quality of each chromatographic peak taking into consideration the retention as well as the peak shape of each compound, a Quality Score (QS) was assigned for each analyte (Table 1). Here, a modification from (Iturrospe et al. 2021) was made, disregarding peak intensity in the overall assessment (Fig. 2).

Figure 3 shows the QS of each compound on both columns. In general terms, polar and moderately polar compounds demonstrate a great performance using the HSS T3 column. However, there are some exceptions such as aspartame (log D − 1.8), 5-fluorouracil (log D − 1.6), melamine (log D − 1.2), sulfaguanidine (log D − 1.0), clofibric acid (log D − 0.9), lincomycin (log D − 0.4), and metoprolol (log D − 0.3) that have higher QS in the HILIC column. That is mainly related to the peak shape of these substances. Among

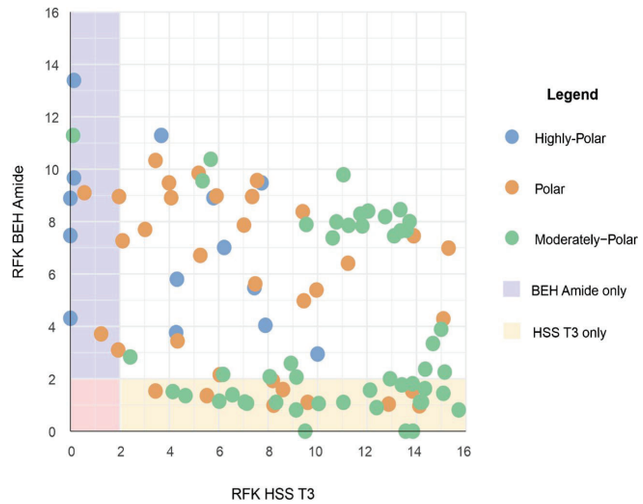


Fig. 2 Relation between the target compounds retention on both columns based on their polarity classification. The red area of the graph shows the non-retained zone for both columns. The orange area shows where the compounds are better retained on the HSST3 column, while the blue zone shows the compounds only retained using BEH amide. The white area shows compounds well retained in both columns

Table 1 Quality Score system for each compound in both chromatographic columns

Peak shape score		Retention factor score	
0	No peak	0	No peak
1	Split peak or multiple peaks	1	RFK ≤ 1
4	Single peak with FWHM ≥ 2 or tailing factor ≥ 2 or ≤ 8	2	1 < RFK ≤ 2
7	Single peak with FWHM < 2 or tailing factor < 2 or > 8	3	RFK > 2

FWHM, full width at half maximum; *RFK*, retention factor.

these substances, melamine was the one demonstrating better performance in both peak shape and retention under HILIC conditions (Figure S3). Except for 5-fluorouracil and sulfaguanidine, whose main difference between columns is based on retention and not on peak shape score, the other four compounds showed greater peak shape improvement using HILIC than using the HSS T3 column. Several mechanisms could affect the peak shape performance, but they are not completely understood yet. On the other hand, for the high-polar compounds, the BEH amide column results in a better performance compared to the HSS T3 column, which demonstrates its ability to retain and provide a Gaussian pattern for the polar compounds.

Given the distinct differences in QS of the analytes for the two column types, the 96 compounds were divided into two groups to ensure high chromatographic performance: 67 were analyzed on the RP column and 29 on the HILIC column (Table 2).

Extraction of polar analytes

As Fig. 4 shows, VAE enrichment provided a satisfactory performance for all three substance classes although there were substances in each class that were lost during the sample preparation. Analytes not recovered at all were codeine (moderately polar), naproxen (moderately polar), aspartame (polar), meprobamate (polar), sulfaguanidine (polar), morphine (polar), and amoxicillin (highly-polar). In the group of moderately polar compounds, tetracycline showed a suboptimal recovery of only 26%.

Occurrence

The analytical method was applied to GW well samples collected in the Besos River (Fig. 1) in order to assess the occurrence of the target analytes. The concentrations spanned a broad range of five orders of magnitude: from sub-ng L^{-1} to double-digit μg L^{-1} (Fig. 5). Then, 53 out of 89 were found above the LOD in at least one of the samples, while a total of 22 compounds were found in all seven GW samples above the LOD (Table S8). The sample SAP2b stood out insofar as the compound concentrations were generally higher than in the other samples because this well is directly impacted by the Besos River (Labad et al. 2023).

It is worth noting that the three fluoroquinolone antibiotics (ciprofloxacin, levofloxacin, and enrofloxacin) were detected in all GW well samples. They are used worldwide for the treatment of several kinds of bacterial infections in humans as well as in veterinary practice. A second group of antibiotics frequently detected were sulfonamides (sulfamethoxazole, sulfapyridine, sulfamerazine, and sulfadiazine). The concentrations of the drugs furosemide, gemfibrozil, hydrochlorothiazide, and valsartan exceed a concentration of 1 μg/L in sample SAP2b. Interestingly, furosemide and gemfibrozil were not measurable in any other sample. Previous studies of pharmaceuticals in groundwater in a pan-survey of wells from all over Europe provided max concentrations of some of them within the same range as detected in this study for sulfamethoxazole and diclofenac (Loos et al. 2010).

Other studies have demonstrated the presence of 5-methyl-1H-benzotriazole, sulfamethoxazole, ibuprofen, 1H-benzotriazole, and highly polar, e.g., melamine in groundwater and surface water in several across Europe and the US (Kruc et al. 2019; Loos et al. 2010; Neuwald et al. 2022; Schaider et al. 2014; Selak et al. 2022). There is a study regarding Barcelona wells made in 2013 (López-Serna et al. 2013), where 95 pharmaceuticals were analyzed and 33 are the same as our study. Similar zones (Besós deltaic area) were also studied. When compared, several agreements in both frequency of detection (FoD) and concentrations are observed. For example, the antibiotics sulfadiazine, sulfamethazine, and sulfamethoxazole showed very similar FoD as well as concentration ranges. Similar behaviors were observed with metoprolol, propranolol, and sotalol which are pharmaceuticals used to treat high blood pressure. Finally, hydrochlorothiazide, a diuretic, in both studies has been reported with a 100% FoD with similar minimum concentrations and close maximum concentrations (665 and 1179 ng L^{-1} in the López-Serna and the present study, respectively). On the other hand, there are some differences between studies, the main one is salicylic acid whose detection is opposite; not detected in the present study and fully detected in the comparison study. Diclofenac, ibuprofen, furosemide, and gemfibrozil are also compounds more detected and more concentrated in the 2013 study than in the present one. However, atenolol was detected in 85.7% of the samples here, while in the other study, it was detected just in one sample. Causes of agreement and disagreement in those molecules could be related to several factors, the main ones, being the year difference between studies, the season of the year, and, the obvious one, the wells are not the same in both studies.

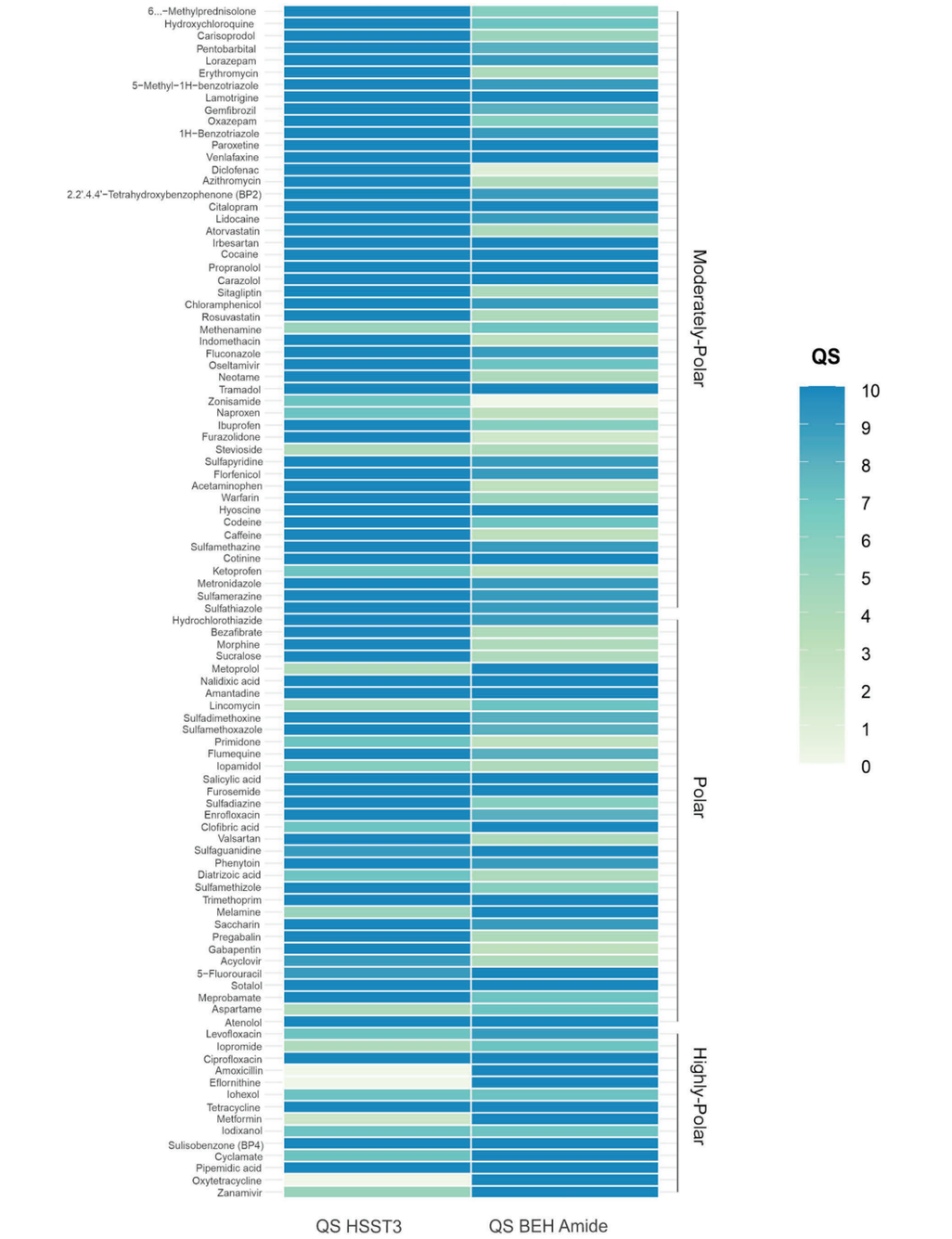


Fig. 3 Quality Scores (QS) heatmap for each compound in both columns, sorted by polarity

Table 2 Target compounds sorted by their polarity class and the chromatographic column selected for analysis

LC column	Polarity	Compounds
HSS T3	Polar	Acyclovir, bezafibrate, diatrizoic acid, enrofloxacin, flumequine, gabapentin, hydrochlorothiazide, meprobamate, morphine, phenytoin, pregabalin, primidone, saccharin, sucralose, sulfadiazine, sulfadimethoxine, sulfamethizole, sulfamethoxazole, valsartan
	Moderately polar	Acetaminophen, atorvastatin, azithromycin, BP2, caffeine, carazolol, chloramphenicol, citalopram, cocaine, codeine, cotinine, florfenicol, fluconazole, furazolidone, hyoscine, ibuprofen, indomethacin, irbesartan, ketoprofen, lidocaine, metronidazole, naproxen, neotame, oseltamivir, propranolol, rosuvastatin, sitagliptin, sulfamerazine, sulfamethazine, sulfapyridine, sulfathiazole, tramadol, warfarin, zonisamide, 1H-benzotriazole, 5-methyl-1H-lamotrigine, 6α-methylprednisolone, carisoprodol, diclofenac, erythromycin, gemfibrozil, hydroxychloroquine, lamotrigine, lorazepam, oxazepam, paroxetine, pentobarbital, venlafaxine
BEH amide	Highly polar	Amoxicillin, BP4, ciprofloxacin, cyclamate, eflornithine, iodixanol, iohexol, iopromide, levofloxacin, metformin, oxytetracycline, pipemidic acid, tetracycline, zanamivir
	Polar	5-Fluorouracil, amantadine, aspartame, atenolol, clofibric acid, furosemide, lincomycin, melamine, metoprolol, nalidixic acid, salicylic acid, sotalol, sulfaguanidine, trimethoprim
	Moderately polar	Methenamine

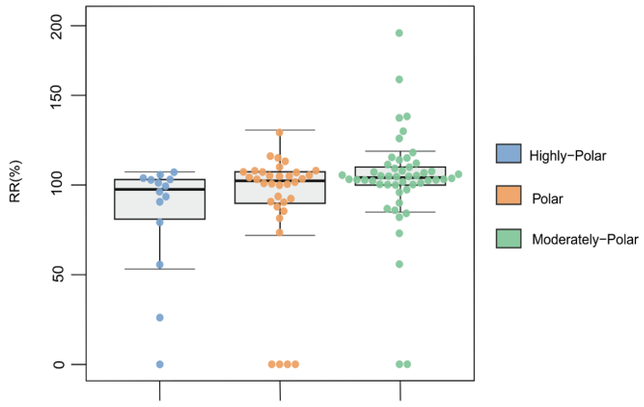


Fig. 4 Relative VAE recoveries of the 96 analytes, expressed in percentage (RR %), as grouped by polarity class

Digging into the results, the substance with by far the highest measured concentration (34,100 ng L^{-1}) was the artificial sweetener sucralose (log $D-0.2$) whose average concentration across all wells was 7220 ng L^{-1}. It has to be mentioned that in the sample point HBAV, sucralose was not detected. The presence of this chlorinated saccharose derivative in GW is a reflection of its extensive use in foodstuff, high water solubility and polarity, resistance to biodegradation over a wide range of pH, and very low affinity to soil particles. Sucralose was previously detected in two studies in non-urban groundwater from Barbados and Rastatt although low concentrations were found (Edwards et al. 2019; Wolf et al. 2012). Sweeteners, in general, are not included in legislation or watch lists due to their low toxicity.

Apart from these pharmaceuticals and artificial sweeteners, a series of pollutants considered of high environmental concern were found that are commonly classified as PMT (persistent—mobile—toxic) contaminants (1H-benzotriazole, 5-methyl-1H-benzotriazole, melamine, phenytoin, sulfadiazine, sulfapyridine, and venlafaxine) and as vPvM (very persistent—very mobile) contaminants (amantadine) (Hale et al. 2020). Among the PMT, the maximum concentrations of 5-methylbenzotriazole and 1H-benzotriazole were reached in sample Sap2b (2122 and 1100 ng L^{-1}, respectively).

Conclusions

In this study, the presence of pollutants with a wide range of polarities in the urban GW of Barcelona city was evaluated. Through the calculation of the QS of each compound on both columns, we can conclude that moderately polar compounds were satisfactorily separated on a C18 column (HSS T3). However, the chromatography of highly polar substances was more challenging due to their poor retention so aspartame, clofibric acid, 5-fluorouracil, melamine, lincomycin, metoprolol, and sulfaguanidine presented higher

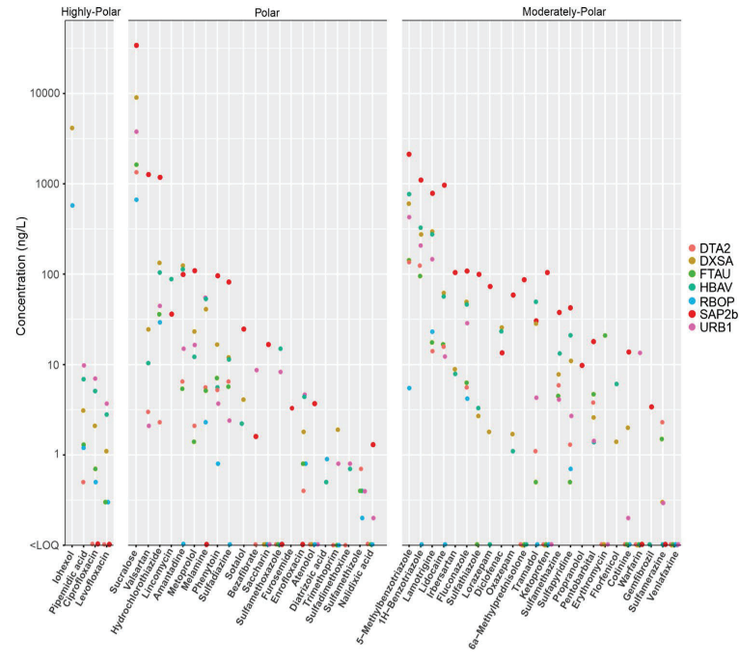


Fig. 5 Concentrations of the analytes in the GW well samples collected in the vicinity of the Besos River. Compounds are grouped according to their polarity class

QS in the HILIC column. That is mainly related to the peak shape of these substances. Finally, the VAE enrichment combined with the chromatographic separation on both columns provided the best performance.

The analytical protocol was applied to real samples from GW wells showing that GW is not only polluted with compounds previously detected but also with highly polar and polar compounds including artificial sweeteners, industrial chemicals, and pharmaceuticals. The concentrations of most of the organic contaminants in GW were less than 100 ng L^{-1}. A notable exception was the artificial sweetener sucralose with a peak concentration of 34,100 ng L^{-1} as well as the highly polar compound, iohexol, with concentrations higher than 1000 ng L^{-1}. The study highlighted a clear need for updating existing monitoring schemes to include very polar substances, which will allow to monitor GW quality in a more comprehensive matter and thus assess potential drinking water sources.

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Author contribution Francesc Labad: methodology, lab work, and writing—original draft. Sandra Pérez: conceptualization, supervision, project administration, writing—review and editing, and funding acquisition.

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Declarations

Ethical approval Ethics approval was not required for this research.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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PUBLICACIÓ CIENTÍFICA #1

SUPPLEMENTARY INFORMATION

LC-MS analysis of polar and highly polar organic pollutants in Barcelona urban groundwater using orthogonal LC separation modes

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Environmental Science and Pollution Research, 2023. 1-11
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Supplementary Data

LC-MS analysis of polar and highly polar organic pollutants in Barcelona urban groundwater using orthogonal LC separation modes

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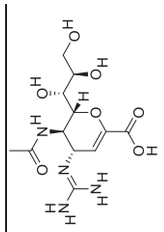
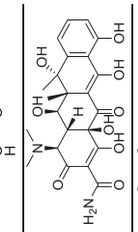
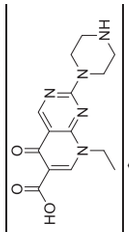
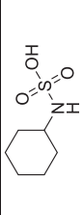
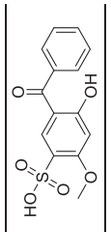
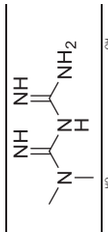
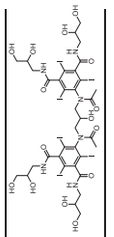
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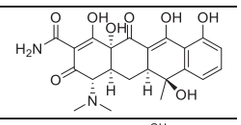
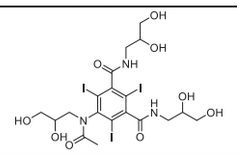
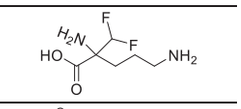
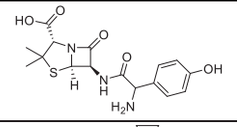
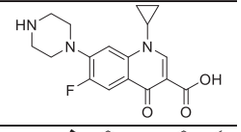
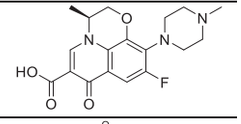
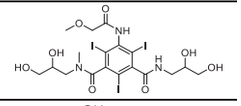
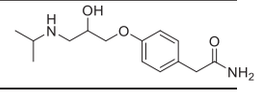
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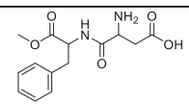
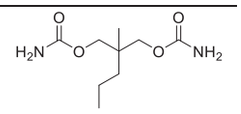
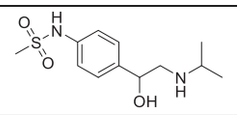
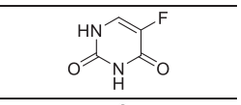
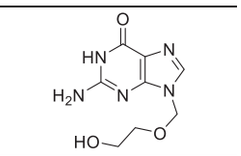
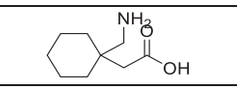
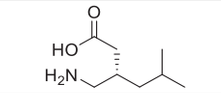
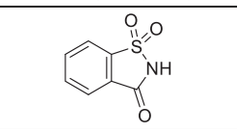
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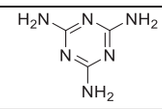
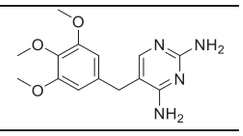
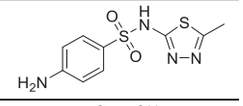
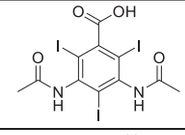
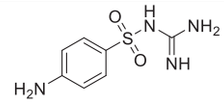
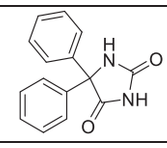
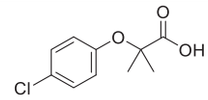
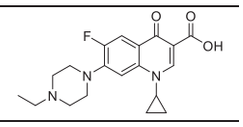
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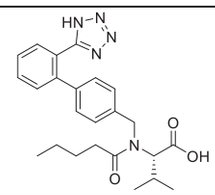
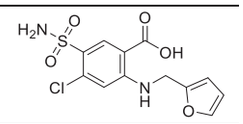
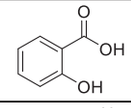
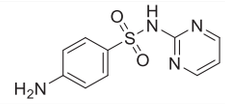
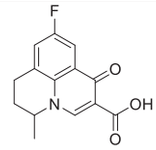
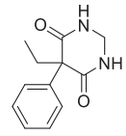
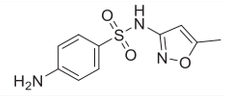
Table S1. List of the 96 target compounds sorted by log*D*

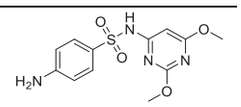
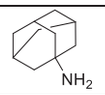
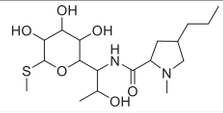
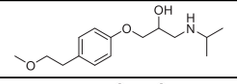
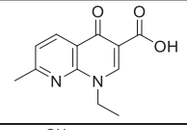
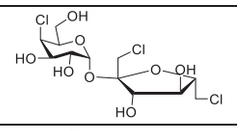
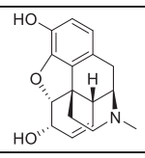
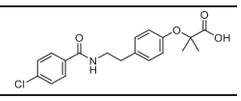
Compound	Main use	CAS	Molecular formula	Molecular weight	Log D[1] at pH 7.4	Structure	Boiling point[1] (°C)	Water Solubility[1] (mg mL^{-1})
Zanamivir	Antiviral	1391180-80-8	$C_{12}H_{20}N_4O_7$	332.31	-6.0		-	18
Oxytetracycline	Antibiotic	79-57-2	$C_{22}H_{24}N_2O_9$	460.40	-4.3		840	31
Pipemidic acid	Antibiotic	51940-44-4	$C_{14}H_{17}N_5O_3$	303.32	-3.6		535	0.32
Cyclamate	Sweetener	100-88-9 (cyclamic acid)	$C_6H_{13}NO_3S$	179.24	-3.5		-	133
Sulisobenzone (BP4)	UV-Filter	4065-45-6	$C_{14}H_{12}O_6S$	308.31	-3.5		498	250
Metformin	Diabetes type 2 treatment agent	657-24-9	$C_4H_{11}N_5$	129.16	-3.4		173	300
Iodixanol	Iodinated contrast media	92339-11-2	$C_{35}H_{44}I_6N_6O_{15}$	1550.20	-3.4		1251	0.19

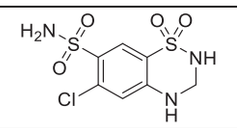
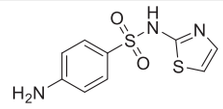
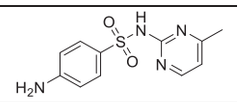
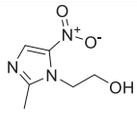
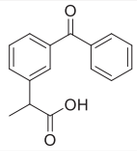
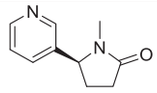
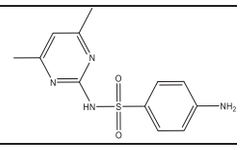
Tetracycline	Antibiotic	60-54-8	$C_{22}H_{24}N_2O_8$	444.40	0.23	738	-3.2	
Iohexol	Iodinated contrast media	66108-95-0	$C_{19}H_{26}I_3N_3O_9$	821.14	350	892	-3.2	
Eflornithine	Facial hirsutism treatment drug	70052-12-9	$C_6H_{12}F_2N_2O_2$	182.17	10	347	-3.0	
Amoxicillin	Antibiotic	26787-78-0	$C_{16}H_{19}N_3O_5S$	365.40	0.96	743	-2.7	
Ciprofloxacin	Antibiotic	85721-33-1	$C_{17}H_{18}FN_3O_3$	331.35	1.4	582	-2.2	
Levofloxacin	Antibiotic	100986-85-4	$C_{18}H_{20}FN_3O_4$	361.40	0.05	572	-2.1	
Iopromide	Iodinated contrast media	73334-07-3	$C_{18}H_{24}I_3N_3O_8$	791.11	0.37	841	-2.1	
Atenolol	β-blocker agent	29122-68-7	$C_{14}H_{22}N_2O_3$	266.34	13	508	-1.9	

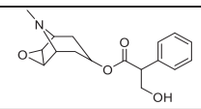
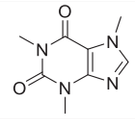
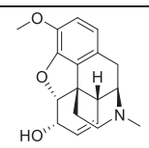
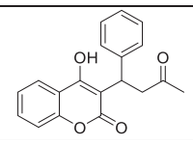
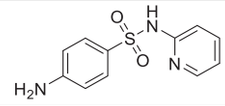
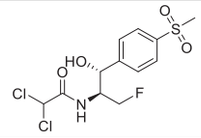
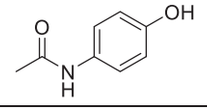
Aspartame	Sweetener	22839-47-0	$C_{14}H_{18}N_2O_5$	294.30	10	536	-1.8	
Meprobamate	Anxiolytic	57-53-4	$C_9H_{18}N_2O_4$	218.25	2.5	334	-1.8	
Sotalol	β-blocker agent	3930-20-9	$C_{12}H_{20}N_2O_3S$	272.36	0.78	443	-1.6	
5-Fluorouracil	Antineoplastic agent	51-21-8	$C_4H_3FN_2O_2$	130.08	5.9	367	-1.6	
Acyclovir	Antiviral	59277-89-3	$C_8H_{11}N_5O_3$	225.20	9.1	500	-1.5	
Gabapentin	Anticonvulsant	60142-96-3	C9H17NO2	171.24	4.5	314	-1.4	
Pregabalin	Anticonvulsant	148553-50-8	$C_8H_{17}NO_2$	159.23	11	274	-1.3	
Saccharin	Sweetener	81-07-2	$C_7H_5NO_3S$	183.18	4.0	389	-1.3	

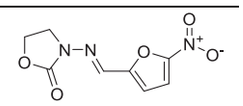
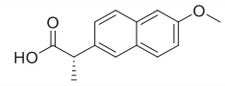
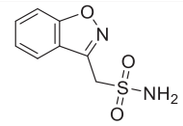
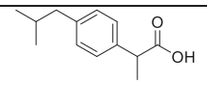
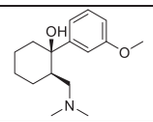
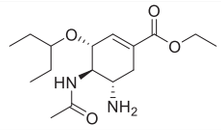
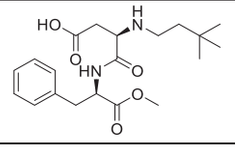
Melamine	Industrial compound	108-78-1	$C_3H_6N_6$	126.12	3.2	558	-1.2	
Trimethoprim	Antibiotic	738-70-5	$C_{14}H_{18}N_4O_3$	290.32	0.62	405	-1.2	
Sulfamethizole	Antibiotic	144-82-1	$C_9H_{10}N_4O_2S_2$	270.33	0.61	505	-1.1	
Diatrizoic acid	Iodinated contrast media	117-96-4	$C_{11}H_9I_3N_2O_4$	613.91	0.11	614	-1.0	
Sulfaguanidine	Antibiotic	57-67-0	$C_7H_{10}N_4O_2S$	214.25	0.81	426	-1.0	
Phenytoin	Anticonvulsant	57-41-0	$C_{15}H_{12}N_2O_2$	252.27	0.07	464	-1.0	
Clofibric acid	Lipid-lowering agent	882-09-7	$C_{10}H_{11}ClO_3$	214.64	-	324	-0.9	
Enrofloxacin	Antibiotic	93106-60-6	$C_{19}H_{22}FN_3O_3$	359.40	0.05	561	-0.9	

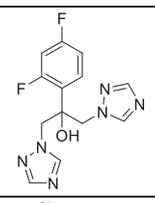
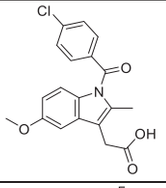
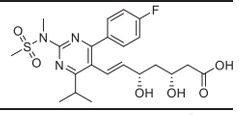
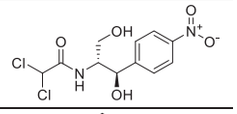
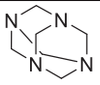
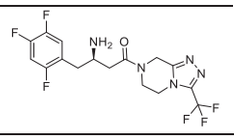
Valsartan	Antihypertensive	137862-53-4	$C_{24}H_{29}N_5O_3$	435.52	0.02	685	-0.9	
Furosemide	Antihypertensive	54-31-9	$C_{12}H_{11}ClN_2O_5S$	330.74	0.07	582	-0.8	
Salicylic acid	Antibacterial	69-72-7	$C_7H_6O_3$	138.12	2.24	336	-0.8	
Sulfadiazine	Antibiotic	68-35-9	$C_{10}H_{10}N_4O_2S$	250.28	0.6	513	-0.8	
Flumequine	Antibiotic	42835-25-6	$C_{14}H_{12}FNO_3$	261.25	<1.0	440	-0.7	
Primidone	Anticonvulsant	125-33-7	$C_{12}H_{14}N_2O_2$	218.25	1.0	443	-0.7	
Sulfamethoxazole	Antibiotic	723-46-6	$C_{10}H_{11}N_3O_3S$	253.28	0.46	482	-0.6	

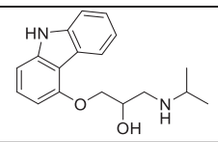
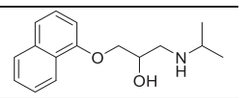
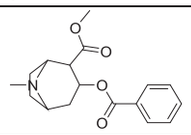
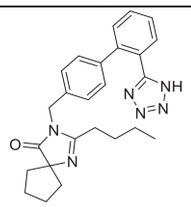
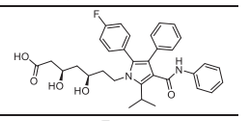
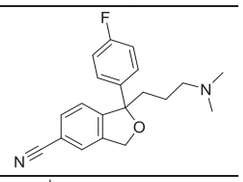
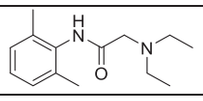
Sulfadimethoxine	Antibiotic	122-11-2	$C_{12}H_{14}N_4O_4S$	310.33	0.34	549	-0.5	
Amantadine	Antiviral	768-94-5	$C_{10}H_{17}N$	151.14	6.3	226	-0.4	
Lincomycin	Antibiotic	154-21-2	$C_{18}H_{34}N_2O_6S$	406.54	-	647	-0.4	
Metoprolol	β-blocker agent	37350-58-6	$C_{15}H_{25}NO_3$	267.36	>1000	399	-0.3	
Nalidixic acid	Antibiotics	389-08-2	$C_{12}H_{12}N_2O_3$	232.24	2.3	413	-0.3	
Sucralose	Sweetener	56038-13-2	$C_{12}H_{19}Cl_3O_8$	397.63	>1000	669	-0.2	
Morphine	Analgesic	57-27-2	$C_{17}H_{19}NO_3$	285.34	10	476	-0.1	
Bezafibrate	Lipid-lowering agent	41859-67-0	$C_{19}H_{20}ClNO_4$	361.82	$2*10^{-3}$	572	-0.1	

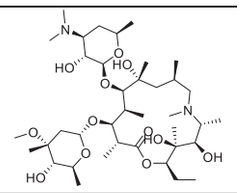
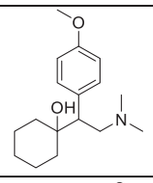
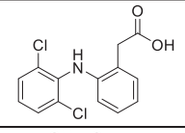
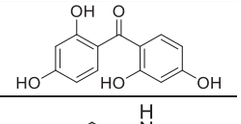
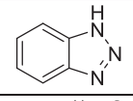
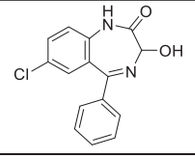
Hydrochlorothiazide	Antihypertensive	58-93-5	$C_7H_8ClN_3O_4S_2$	297.74	0.72	577	0.0	
Sulfathiazole	Antibiotic	72-14-0	$C_9H_9N_3O_2S_2$	255.32	0.37	480	0.0	
Sulfamerazine	Antibiotic	127-79-7	$C_{11}H_{12}N_4O_2S$	264.30	0.20	519	0.0	
Metronidazole	Antibacterial	443-48-1	$C_6H_9N_3O_3$	171.15	5.9	405	0.1	
Ketoprofen	NSAID	22071-15-4	$C_{16}H_{14}O_3$	254.28	0.02	431	0.1	
Cotinine	Stimulant	486-56-6	$C_{10}H_{12}N_2O$	176.22	-	329	0.2	
Sulfamethazine	Antibiotics	57-68-1	$C_{12}H_{14}N_4O_2S$	278.33	0.23	526	0.2	

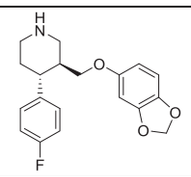
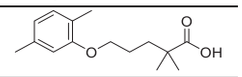
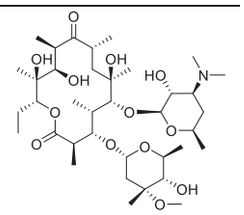
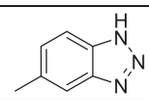
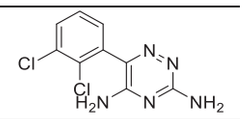
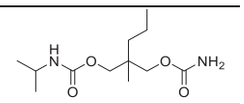
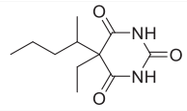
Hyoscine	Anticholinergic	149-64-4	$C_{21}H_{29}NO_4$	359.46	100	460	0.3	
Caffeine	Stimulant	58-08-2	$C_8H_{10}N_4O_2$	194.19	22	417	0.3	
Codeine	Analgesic	76-57-3	$C_{18}H_{21}NO_3$	299.36	0.58	462	0.3	
Warfarin	Anticoagulant	81-81-2	$C_{19}H_{16}O_4$	308.30	0.02	515	0.3	
Sulfapyridine	Antibiotic	144-83-2	$C_{11}H_{11}N_3O_2S$	249.29	0.27	474	0.4	
Florfenicol	Antibiotic	73231-34-2	$C_{12}H_{14}Cl_2FNO_4S$	358.21	-	-	0.4	
Acetaminophen	Analgesic	103-90-2	$C_8H_9NO_2$	151.16	14	388	0.4	

Furazolidone	Antibiotics	67-45-8	$C_8H_7N_3O_5$	225.16	0.36	353	0.4	
Naproxen	NSAID	22204-53-1	$C_{14}H_{14}O_3$	230.26	0.02	404	0.5	
Zonisamide	Anticonvulsant	68291-97-4	$C_8H_8N_2O_3S$	212.23	2.1	457	0.5	
Ibuprofen	NSAID	15687-27-1	$C_{13}H_{18}O_2$	206.28	0.02	320	0.5	
Tramadol	Analgesic	3715-90-0	$C_{13}H_{18}ClN_3$	251.75	0.75	388	0.5	
Oseltamivir	Antiviral	196618-13-0	$C_{16}H_{28}N_2O_4$	312.40	0.69	473	0.6	
Neotame	Sweetener	165450-17-9	$C_{20}H_{30}N_2O_5$	378.46	0.01	572	0.6	

Fluconazole	Antifugals	86386-73-4	$C_{13}H_{12}F_2N_6O$	306.27	1.4	580	0.7	
Indomethacin	NSAID	53-86-1	$C_{19}H_{16}ClNO_4$	357.79	$0.9*10^{-3}$	499	0.8	
Rosuvastatin	NSAID	287714-41-4	$C_{22}H_{28}FN_3O_6S$	481.54	0.09	746	1.0	
Chloramphenicol	Antibiotic	56-75-7	$C_{11}H_{12}Cl_2N_2O_5$	323.13	2.5	645	1.0	
Methenamine	Antibacterial	100-97-0	$C_6H_{12}N_4$	140.19	449	253	1.0	
Sitagliptin	Diabetes type 2 treatment	486460-32-6	$C_{16}H_{15}F_6N_5O$	407.31	0.03	530	1.1	

Carazolol	β-blocker agent	57775-29-8	$C_{18}H_{22}N_2O_2$	298.38	0.01	469	1.1	
Propranolol	β-blocker agent	525-66-6	$C_{16}H_{21}NO_2$	259.34	0.06	435	1.2	
Cocaine	Stimulant	50-36-2	$C_{17}H_{21}NO_4$	303.35	1.8	395	1.2	
Irbesartan	Antihypertensive	138402-11-6	$C_{25}H_{28}N_6O$	428.53	0.01	649	1.2	
Atorvastatin	Lipid-lowering agent	134523-00-5	$C_{33}H_{35}FN_2O_5$	558.60	<1	722	1.3	
Citalopram	Antidepressant	59729-33-8	$C_{20}H_{21}FN_2O$	324.16	0.02	352	1.3	
Lidocaine	Anesthetic	137-58-6	$C_{14}H_{22}N_2O$	234.34	0.59	373	1.3	

Azithromycin	Antibiotic	83905-01-5	$C_{38}H_{72}N_2O_{12}$	748.98	-	822	1.4	
Venlafaxine	Antidepressant	93413-69-5	$C_{17}H_{27}NO_2$	277.40	572	398	1.4	
Diclofenac	NSAID	15307-86-5	$C_{14}H_{11}Cl_2NO_2$	296.15	$2.3*10^{-3}$	412	1.4	
2.2'.4.4'-Tetrahydroxybenzophenone (BP2)	UV-Filter	131-55-5	$C_{13}H_{10}O_5$	246.22	0.01	559	1.4	
1H-Benzotriazole	Industrial compound	95-14-7	$C_6H_5N_3$	119.12	20	359	1.5	
Oxazepam	Antidepressant	604-75-1	$C_{15}H_{11}N_2O_2Cl$	286.71	0.02	517	1.5	

Paroxetine	Antidepressant	61869-08-7	$C_{19}H_{20}FNO_3$	329.37	$1.1*10^{-3}$	452	1.5	
Gemfibrozil	Lipid-lowering drug	25812-30-0	$C_{15}H_{22}O_3$	250.33	0.03	395	1.6	
Erythromycin	Antibiotic	114-07-8	$C_{37}H_{67}NO_{13}$	733.93	2.0	720	1.7	
5-Methyl-1H-benzotriazole	Industrial compound	136-85-6	$C_7H_7N_3$	133.15	3.1	211	1.7	
Lamotrigine	Antidepressant	84057-84-1	$C_9H_7Cl_2N_5$	256.09	0.17	503	1.7	
Carisoprodol	Muscle relaxant	78-44-4	$C_{12}H_{24}N_2O_4$	260.33	0.30	423	1.9	
Pentobarbital	Sedative	76-74-4	$C_{11}H_{18}N_2O_3$	226.28	0.68	-	1.9	

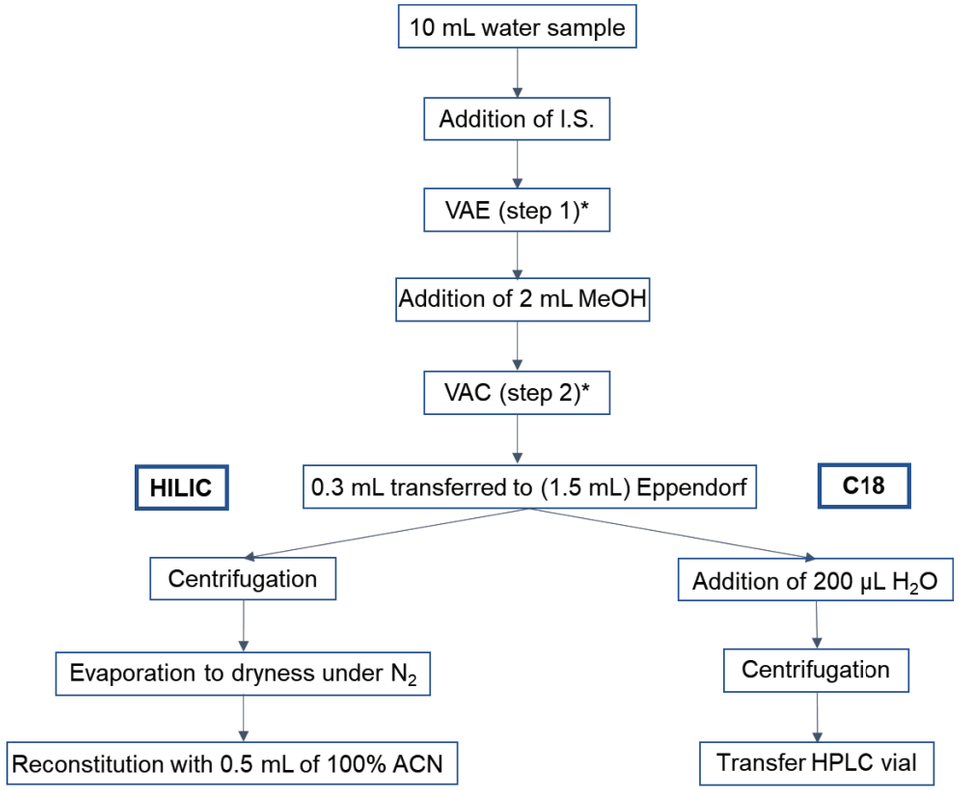
Lorazepam	Anxiolytic	846-49-1	$C_{15}H_{10}Cl_2N_2O_2$	321.20	1.9	534	0.08
Hydroxychloroquine	Antimalarial drug	118-42-3	$C_{18}H_{26}ClN_3O$	335.87	2.0	517	0.03
6α-Methylprednisolone	Antiinflammatory	83-43-2	$C_{22}H_{30}O_5$	374.47	2.0	572	0.12

[1]Log D, solubility and boiling point values were obtained from the ChemSpider database http://www.chemspider.com/.

Table S2. In situ parameters of the seven GW samples.

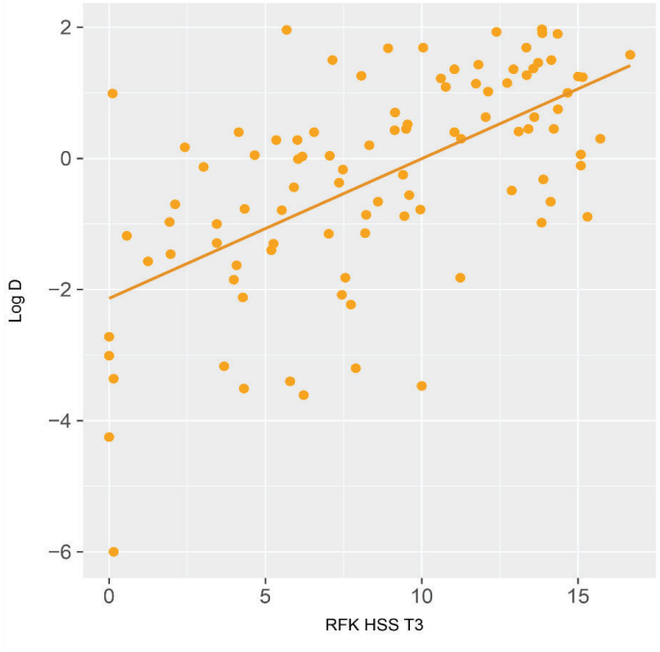
Site	pH	EC[1] (µS cm^{-1})	T (ºC)	Hardness (mg L^{-1})
HBAV	6.7	1163	25.0	305.2
DXSA	6.9	1270	19.7	291.2
RBOP	5.5	580	21.8	201.2
URB1	6.7	1422	19.7	375.2
SAP2b	6.9	2541	21.3	537.6
DTA2	6.8	1730	20.1	479.2
FTAU	6.6	1699	21.5	429.6

[1]Electric conductivity.



* For further information see Mechelke et al. (Mechelke et al., 2019).

Figure S1. Flow-chart for enrichment by VAE followed by HILIC (left) and C18 (right) chromatographic separation before HPLC-MS/MS analysis.



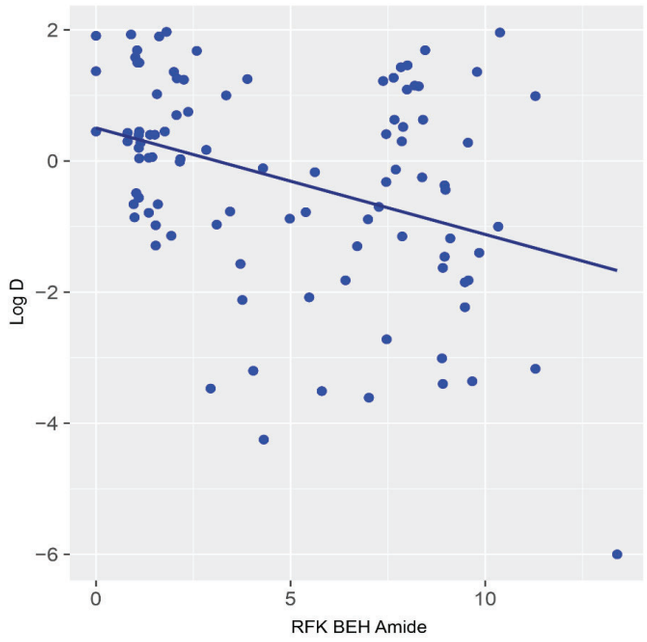


Figure S2. Retention differences between columns and compounds polarities.

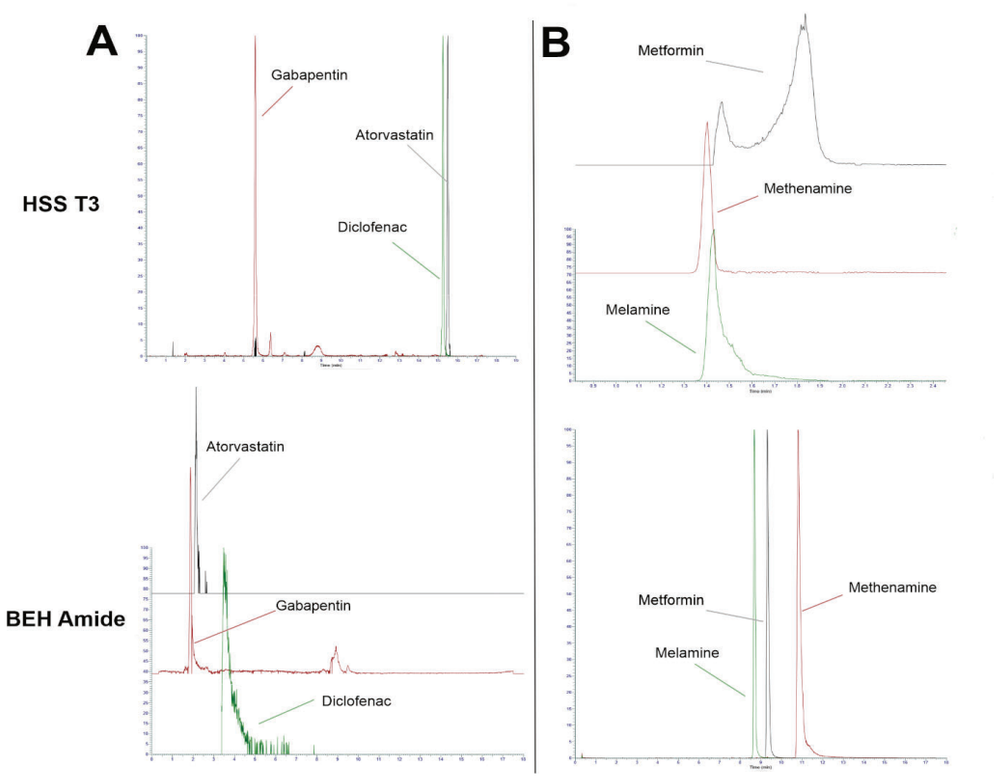


Figure S3. A: Chromatograms of diclofenac, atorvastatin and gabapentin; B: Chromatograms of melamine, metformin and methenamine. A shows great performance using the HSS T3 column (Upper) while B shows great BEH Amide column (Lower) performance for the selected compounds shown.

Table S3. Parameters of the optimised gradients.

Optimised Gradient HSS T3			
Flow (mL/min)	Time (min)	Solvent A* (%)	Solvent B* (%)
0.2	0	5	95
0.2	0.3	5	95
0.2	10	30	70
0.2	13.3	65	35
0.2	15.5	100	0
0.2	17.3	100	0
0.2	17.7	5	95
0.2	19	5	95

Optimised Gradient HILIC			
Flow (mL/min)	Time (min)	Solvent A** (%)	Solvent B** (%)
0.2	0	100	0
0.2	1	100	0
0.2	8	50	50
0.2	11	50	50
0.2	12	100	0
0.2	15	100	0

* A (ESI+): H_2O 5mM ammonium formate 0.1% formic acid
A (ESI-): H_2O 2mM ammonium fluoride
B (ESI+/-): 100% ACN
** A (ESI+/-): H_2O 5mM ammonium formate
B (ESI+/-): H_2O:ACN (2:98, v/v) 5mM ammonium formate

Table S4. MS parameters, chromatographic retention times (RT) and retention factors (RFK) of target compounds sorted by alphabetical order. The t_0 for the HSS T3 column was 0.90 min.

Analyte	ESI mode	Precursor (m/z)	Product Ion (m/z)	CE (eV)	RT (min)	RFK	Internal Standard
1H-Benzotriazole	+	120.0557	65.0387	20	7.33	7.14	Benzotriazole D4
2,2',4,4'-Tetrahydroxybenzophenone (BP2)	-	245.0454	109.0294	19	12.54	12.93	Irbesartan D6
5-Fluorouracil	-	129.0106	85.0290	37	2.02	1.24	Gabapentin D10
5-methyl-1H-benzotriazole	+	134.0712	79.0542	25	9.94	10.04	Cotinine D3
6αmethylprednisolone	+	375.2162	357.2063	22	13.36	13.84	Paroxetine D4
Acetaminophen	+	152.0706	110.0602	20	4.63	4.14	Acetaminophen D4
Acyclovir	-	224.0789	150.0419	35	2.67	1.97	Gabapentin D10
Amantadine	+	152.1431	135.1167	15	7.52	7.36	Aspartame D5
Amoxicillin	+	366.1118	114.0008	12	3.45	2.83	Cotinine D3
Aspartame	+	295.1292	180.1019	25	7.70	7.56	Sotalol D6
Atenolol	+	267.1701	190.0861	25	4.49	3.99	Propranolol D7
Atorvastatin	+	559.2603	440.2248	38	14.40	15.00	Climbazole D4

Analyte	ESI mode	Precursor (m/z)	Product Ion (m/z)	CE (eV)	RT (min)	RFK	Internal Standard
Azithromycin	+	749.5146	591.4214	44	10.84	11.04	Ciprofloxacin D8
Bezafibrate	+	362.1147	316.1096	14	14.48	15.09	Bezafibrate D4
Caffeine	+	195.0877	138.0664	27	6.32	6.02	Caffeine 13C3
Carazolol	+	299.1754	116.1068	40	11.46	11.73	Propranolol D7
Carisoprodol	+	261.1805	62.0238	20	12.05	12.39	Carisoprodol D7
Chloramphenicol	-	321.0045	152.0352	13	11.81	12.12	Irbesartan D6
Ciprofloxacin	+	332.1403	288.1508	19	7.86	7.73	Ciprofloxacin D8
Citalopram	+	325.1706	109.0446	26	12.92	13.36	Midazolam 13C6
Clofibric acid	-	213.0323	126.9956	10	9.40	9.44	Bezafibrate D4
Cocaine	+	304.1538	182.1174	30	10.45	10.61	Cocaine D5
Codeine	+	300.1597	165.0697	42	5.71	5.34	Codeine D3
Cotinine	+	177.1021	80.0494	28	3.08	2.42	**Cotinine** D3
Cyclamate	-	178.0543	79.9577	34	4.78	4.31	Acetaminophen D4
Diatrizoic acid	+	631.8031	360.9680	25	4.00	3.44	Metronidazole D4
Diclofenac	+	296.0245	215.0496	30	13.11	13.57	Diclofenac 13C6
Eflornithine	+	183.0940	120.1000	25	0.90	0.00	Cotinine D3

Analyte	ESI mode	Precursor (m/z)	Product Ion (m/z)	CE (eV)	RT (min)	RFK	Internal Standard
Enrofloxacin	+	360.1723	316.1824	28	8.30	8.22	Lamotrigine 13C3
Erythromycin	+	734.4666	158.1174	29	12.91	13.34	Ciprofloxacin D8
Florfenicol	-	355.9927	119.0501	14	10.84	11.04	Sulfamethoxazole 13C6
Fluconazole	-	305.0966	68.0252	12	9.13	9.14	Fluconazole 13C3
Flumequine	+	262.0874	244.0766	30	13.61	14.12	Carbamazepine D10
Furazolidone	+	226.0458	95.0366	18	9.12	9.13	Fluconazole 13C3
Furosemide	-	329.0004	204.9823	30	9.86	9.96	Valsartan D3
Gabapentin	+	172.1337	154.1226	17	5.57	5.19	Gabapentin D10
Gemfibrozil	-	249.1496	121.0659	14	15.90	16.67	Gemfibrozil D6
Hydrochlorothiazide	-	295.9568	268.9457	29	6.34	6.04	Hydrochlorothiazide 13CD2
Hydroxychloroquine	+	336.1835	247.0996	30	6.01	5.68	Chlorpromazine D3
Hyoscine	+	360.2164	138.0913	30	11.03	11.26	Cocaine D5
Ibuprofen	-	205.1234	159.1172	10	13.70	14.22	Gemfibrozil D6
Indomethacin	-	356.0689	297.0560	30	13.82	14.36	Indomethacin D4
Iodixanol	-	773.8494	126.9042	50	6.11	5.79	Sulfadiazine D4
Iohexol	+	821.8868	803.8744	21	3.39	2.77	Acetaminophen D4

Analyte	ESI mode	Precursor (m/z)	Product Ion (m/z)	CE (eV)	RT (min)	RFK	Internal Standard
Iopromide	+	791.8755	372.9690	50	4.75	4.28	Acetaminophen D4
Irbesartan	+	429.2392	207.0914	25	14.53	15.14	Irbesartan D6
Ketoprofen	+	255.1012	105.0334	25	14.48	15.09	Valsartan D3
Lamotrigine	+	256.0151	172.9667	40	8.93	8.92	Lamotrigine 13C3
Levofloxacin	+	362.1511	216.1042	21	7.60	7.44	Ofloxacin D8
Lidocaine	+	235.1803	86.0963	18	8.16	8.07	Lamotrigine 13C3
Lincomycin	+	407.2206	126.1276	24	6.22	5.91	Caffeine 13C3
Lorazepam	-	319.0040	283.0274	19	13.81	14.34	Lorazepam D4
Melamine	+	127.0727	85.0515	20	1.41	0.57	Cotinine D3
Meprobamate	+	219.1339	158.1175	13	11.01	11.23	Carisoprodol D7
Metformin	+	130.1087	60.0559	15	1.83	1.03	Lamotrigine 13C3
Methenamine	+	141.1135	112.0870	16	1.00	0.11	Cotinine D3
Metoprolol	+	268.1906	116.1068	21	9.36	9.40	Metoprolol D7
Metronidazole	+	172.0716	128.0453	17	5.09	4.66	Metronidazole D4
Morphine	+	286.1436	201.0909	40	3.62	3.02	Gabapentin D10
Nalidixic acid	+	233.0920	205.0606	32	13.40	13.89	Carbamazepine D10

Analyte	ESI mode	Precursor (m/z)	Product Ion (m/z)	CE (eV)	RT (min)	RFK	Internal Standard
Naproxen	-	229.0864	158.0373	13	12.97	13.41	Naproxen D3
Neotame	+	379.2226	172.1330	30	13.14	13.60	Midazolam 13C6
Oseltamivir	+	313.2116	166.0861	18	11.74	12.04	Oseltamivir D3
Oxazepam	+	287.0581	241.0524	25	13.63	14.14	Lorazepam D4
Oxytetracycline	+	461.1555	426.1183	25	7.40	7.22	Ofloxacin D8
Paroxetine	+	330.1502	192.1183	33	13.25	13.72	Paroxetine D4
Pentobarbital	-	225.1242	122.0975	60	13.37	13.86	Irbesartan D6
Phenytoin	-	251.0821	102.0349	25	13.35	13.83	Irbesartan D6
Pipemidic acid	+	304.1409	217.1084	25	6.50	6.22	Caffeine 13C3
Pregabalin	+	160.1337	142.1227	12	5.63	5.26	Sulfadiazine D4
Primidone	+	219.1128	162.0912	19	8.64	8.60	Acetaminophen D4
Propranolol	+	260.1642	116.1068	23	12.36	12.73	Propranolol D7
Rosuvastatin	+	482.1755	258.1400	43	14.10	14.67	Bezafibrate D4
Saccharin	-	181.9917	61.9703	36	4.00	3.44	Hydrochlorothiazide 13CD2
Salicylic acid	-	137.0244	93.0350	16	4.80	4.33	Acetaminophen D4
Sitagliptin	+	408.1253	174.0524	24	10.59	10.77	Fluconazole 13C3

Analyte	ESI mode	Precursor (m/z)	Product Ion (m/z)	CE (eV)	RT (min)	RFK	Internal Standard
Sotalol	+	273.1265	213.0690	24	4.57	4.08	Sotalol D6
Sucralose	-	395.0066	59.0134	22	7.63	7.48	Gemfibrozil D6
Sulfadiazine	+	251.0596	156.0111	20	5.87	5.52	Sulfadiazine D4
Sulfadimethoxine	+	311.0801	156.0766	35	12.49	12.88	Sulfamethoxazole 13C6
Sulfaguanidine	+	214.0524	156.0115	41	2.64	1.93	Valsartan D3
Sulfamerazine	+	265.0753	156.0113	21	7.25	7.06	Sulfamethazine D4
Sulfamethazine	+	279.0908	204.0436	22	8.39	8.32	Sulfamethazine D4
Sulfamethizole	+	271.0319	156.0113	16	8.27	8.19	Sulfamethoxazole 13C6
Sulfamethoxazole	-	252.0445	156.0124	15	9.54	9.60	Sulfamethoxazole 13C6
Sulfapyridine	+	250.0644	156.0112	22	6.80	6.56	Sulfamethoxazole 13C6
Sulfathiazole	-	254.0062	156.0124	20	6.46	6.18	Sulfamethoxazole 13C6
Sulisobenzone (BP4)	-	307.0279	211.0398	34	9.90	10.00	Sulfamethoxazole 13C6
Tetracycline	+	445.1605	410.1234	25	8.00	7.89	Sulfamethazine D4
Tramadol	+	264.1956	58.0654	15	9.49	9.54	Tramadol 13C3D3
Trimethoprim	+	291.1450	230.1161	29	7.22	7.02	Trimethoprim D9
Valsartan	+	436.2332	207.0915	17	14.67	15.30	Valsartan D3

Analyte	ESI mode	Precursor (m/z)	Product Ion (m/z)	CE (eV)	RT (min)	RFK	Internal Standard
Venlafaxine	+	278.2113	58.0654	27	11.53	11.81	Venlafaxine D6
Warfarin	+	309.1117	163.0388	18	15.04	15.71	Carbamazepine D10
Zanamivir	+	333.1405	60.2418	22	1.39	0.54	Cotinine D3
Zonisamide	+	213.0325	150.0549	12	9.45	9.50	Zonisamide 13C6

Table S5. Validation parameters of the target compounds enriched by the VAE approach at 1, 50 and 200 µg/L (n = 3), sorted by alphabetical order.

Compound	Low Level 1 µg L^{-1}			Intermediate Level 50 µg L^{-1}			High Level 200 µg L^{-1}		
	RR (%)	RSD (%)	ME (%)	RR (%)	RSD (%)	ME (%)	RR (%)	RSD (%)	ME (%)
1H-Benzotriazole	93	19	17	100	3.0	5.3	89	1.8	8.0
2,2',4,4'-Tetrahydroxybenzophenone (BP2)	73	3.1	518	138	42	34	89	15	101
5-Fluorouracil	114	5.6	55	100	3.3	5.3	111	3.3	107
5-methyl-1-H-benzotriazole	69	8.2	323	84	9.3	5.3	79	7.6	-13
6αmethylprednisolone	37	8.0	333	101	4.7	7.4	107	5.0	3.9
Acetaminophen	99	4.3	1.2	103	0.6	7.8	104	1.8	-4.8
Acyclovir	103	6.0	68	108	3.2	-8.6	108	3.5	156
Amantadine	59	11	371	85	9.1	2.9	96	7.0	-10
Amoxicillin	0	0.0	0	0	0	-69	0	0	-64
Aspartame	0	0.0	0	0	0	-92	0	0	-92
Atenolol	54	6.1	209	107	4.1	0.9	106	7.2	4.1
Atorvastatin	31	40	343	102	4.9	10	47	3.9	114
Azithromycin	0	0	0	118	48	1637	49	48	-47
Bezafibrate	71	7.7	205	100	2.1	6.0	108	1.7	-5.6
Caffeine	8.7	503	79	114	5.8	4.5	102	1.2	-0.2
Carazolol	70	13	376	190	55	1128	92	0.6	5.2
Carisoprodol	37	5.3	416	108	0.9	0.4	88	1.6	14

Chloramphenicol	127	2.3	73	115	53	13	121	26	189
Ciprofloxacin	1085	117	0	104	4.4	10	73	3.8	26
Citalopram	47	17	665	100	4.3	18	92	4.5	49
Clofibric acid	108	4.4	86	94	6.3	15	122	3.2	133
Cocaine	19	9.3	1270	107	2.6	5.4	34	2.5	208
Codeine	0	0.0	0	0	0	0	0	0	0
Cotinine	43	13	684	104	1.4	5.5	106	1.0	-5.1
Cyclamate	78	11	109	106	1.7	3.5	110	6.0	186
Diatrizoic acid	112	1.8	189	101	2.7	-1.7	99	4.9	-0.2
Diclofenac	0	0.0	0	105	0.5	4.6	138	1.5	-29
Eflornithine	0	0.0	0	79	8.0	-49	142	4.2	-96
Enrofloxacin	627	108	93	81	5.2	375	78	20	128
Erythromycin	17	36	-89	73	21	-2.4	63	42	-23
Florfenicol	69	12	257	159	11	-38	116	3.0	212
Fluconazole	118	4.0	85	87	3.3	-7.0	110	1.3	177
Flumequine	120	72	412	113	3.8	-4.0	102	0.8	14
Furazolidone	60	6.1	238	90	3.1	6.1	105	7.1	2.4
Furosemide	102	3.5	73	73	62	-43	97	15	141
Gabapentin	49	19	409	105	1.9	4.3	104	1.6	-7.5
Gemfibrozil	65	8.1	225	105	1.0	1.1	89	2.1	244

Hydrochlorothiazide	100	3.9	101	88	6.0	-1.6	103	1.4	180
Hydroxychloroquine	2695	88	0	56	16	104077	58	34	335
Hyoscine	39	9.6	3305	82	11	-11	98	18	552
Ibuprofen	89	26	5557	115	1.5	1.0	103	5.9	124
Indomethacin	182	0.4	7.5	130	8.5	-20	83	4.3	165
Iodixanol	181	0.9	13	107	5.0	2.4	112	5.1	146
Iohexol	159	1.9	42	99	6.6	4.5	94	5.8	-17
Iopromide	0	0.0	0	96	18	-1.4	104	4.4	-23
Irbesartan	28	51	1832	107	0	2.8	66	1.1	51
Ketoprofen	54	17	108	103	1.2	-0.1	100	16	-12
Lamotrigine	69	12	230	102	2.5	1.9	109	1.1	-6.0
Levofloxacin	355	44	5720	103	3.2	0.1	74	7.9	24
Lidocaine	45	5.9	182	105	12	-76	102	2.2	-17
Lincomycin	51	14	211	92	5.6	6.5	103	3.6	-4.2
Lorazepam	101	8.6	82	97	15	-0.4	95	1.5	224
Melamine	112	0.1	3618	116	5.5	0.0	130	3.7	26
Meprobamate	0	0.0	0	0	0	0	0	0	0
Metformin	63	8.1	234	94	11	2.6	124	1.6	-3.8
Methenamine	59	8.6	-91	112	4.8	341	69	3.4	2.8
Metoprolol	53	3.5	291	115	3.3	8.0	111	3.1	-7.3

Metronidazole	97	8.2	43	102	7.3	1.4	107	2.0	-4.4
Morphine	0	0.0	0	0	0	0	0	0	0
Nalidixic Acid	87	47	358	108	1.0	0.2	111	2.4	1.7
Naproxen	201	1.1	-7.1	0	4.1	0.0	112	8.2	84
Neotame	0	0.0	188	100	15.5	-69	25	25	-19
Oseltamivir	41	5.1	424	105	3.8	4.5	99	0.7	2.1
Oxazepam	0	0.0	0	96	3.7	-2.9	100	2.1	-1.0
Oxytetracycline	0	0.0	0	56	4.3	-6.7	75	18	-47
Paroxetine	162	1.4	23	103	1.1	2.8	50	25	-38
Pentobarbital	0	0.0	0	105	5.3	3.1	106	4.9	2.9
Phenytoin	67	12	346	129	5.6	12	115	29	194
Pipemidic acid	600	102	68	101	5.1	136	83	5.2	46
Pregabalin	178	22	30	103	3.2	6.3	121	4.5	-15
Primidone	0	0.0	0	90	7.7	5.3	101	6.3	-18
Propranolol	53	6.2	296	105	2.7	7.6	99	3.3	1.9
Rosuvastatin	80	5.3	160	126	2.6	1.7	111	2.9	0.9
Saccharin	93	5.7	279	110	4.2	4.2	101	2.6	183
Salicylic acid	83	3.9	347	107	0.9	15	108	5.7	195
Sitagliptin	68	8.4	162	106	3.4	1.6	104	1.4	-10
Sotalol	58	2.3	252	105	3.2	1.8	103	0.5	-4.2

Sucralose	186	1.8	160	91	7.0	8.4	124	7.9	82
Sulfadiazine	63	1.7	223	104	5.4	1.8	111	1.8	-7.9
Sulfadimethoxine	59	3.1	368	101	5.8	17	120	0.8	-6.0
Sulfaguanidine	0	0.0	0	0	0	0	0	0	0
Sulfamerazine	66	3.5	184	107	6.4	2.0	102	5.3	-5.8
Sulfamethazine	51	11	295	137	9.3	48	109	3.2	-2.3
Sulfamethizole	43	17	217	102	6.6	10	116	6.0	-8.9
Sulfamethoxazole	63	4.6	168	107	1.5	1.8	111	7.5	179
Sulfapyridine	59	7.6	308	100	4.0	5.4	107	12	-2.2
Sulfathiazole	75	13	138	111	5.2	2.2	109	3.0	210
Sulisobenzone (BP4)	97	1.9	121	91	10	13	114	2.1	214
Tetracycline	0	0.0	0	26	14	-31	42	30	-25
Tramadol	30	26	687	109	2.8	5.6	112	4.2	-9.4
Trimethoprim	55	3.9	257	105	2.8	4.7	119	3.3	-4.2
Valsartan	82	13	365	105	0.9	3.3	93	1.9	11
Venlafaxine	46	5.9	361	103	4.9	7.3	105	1.6	-5.0
Warfarin	40	15	536	110	1.8	-1.8	109	3.3	5.6
Zanamivir	0	0.0	0	103	2.8	-3.5	92	12	-94
Zonisamide	0	0.0	0	103	2.8	-3.5	118	3.1	-17

Table S6. Sample location in coordinates.

Sample name	Latitude (UTM)	Longitude (UTM)
SAP2bis	41.42999	2.215175
HBAV	41.45036842	2.19982326
DXSA	41.44558850	2.20261138
RBOP	41.43877969	2.20583093
URB1	41.43283058	2.20366017
DTA2	41.42092226	2.21613223
FTAU	41.41963968	2.22703186

Table S7. Limits of detection (LOD) and quantification (LOQ) of the target analytes, sorted by alphabetical order.

Compounds	LOD (ng L^{-1})	LOQ (ng L^{-1})
1H-Benzotriazole	0.07	0.21
2,2',4,4'-Tetrahydroxybenzophenone (BP2)	0.16	0.50
5-Fluorouracil	0.45	1.34
5-methyl-1-H-benzotriazole	0.12	0.37
6α-methylprednisolone	0.14	0.43
Acetaminophen	0.16	0.49
Acyclovir	0.16	0.48
Amantadine	0.15	0.45
Amoxicillin	0.00	0.00
Aspartame	0.10	0.30
Atenolol	0.03	0.09
Atorvastatin	0.16	0.47
Azithromycin	0.15	0.44
Bezafibrate	0.13	0.40
Caffeine	0.16	0.47
Carazolol	0.07	0.21
Carisoprodol	0.12	0.37
Chloramphenicol	0.07	0.20
Ciprofloxacin	0.16	0.48
Citalopram	0.14	0.41
Clofibric acid	0.17	0.49
Cocaine	0.12	0.36
Codeine	0.14	0.43
Cotinine	0.09	0.26
Cyclamate	0.09	0.27
Diatrizoic acid	0.31	0.92
Diclofenac	0.10	0.29
Eflornithine	0.44	1.20
Enrofloxacin	0.09	0.26
Erythromycin	0.27	0.82
Florfenicol	0.10	0.31
Fluconazole	0.13	0.38
Flumequine	0.13	0.39
Furazolidone	0.11	0.35
Furosemide	0.10	0.29
Gabapentin	0.09	0.28
Gemfibrozil	0.11	0.32
Hydrochlorothiazide	0.11	0.33
Hydroxychloroquine	0.15	0.44
Hyoscine	0.13	0.40
Ibuprofen	0.26	0.77

Indomethacin	0.06	0.19
Iodixanol	0.11	0.32
Iohexol	0.22	0.67
Iopromide	0.23	0.72
Irbesartan	0.12	0.35
Ketoprofen	0.13	0.38
Lamotrigine	0.11	0.33
Levofloxacin	0.10	0.30
Lidocaine	0.11	0.33
Lincomycin	0.13	0.39
Lorazepam	0.14	0.42
Melamine	0.34	1.00
Meprobamate	0.08	0.23
Metformin	0.29	0.86
Methenamine	0.17	0.50
Metoprolol	0.10	0.31
Metronidazole	0.14	0.43
Morphine	0.11	0.33
Nadixilic Acid	0.14	0.42
Naproxen	0.11	0.32
Neotame	0.14	0.42
Oseltamivir	0.09	0.28
Oxazepam	0.13	0.40
Oxytetracycline	0.12	0.36
Paroxetine	0.15	0.44
Pentobarbital	0.13	0.39
Phenytoin	0.13	0.39
Pipemidic acid	0.19	0.58
Pregabalin	0.16	0.49
Primidone	0.04	0.12
Propranolol	0.15	0.46
Rosuvastatin	0.14	0.43
Saccharin	0.14	0.41
Salicylic acid	0.41	1.23
Sitagliptin	0.16	0.49
Sotalol	0.14	0.42
Sucralose	0.12	0.36
Sulfadiazine	0.12	0.36
Sulfadimethoxine	0.06	0.17
Sulfaguanidine	0.17	0.52
Sulfamerazine	0.09	0.26
Sulfamethazine	0.10	0.29
Sulfamethizole	0.16	0.48
Sulfamethoxazole	0.11	0.32
Sulfapyridine	0.12	0.37
Sulfathiazole	0.13	0.40
Sulisobenzone (BP4)	0.06	0.18
Tetracycline	0.40	1.19
Tramadol	0.11	0.33
Trimethoprim	0.11	0.35
Valsartan	0.10	0.29
Venlafaxine	0.10	0.30
Warfarin	0.15	0.45
Zanamivir	0.22	0.65
Zonisamide	0.28	0.84

Table S8. Results of the seven wells samples studied sorted by Log D (pH 7.4). The concentration values shown are in ng L^{-1}.

Compounds	SAP2bis	HBAV	DXSA	RBOP	URB1	DTA2	FTAU
1H-Benzotriazole	1100	326	275	<LOQ	207	124	95.1
2,2',4,4'-Tetrahydroxybenzophenone (BP2)	<LOQ	<LOQ	N/F	N/F	N/F	N/F	N/F
5-Fluorouracil	N/F	N/F	N/F	N/F	N/F	N/F	N/F
5-Methylbenzotriazole	2122	768	602	5.5	427	137	142
6α-Methylprednisolone	86.6	<LOQ	<LOQ	N/F	N/F	<LOQ	<LOQ
Acetaminophen	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Acyclovir	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Amantadine	99.0	113	124	<LOQ	15.0	6.5	5.4
Atenolol	3.7	0.1	<LOQ	<LOQ	0.1	0.1	N/F
Atorvastatin	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Azithromycin	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Bezafibrate	1.6	N/F	N/F	N/F	8.7	<LOQ	N/F
Caffeine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Carazolol	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Carisoprodol	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Chloramphenicol	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Ciprofloxacin	<LOQ	5.1	2.1	0.5	7.0	<LOQ	0.7
Citalopram	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Clofibric acid	N/F	<LOQ	N/F	N/F	<LOQ	<LOQ	N/F
Cocaine	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	N/F	<LOQ
Cotinine	13.8	<LOQ	2.0	<LOQ	0.2	<LOQ	<LOQ
Cyclamate	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Diatrizoic acid	N/F	0.5	N/F	0.9	N/F	N/F	N/F
Diclofenac	13.5	23.2	25.6	N/F	N/F	N/F	N/F
Eflornithine	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Enrofloxacin	<LOQ	4.4	1.8	0.8	4.6	0.4	0.8
Erythromycin	N/F	N/F	<LOQ	N/F	<LOQ	<LOQ	20.9
Florfenicol	N/F	6.1	1.4	N/F	N/F	N/F	N/F
Fluconazole	108	46.1	49.2	4.2	28.6	5.6	6.3
Flumenquine	N/F	<LOQ	<LOQ	N/F	N/F	<LOQ	<LOQ
Furazolidone	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Furosemide	3.292	N/F	N/F	N/F	N/F	N/F	N/F
Gabapentin	<LOQ	<LOQ	N/F	N/F	N/F	N/F	N/F
Gemfibrozil	3.404	<LOQ	N/F	N/F	N/F	N/F	N/F
Hydrochlorothiazide	1179	104	133	29.2	44.4	2.3	35.9
Hydroxychloroquine	N/F	N/F	N/F	<LOQ	N/F	N/F	N/F
Hyoscine	<LOQ	N/F	N/F	N/F	N/F	N/F	N/F
Ibuprofen	N/F	N/F	N/F	<LOQ	N/F	N/F	N/F
Indomethacin	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Iodixanol	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Iohexol	N/F	N/F	4148	576	N/F	N/F	N/F
Iopromide	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Irbersartan	104	7.9	8.9	N/F	N/F	N/F	N/F
Ketoprofen	104	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Lamotrigine	784	276	296	23.0	146	14.1	17.6
Levofloxacin	<LOQ	2.8	1.1	0.3	3.7	<LOQ	0.3
Lidocaine	965	56.5	61.7	<LOQ	12.3	15.8	16.6
Lincomycin	36.0	88.0	N/F	N/F	N/F	N/F	N/F
Lorazepam	72.9	<LOQ	1.8	N/F	N/F	N/F	N/F
Melamine	<LOQ	53.1	40.8	2.3	53.7	5.6	5.2
Metformin	<LOQ	N/F	<LOQ	N/F	N/F	N/F	N/F
Methenamine	<LOQ	N/F	N/F	N/F	N/F	N/F	N/F
Metoprolol	109	12.2	23.1	N/F	16.5	2.1	1.4
Metronidazole	N/F	N/F	N/F	<LOQ	N/F	N/F	N/F
Nalidixic acid	1.3	N/F	0.1	<LOQ	0.2	0.1	0.1
Neotame	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Oseltamivir	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Oxazepam	58.6	1.1	1.7	N/F	N/F	N/F	N/F
Oxytetracycline	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Paroxetine	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Pentobarbital	18.0	1.4	2.6	N/F	1.4	3.8	4.7
Phenytoin	95.8	5.6	16.7	0.8	3.7	5.3	7.1
Pipemidic acid	N/F	6.9	3.1	1.2	9.8	0.5	1.3
Pregabalin	<LOQ	<LOQ	<LOQ	N/F	<LOQ	<LOQ	<LOQ
Primidone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Propranolol	9.8	N/F	N/F	N/F	N/F	N/F	N/F
Rosuvastatin	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Saccharin	16.7	N/F	<LOQ	<LOQ	<LOQ	N/F	<LOQ
Salicylic acid	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Sitagliptin	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Sotalol	24.6	2.2	4.3	N/F	N/F	N/F	N/F
Sucralose	34099	N/F	9021	666	3775	1342	1626
Sulfadiazine	81.6	11.4	11.9	<LOQ	2.4	6.5	5.7
Sulfadimethoxine	N/F	0.7	N/F	N/F	0.8	<LOQ	N/F
Sulfamerazine	<LOQ	0.1	0.3	<LOQ	0.3	2.3	1.5
Sulfamethazine	37.6	13.3	7.8	N/F	4.1	5.9	4.5
Sulfamethizole	N/F	0.4	N/F	0.2	0.4	0.7	0.4
Sulfamethoxazole	<LOQ	15.0	<LOQ	<LOQ	8.3	<LOQ	<LOQ
Sulfapyridine	42.3	21.0	11.0	0.7	2.7	1.3	0.5
Sulfathiazole	99.3	3.3	2.7	N/F	N/F	N/F	<LOQ
Sulisobenzone (BP4)	N/F	N/F	N/F	N/F	N/F	N/F	N/F
Tetracycline	N/F	<LOQ	N/F	N/F	<LOQ	N/F	N/F
Tramadol	30.0	49.3	28.3	0.1	4.3	1.1	0.5
Trimethoprim	N/F	N/F	1.9	0.1	0.8	<LOQ	0.1
Valsartan	1266	10.4	24.4	N/F	2.1	3.0	N/F
Venlafaxine	<LOQ	0.1	<LOQ	<LOQ	0.1	<LOQ	<LOQ

Table S9. Quality Score for each compound in both columns, sorted by log D.

Compound	QS HSST3	QS BEH Amide	Log D (pH 7.4)
Zanamivir	5	10	-6,0
Oxytetracycline	0	10	-4,3
Pipemidic acid	10	10	-3,6
Cyclamate	7	10	-3,5
Sulisobenzone (BP4)	10	10	-3,5
Iodixanol	7	7	-3,4
Metformin	2	10	-3,4
Tetracycline	10	10	-3,2
Iohexol	7	7	-3,2
Eflornithine	0	10	-3,0
Amoxicillin	0	10	-2,7
Ciprofloxacin	10	10	-2,2
Iopromide	4	7	-2,1
Levofloxacin	7	9	-2,1
Atenolol	10	10	-1,9
Aspartame	4	7	-1,8
Meprobamate	10	7	-1,8
Sotalol	10	10	-1,6
5-Fluorouracil	9	10	-1,6
Acyclovir	9	4	-1,5
Gabapentin	10	3	-1,4
Pregabalin	10	4	-1,3
Saccharin	10	9	-1,3
Melamine	5	10	-1,2
Trimethoprim	10	10	-1,2
Sulfamethizole	10	6	-1,1
Diatrizoic acid	7	4	-1,0
Phenytoin	10	9	-1,0
Sulfaguanidine	9	10	-1,0
Valsartan	10	4	-0,9
Clofibric acid	7	10	-0,9
Enrofloxacin	10	8	-0,9
Sulfadiazine	10	6	-0,8
Furosemide	10	10	-0,8
Salicylic acid	10	10	-0,8
Flumequine	10	8	-0,7
Primidone	7	3	-0,7
Sulfamethoxazole	10	8	-0,6
Sulfadimethoxine	10	8	-0,5
Lincomycin	4	7	-0,4
Amantadine	10	10	-0,4
Nalidixic acid	10	10	-0,3
Metoprolol	4	10	-0,3
Sucralose	10	4	-0,2
Morphine	10	4	-0,1
Bezafibrate	10	4	-0,1
Hydrochlorothiazide	10	9	0,0
Sulfathiazole	10	9	0,0
Sulfamerazine	10	9	0,0
Metronidazole	10	9	0,1
Ketoprofen	7	3	0,1
Cotinine	10	10	0,2

Sulfamethazine	10	9	0,2
Caffeine	10	3	0,3
Codeine	10	7	0,3
Hyoscine	10	10	0,3
Warfarin	10	5	0,3
Acetaminophen	10	3	0,4
Florfenicol	10	9	0,4
Sulfapyridine	10	9	0,4
Furazolidone	10	2	0,4
Ibuprofen	10	6	0,5
Naproxen	7	3	0,5
Zonisamide	7	0	0,5
Tramadol	10	10	0,5
Neotame	10	4	0,6
Oseltamivir	10	7	0,6
Fluconazole	10	9	0,7
Indomethacin	10	3	0,8
Methenamine	5	7	1,0
Rosuvastatin	10	4	1,0
Chloramphenicol	10	9	1,0
Sitagliptin	10	4	1,1
Carazolol	10	10	1,1
Propranolol	10	10	1,2
Cocaine	10	10	1,2
Irbesartan	10	10	1,2
Atorvastatin	10	4	1,3
Lidocaine	10	9	1,3

Citalopram	10	10	1,3
2.2'.4.4'-Tetrahydroxybenzophenone (BP2)	10	9	1,4
Azithromycin	10	4	1,4
Diclofenac	10	1	1,4
Venlafaxine	10	10	1,4
Paroxetine	10	10	1,5
1H-Benzotriazole	10	9	1,5
Oxazepam	10	6	1,5
Gemfibrozil	10	8	1,6
Lamotrigine	10	10	1,7
5-Methyl-1H-benzotriazole	10	9	1,7
Erythromycin	10	4	1,7
Lorazepam	10	9	1,9
Pentobarbital	10	8	1,9
Carisoprodol	10	5	1,9
Hydroxychloroquine	10	7	2,0
6∝-Methylprednisolone	10	6	2,0

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Qualitative and quantitative analysis of highly-polar contaminants in Atlanta urban water

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ABSTRACT

This study presents an integrated analytical approach combining liquid chromatography (LC) and travelling-wave ion mobility spectrometry (TWIMS) coupled with high-resolution mass spectrometry (HRMS) for the separation, detection, and quantification of 45 challenging contaminants in urban water matrices. The targeted analytes, including 41 very mobile compounds and 37 highly polar substances (log D_{ow} < 0), represent compounds that are often poorly retained under conventional reversed-phase and normal-phase LC conditions. In cases where LC provided inadequate retention, TWIMS proved to be an effective complementary technique by exploiting differences in molecular size, shape, and charge to resolve compounds based on their collision cross-section (CCS) values.

TWIMS was used to determine the CCS of 33 small organic molecules (120–500 Da). A ΔCCS threshold of ≥0.5% was identified as sufficient for proper separation on second-generation IMS instruments (resolving power >300 Rp).

Surface water samples from the Chattahoochee River and tap water from Midtown Atlanta (USA) were analyzed, revealing that over 50% of the targeted contaminants were detected in at least one matrix. Notably, compounds such as naphthalene-1-sulfonic acid, nicotine, and several per- and poly-fluoroalkyl substances (PFAS) were consistently observed, highlighting their ubiquitous occurrence in urban water impacted by industrial activities and heavy traffic. The methodology employed not only improved the resolution and identification of small, highly polar molecules but also provided robust quantitative data essential for environmental monitoring and risk assessment. This approach underscores the potential of IMS as a valuable complementary tool to traditional LC-MS workflows in complex environmental analyses.

1. Introduction

Liquid chromatography (LC) coupled to a mass spectrometer (MS) has been an excellent instrument used for the analysis of small molecules (López-Ruiz et al., 2019). Specifically, the entry of high-resolution MS (HRMS) into the market opened a new door to deep-through structural information of small molecules by unveiling molecular formulas. Recently, ion mobility (IM) has expanded its applicability area, traditionally focused on large molecules such as proteins and lipids, entering into the analysis of small molecules (e.g. > 1,000 Da) (Paglia et al., 2015; Uetrecht et al., 2010). IM offers the potential to resolve the structural and conformational dynamics of molecules, providing an additional separation dimension beyond retention time, m/z, and intensity (Lanucara et al., 2014). In an ion mobility spectrometer (IMS), ions are subjected to an electric field as they traverse through a neutral gas, with the separation governed by interactions between the ions and gas molecules (Lanucara et al., 2014). These interactions are influenced by the ion charge (z), size, and three-dimensional shape, which together determine its drift time (DT), allowing the calculation of collision cross-section (CCS) values (Lanucara et al., 2014). However, several IMS techniques with distinct separation principles, such as drift-time IMS (DTIMS), travelling-wave IMS (TWIMS), trapped IMS, and others, complicate the standardization of CCS measurements, since DT are not comparable between IMS techniques (Lanucara et al., 2014). Currently, aligning with community standards, only DTIMS enables the direct calculation of CCS for a specific molecule, while TWIMS requires calibrant ions with accurately characterized CCS values (usually poly-$_{DL}$-alanine), previously measured on DTIMS instruments, to generate a calibration curve for determining the CCS of unknown analytes (Ahmed et al., 2011; Dodds and Baker, 2019). In contrast, TWIMS offers key advantages, including low voltage requirements and the ability to achieve extended path lengths for enhanced ion mobility separation with minimal ion loss (Dodds and Baker, 2019). These longer paths increase analyte-gas interactions, enabling high resolving power and the

separation of ions that were previously unresolvable with DTIMS instrumentation (Dodds and Baker, 2019). Thus, TWIMS may offer superior performance in targeting small molecules within environmental matrices, which are often embedded in complex chemical mixtures.

Although LC can operate under both reversed-phase conditions, designed for retaining polar and moderately polar compounds, and normal-phase conditions, intended for separating highly polar and polar compounds, some molecules exhibit poor retention in both settings (McCalley, 2017; Menger et al., 2020; Reemtsma et al., 2016). IM does not incorporate polarity characteristics in the separation process, a factor that could be beneficial for molecules that are challenging to resolve under LC conditions. The limiting factor refers to the three-dimensional shape of small molecules, often very similar between them. Dodds and co-workers determined Eq. 1 and concluded that a ΔCCS ≥ 0.5 % between two consecutive ions is considered sufficient for proper separation when using second-generation IMS instruments, which offer resolving powers higher than 300 Rp (Dodds et al., 2017).

$$\Delta CCS\% = \frac{CCS_B - CCS_A}{\text{average } CCS_{A,B}} \times 100 \quad \text{Equation 1}$$

Where A and B represent two consecutive compounds. Notably, ΔCCS is independent of molecular size, enabling direct comparisons of separation efficiency across molecules with varying dimensions.

Thus, being able to detect and quantify highly polar compounds is vital for preserving environmental quality, especially for water, a resource deeply affected by climate change (Rodell et al., 2018). These compounds tend to remain in water compartments due to their low ability to accumulate into organic matter such as soils and sludge, compromising water quality and its possible reuse (Reemtsma et al., 2016). Additionally, highly polar compounds, also referred to as very mobile substances by the European Chemicals Agency for compounds with log D_{ow} < 2.5, have been underestimated for their low capacity to bioaccumulate and the analytical challenge they pose (Peter Arp et al., 2023).

In this study, 45 contaminants, 41 within the very mobile compounds range, and 37 highly polar (log D_{ow} < 0), have been analyzed in urban surface water and tap water using two different LC column chemistries, namely reversed-phase and normal-phase conditions, and a TWIMS instrument. The selected study area was Atlanta, GA (USA), a densely populated, water-stressed city with heavy traffic, relying on the Chattahoochee River as a primary source of drinking water. The aims of this study were: (i) to achieve effective separation of 45 challenging analytes using both LC and IM strategies; (ii) to assess the performance of each technique in terms of separation and detection capabilities; (iii) to determine the CCS of 33 highly polar compounds; and (iv) to quantify the compounds optimized via LC-HRMS analysis and qualitatively assess their presence by IMS in urban waters.

2. Materials and methods

2.1. Chemicals and reagents

The 45 contaminants were selected based on their mobility (polarity) and they comprise a variety of classes. All 45 analytical reference standards used for method development were of high purity and purchased from Sigma Aldrich (St. Louis, MO, U.S.). The relevant physicochemical properties of the target compounds including CAS numbers, molecular formulas, molecular weight, and log D_{ow} (at pH 7.4), are reported in Table S1 of the Supplementary Information.

LC-MS grade acetonitrile (≥ 99.9%), methanol (≥ 99.9%), dimethyl sulfoxide (≥ 99.9%), and HPLC-grade water were obtained from Merck (Darmstadt, Germany). Sigma-Aldrich supplied formic acid (≥ 96.0%, ACS grade), ammonium formate, and concentrated ammonia solution (29.0%, ACS grade). Additionally, LC/MS Optima™ grade acetonitrile, water, and formic acid used for mobile phase preparation were purchased from Fisher Chemical (Fisher Scientific SL, Germany). Poly-$_{DL}$-alanine (P9003) and polyglycine (P8791) were purchased from Sigma-Aldrich.

Individual stock solutions of the target analytes were prepared at concentrations of 1000 µg mL^{-1} in methanol, acetonitrile, dimethyl sulfoxide, or HPLC-grade water, depending on compound solubility. These stock solutions were stored at -20 °C, protected from light, to minimize potential degradation. For calibration, method development, and validation processes, mixed working solutions containing both pollutants and isotopically labelled standards were diluted to 2 µg mL^{-1} in methanol.

2.2. Instrumental analysis

Two different instruments were employed to ensure quality control, assess separation performance, and analyze the samples. For qualitative purposes, the TWIMS and the ultra-high-performance liquid chromatography (UPLC), both coupled to HRMS instruments, were used. For quantification, the UPLC-HRMS was the unique instrument employed.

2.2.1. TWIMS qualitative analysis

A q-traveling wave IM-ToF Synapt G2-Si HDMS (Waters, Milford, MA) equipped with a triboelectric nanogenerator (TENG) as an ionization source operating in both ionization modalities (positive and negative) was used for qualitative purposes (Li et al., 2017). The system was operated using MassLynx software (version 4.1 SCN 781), with daily tuning and calibration performed for both IM and MS analyses. The TENG parameters were reported previously by the group (Li et al., 2017; Vallejo et al., 2023). Important parameters for further CCS comparison are described: wave velocity was set to 300 m/s at a wave height of 5.0 V, the carrier gas was pure nitrogen (N_2), and the radio frequency step wave and ion guide was set to 150 and 200, respectively (Belova et al., 2022). For calibration purposes, poly-$_{DL}$-alanine was used and a mixture was injected every day before standard/sample injections. After recalibrating with the added lock-mass of leucine-enkephalin, extracted ion mobilograms for each standard including several alanine oligomers, used as calibrants, were generated using TWIMExtract software, to determine their respective drift time values (Haynes et al., 2017). These values were subsequently used to construct calibration curves for both positive and negative ionization modes (Table S2), enabling the calculation of $^{TWIMS}CCS_{N2}$ values for the target standards selected in the study, using the CCS values reported previously elsewhere (Bush et al., 2012; Forsythe et al., 2015).

2.2.2. UPLC-HRMS quantitative analysis

A Vanquish Horizon UHPLC system coupled to an Orbitrap QEHF mass spectrometer (Thermo Fisher Scientific, Waltham, MA, USA) was used for quantitative purposes using an ESI source working in both positive and negative ionization modes. Two different column chemistries were used in order to separate the maximum number of polar analytes by LC. The C18 column used was a Cortecs UPLC T3 (150 mm x 2.1 mm, 1.6 µm), while the normal phase column employed was a BEH Z-HILIC (100 mm x 2.1 mm, 1.7 µm), both acquired from Waters. Both gradients are reported in Table S3 of the Supplementary Information and the column temperature was set to 40 °C with volume injection of 1µL. The mobile phases of the reversed-phase conditions were: A; HPLC H_2O with 0.1 % formic acid and, B; acetonitrile with 0.1 % formic acid. For the normal-phase conditions, mobile phases were slightly different: A; HPLC H_2O:acetonitrile (80:20, v/v) with 10 mM ammonium formate plus 0.1 % formic acid and, B; acetonitrile with 0.1 % formic acid. Procedural blanks containing HPLC-grade water, and cleaning solvent vials containing methanol were injected after every five samples to check for any possible carryover or cross-contamination. The corresponding concentration values were subtracted from the sample measurements if positive signals were detected. In addition, to ensure the analysis's integrity and compensate for any analytical discrepancies, quality control samples (QC) were also injected every five samples. QCs were prepared by spiking standards for a final concentration of 50 µg L^{-1}.

The MS tuning methods and parameters were optimized under specific conditions. A Full MS-SIM experiment was conducted to determine the parent ion of each compound, with a scan range of 70-1000 m/z and a resolution of 60,000. Simultaneously, a parallel reaction monitoring experiment was carried out to acquire MS^2 spectra exclusively for precursor ions specified in an inclusion list, using an isolation window of 0.8 m/z. This approach provided high-quality MS^2 spectra with individual m/z and retention times (RT) windows at a resolution of 15,000. Collision energy (CE) was set to normalized CE (NCE) values of 35 and 50 eV. Optimization was achieved by injecting a solution containing all target compounds at 10 µg mL^{-1} in the appropriate solvent for each LC column (refer to Section 2.3).

Instrument control, qualitative validation, and quantitative analysis were performed using Thermo Xcalibur software version 4.1, following the validation and quantification guidelines outlined in SANTE/12682/2019 (Pihlström et al., 2019).

2.3. Extraction method

Atlanta, the capital of Georgia, has a population density of 3,882 people per km² and a total population of 525,050. It is a highly urbanized city with residential and commercial growth, including heavy traffic (Hu and Lo, 2007). Atlanta experiences a humid subtropical climate with humid summers and mild winters (average temperature of 19 °C). The city receives approximately 1,200 mm of annual rainfall, with no distinct dry season, making precipitation fairly evenly distributed throughout the year.

The Chattahoochee River, about 690 km long, originates in the Appalachian Mountains and flows southwest through Georgia, passing near Midtown and Downtown Atlanta. It provides drinking water for over 5 million people and supports regional ecosystems and recreational activities (Ghosh, 2021; Lynn Willoughby, 2020). This study focuses on the surface water of the Chattahoochee near urbanized areas in different spots as seen in Figure 1. Coordinates are reported in Table S4 of the Supplementary Information.



Fig. 1. Map of the surface water and the tap water sampled for this study. Black dots: Surface water; Blue dot: Tap water

All samples were collected in Atlanta (GA, USA) in autumn 2023. The Chattahoochee River was the main target of this study, obtaining eight surface water samples from the periphery of the city (Figure 1). Sample collection was conducted using the grab sampling method with a 50 mL Eppendorf tube. Before sampling, the tube was rinsed three times with the target water to minimize contamination. Tap water samples were collected directly from a faucet in an apartment located in Midtown Atlanta, following the same procedure as for surface water collection (Figure 1). While automatic and passive samplers can capture contaminants from a river flow site more specifically, they have notable drawbacks compared to grab samples, including higher costs and limited effectiveness in retaining highly mobile, polar compounds (Fialová et al., 2023; Gong et al., 2018).

2.4. Sample treatment

All samples were collected and treated on the same day. Once the samples arrived at the laboratory, they were centrifugated at 4000 rpm for 5 minutes to remove the solid impurities of the sampling by collecting 20 mL of the supernatant and stored at 4 °C. The enrichment procedure was performed the day after which consisted of an evaporative technique to avoid possible losses of the polar analytes (Labad and Pérez, 2024). Briefly, a 20-mL aliquot of each sample of surface and tap water was concentrated using an Eppendorf Concentrator Plus (Eppendorf AG, Hamburg, Germany). After the enrichment, the dry Eppendorf tubes were mixed with 300 µL of methanol, then centrifugated to 4000 rpm, and the supernatant was transferred to HPLC vials and evaporated

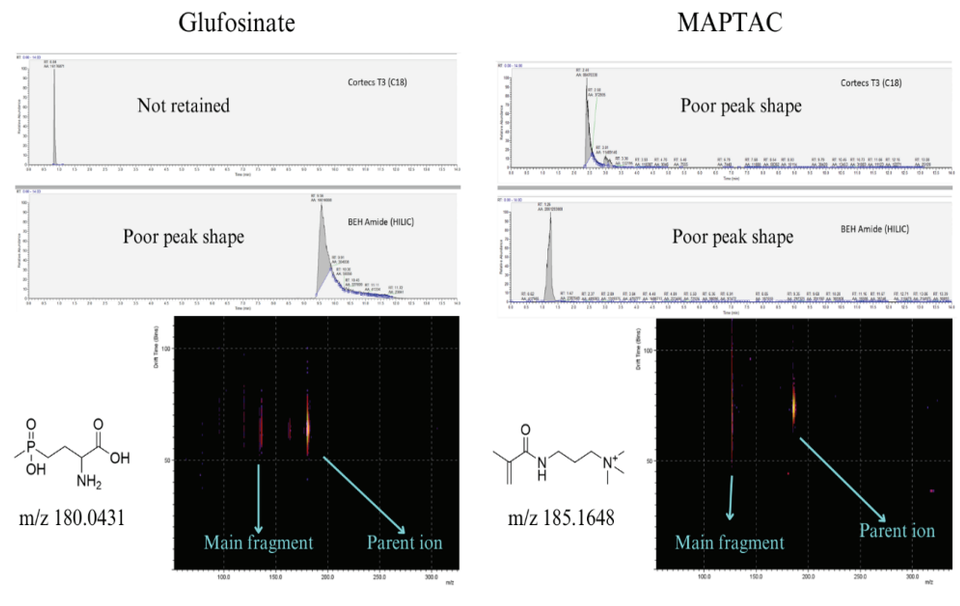


Figure 2. Performance of glufosinate and MAPTAC analytes in LC using RP and HILIC chemistries, compared to IM.

to dryness using a gentle stream of N_2. All samples were processed twice and reconstituted depending on their LC separation chemistries; acetonitrile:water (98:2, v/v) for the normal-phase separation and 100 % water for the reversed-phase separation (Labad and Pérez, 2024). The total enrichment factor achieved was 20 allowing the proper detection and quantification of the target compounds of this study.

2.5. Quality assurance

Instrumental and separation parameters such as retention time, precursor ion selected for quantification, product ion selected for confirmation, linearity, and method limits of detection and quantification (mLOD and mLOQ, respectively) are summarized in the Supplementary Information (Tables S1 and S5). The level used was 50 ng mL^{-1} as similar validation was performed previously for other polar substances (Labad and Pérez, 2024). The mLOD and mLOQ were calculated using the least detectable value of the calibration curve.

2.6. Statistical analysis

A Shapiro-Wilk ($p > 0.05$) was performed for all analytes to assess the distribution of the data, resulting in non-normal distributions. Non-parametric tests were further applied to the data. Then, a Kruskal-Wallis test ($p < 0.05$) was done for all samples and compounds to see patterns in the medians of the concentration distribution of the compounds across all samples. All tests were run in R software (version 2024.09.0 + 375) using the packages "dplyr", "tidyr", "readxl", and "ggplot2".

3. Results and discussion

3.1. IM vs LC

Expanding the knowledge provided by an additional dimension beyond LC and m/z is crucial for separating molecules that are challenging to resolve under liquid-phase conditions. For example, 1-(2-aminoethyl) piperazine (log D_{ow} -4.53), glufosinate (log D_{ow} -6.67), N-(1,3-Dimethylbutyl)-N′-phenyl-p-phenylenediamine (log D_{ow} -1.22), MAPTAC (log D_{ow} -3.74), and, tributyltin (log D_{ow} 3.68) were neither adequately separated nor effectively retained in any of the tested columns, including reversed-phase and normal-phase configurations but properly analyzed and separated using IMS (Figure 2).

3.2. Determination of CCS values

IM best performance has traditionally been achieved with large biomolecules, such as proteins and lipids with molecular masses exceeding 1,000 Da (Paglia

Figure 1. Map of the surface water and the tap water sampled for this study.

et al., 2015; Uetrecht et al., 2010). However, its application in the detection of small molecules has expanded significantly over the past decade (Lanucara et al., 2014). In this study, the CCS of 33 small organic compounds (120 – 500 Da) has been determined using a TWIMS instrument. Table 1 shows the values of the drift time observed and the $^{TWIMS}CCS_{N2}$ calculated using a poly-DT-alanine calibration curve (Table S2) considering CCS values previously reported elsewhere (Bush et al., 2012; Forsythe et al., 2015).

Notably, few CCS for highly polar compounds have been reported previously in the literature. However, Erin Baker's group focused on analyzing PFAS using IMS in environmental matrices. They determined the CCS values of several PFAS using a DTIMS instrument, resulting in CCS values closely related to the present study (Dodds et al., 2020). Specifically, the CCS values for PFBS, PFHxS, and PFOS were reported as 133.6, 150.5, and 168.3 Å^2, respectively, while in this study, they were measured as 134.0, 150.4, and 168.0 Å^2 (Dodds et al., 2020). The observed differences were minimal, at 0.3, -0.1, and -0.2 Å^2, respectively. These examples showed the possible comparison between DTIMS and TWIMS instruments regarding the CCS values determined for small molecules.

3.3. Is ion mobility useful for highly polar and small organic compounds?

Although molecular size and CCS are correlated, their relationship is not strictly linear, as illustrated in Table 1. Positive ions consistently exhibit larger CCS than negative ions with comparable m/z values. In this study, where the target analytes undergo only protonation or deprotonation, positive ions exhibit larger sizes due to increased molecular volume from protonation. In contrast, negative ions are smaller due to deprotonation. For instance, PFBA, PFBS, PFHxS, PFOA, and PFOS exhibit higher m/z values compared to other target analytes. This effect may be attributed to fluorine atoms, which are heavier and smaller than carbon, nitrogen, and oxygen atoms, thereby reducing the overall three-dimensional shape of PFAS molecules. In Figure 3 the relation of CCS with m/z is shown.

Several trends are evident in Figure 3, with each family, PFAS (purple triangles), sulfonic acids (blue triangles), and amines (yellow circles), independently following a consistent pattern. Previous studies determined trends depending on functional groups and specific molecule structures using IMS (Dodds et al., 2020; Paglia et al., 2014). Structural information using IMS could be important for non-targeted analysis in the identification of unknowns by determining their primary functional groups.

Additionally, Eq. 1 serves as an indicator of the resolution between two compounds with similar DT and, consequently, CCS (Dodds et al., 2017). In this study, the ΔCCS was assessed for all 33 compounds analyzed using IMS, considering the ionization mode and ordered by CCS (Table S6). Among the 33 small compounds, only four pairs were not properly separated (ΔCCS < 0.5 %), being 25 contaminants (75.8 %) resolved enough to be analyzed by IMS. The unresolved molecules were the following: 3-(methylphosphinic)propionic acid – PFBA; Aniline-3-sulfonic acid - Aniline-4-sulfonic acid; 2,3-dimethylbenzenesulfonic acid – PFBS; and Acrylamide-

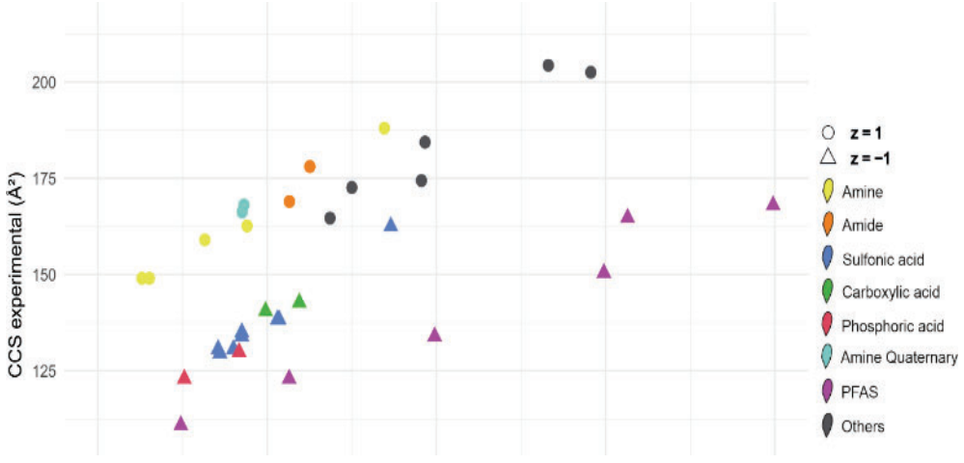


Figure 3. Relationship between CCS and m/z for the 33 compounds analyzed using TWIMS. The functional groups present in each molecule influence the CCS value. Circles represent positive ions while triangles show negative ions.

Table 1. Compound name, m/z, z, drift-time, and CCS_{TWIMS} of 33 analytes using TWIMS.

Compound name	m/z	z	DT (ms)	$^{TWIMS}CCS_{N2}$ (Å^2)	$^{DTIMS}CCS_{N2}$[1] (Å^2)
6-methyl-1,2,3-triazine-2,4-diamine	126.0774	+1	2.038	149.1	-
1-(2-aminoethyl) piperazine	130.1339	+1	2.068	149.8	-
Nicotine	163.1230	+1	2.453	159.0	-
6-phenyl-1,3,5-triazine-2,4-diamine	188.0931	+1	2.604	162.7	-
Carbamazepine	237.1022	+1	2.688	164.7	-
MAPTAC	185.1648	+1	2.755	166.3	-
Tetrapropylammonium chloride	186.2216	+1	2.830	168.1	-
1,3-diphenylurea	213.1022	+1	2.868	169.0	-
Clothianidin	250.0160	+1	3.019	172.6	-
Tributyltin	291.1129	+1	3.095	174.5	-
N,N'-dicyclohexylurea	225.1961	+1	3.246	178.1	-
Quadrol	293.2435	+1	3.510	184.4	-
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine	269.2012	+1	3.661	188.1	-
Hexa(methoxymethyl)melamine	391.2300	+1	4.264	202.6	-
Amoxicillin	366.1118	+1	4.340	204.4	-
Trifluoromethanesulfonic acid	148.9526	-1	1.698	110.9	-
3-(methylphosphinic)propionic acid	151.0166	-1	2.113	123.0	-
PFBA	212.9792	-1	2.113	123.0	-
Aniline-3-sulfonic acid	172.0074	-1	2.340	129.6	-
Aniline-4-sulfonic acid	172.0074	-1	2.340	129.6	-
Glufosinate	180.0431	-1	2.378	130.7	-
p-toluenesulfonic acid	171.0122	-1	2.409	131.4	-
2,3-dimethylbenzenesulfonic acid	185.0278	-1	2.491	134.0	-
PFBS	298.9430	-1	2.491	134.0	133.6
2,5-xylenesulfonic acid	185.0278	-1	2.528	135.1	-
Acrylamide-2-methyl-1-propane sulfonic acid	206.0493	-1	2.642	138.4	-
Naphthalene-1-sulfonic acid	207.0121	-1	2.642	138.4	-
(4-chloro-2-methylphenoxy)acetic acid	199.0168	-1	2.717	140.6	-
2,4-dicholorophenoxyacetic acid	218.9621	-1	2.793	142.8	-
PFHxS	398.9366	-1	3.057	150.4	150.4
Ensulizole	273.0339	-1	3.472	162.5	-

2-methyl-1-propanesulfonic acid – Naphthalene-1-

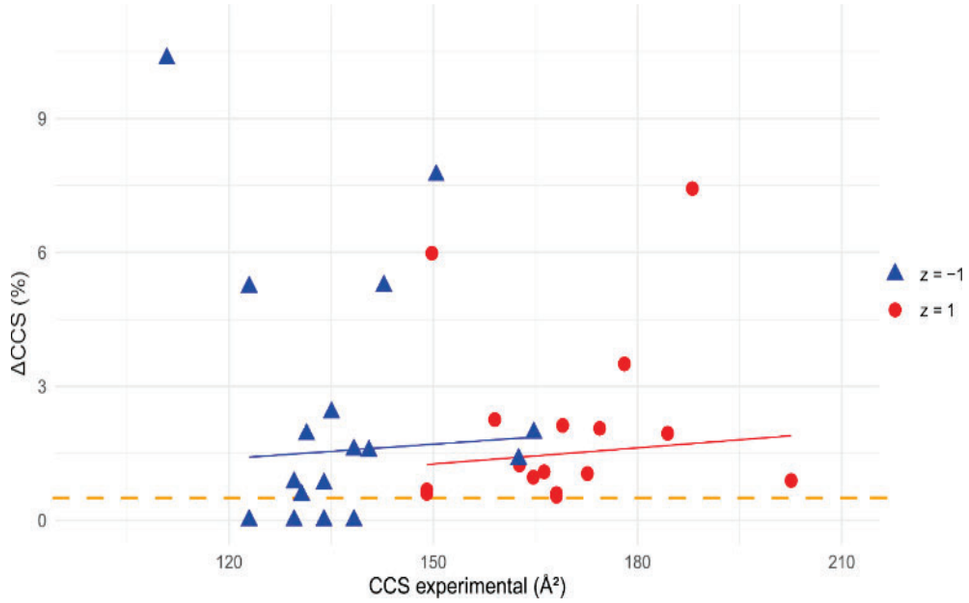


Figure 4. Relationship between ΔCCS and CCS for the 33 compound pairs analyzed using TWIMS. The orange-dotted line represents the threshold of 0.5 %. Blue and red lines show the tendencies, ignoring outliers, of each ionization mode.

sulfonic acid. Note that IMS coupled to an HRMS could identify each of those pairs of compounds except for the isomers (Aniline-3-sulfonic acid, and Aniline-4-sulfonic acid) due to the m/z differences between them. Among the target analytes, another pair of isomers, namely 2,3-dimethylbenzenesulfonic acid and 2,5-xylenesulfonic acid, are included and properly separated (ΔCCS = 0.82 %). The variation in the position of the isomer may significantly impact the CCS values, potentially affecting the ability of IMS to properly separate them. Curiously, all ESI + ions present enough CCS differences, probably

due to the higher m/z difference compared with ESI – ions. Figure 4 shows the ΔCCS vs CCS of the 33 compounds, differentiated by ESI modes. A slight trend is observed, where ΔCCS increases as CCS increases. This trend aligns with the initial application of IMS for the separation of larger molecules, as IMS demonstrates higher resolution for larger compounds compared to smaller ones (Dodds and Baker, 2019). Nonetheless, the overall ΔCCS values are sufficiently high to underscore IMS's capability to effectively analyze small molecules (Dodds et al., 2017).

Thus, IMS demonstrates its capability to analyze small molecules effectively, addressing the initial question. It proves to be a [1] (Dodds et al., 2020) valuable complementary technique to UPLC-HRMS, providing an additional separation dimension to enhance analytical performance.

3.4. Target analyte occurrence in urban surface and tap water

The occurrence and concentrations of the target analytes were performed by UPLC-HRMS for both surface and tap water. Of 42 compounds, 22 compounds (52.4 %) were detected at least once in the surface water while in tap water were 19 (45.2 %). Table 2 shows the concentrations of the 22 target analytes detected using LC-MS. Naphthalene-1-sulfonic acid (log D_{ow} = -2.70), triethylenediamine (log D_{ow} = -1.28), ethylenethiourea (log D_{ow} = -0.52), nicotine (log D_{ow} = -0.37), PFBA (log D_{ow} = -1.13), and methyl sulfate (log D_{ow} = -2.84) are among the compounds with higher mean concentrations in surface water, all above 100 ng L^{-1}. Except for nicotine, a well-known daily-used drug, the five other substances mentioned above are widely used in industry, demonstrating their ubiquitous presence in urban surface water with a 100% frequency of detection (FD). A previous study also detected naphthalene-1-sulfonic acid and triethylenediamine in 113 urban stormwater samples (Labad et al., 2025). Nicotine, alongside its main human

metabolites as cotinine, has been monitored for years in urban surface waters with concentrations above the µg L^{-1} levels, one order of magnitude higher than the present study (Buerge et al., 2008; Riva et al., 2019). Compounds exhibiting lower concentrations should also be considered due to their high occurrence in the Chattahoochee River. In that way, carbamazepine (log D_{ow} = 2.77, FD = 100 %) showed a mean concentration of 14.2 ng L^{-1} and a maximum concentration of 20.1 ng L^{-1}, which is in concordance with previous concentrations reported in surface water of North America, 54.0 and 114 ng L^{-1} (Pal et al., 2010; Quesada et al., 2019). Trifluoromethanesulfonic acid was also detected in urban waters (stormwater runoff) at a comparable median concentration of 18.8 ng L^{-1}, closely aligning with the 18.5 ng L^{-1} observed in this study, despite the differing water matrices analyzed (Labad et al., 2025). Focusing on the widely recognized family of PFAS, these compounds have been extensively studied in recent years. Concretely, in North America, the surface water of different states has been selected for several studies targeting PFAS. Podder et al. collected the mean concentration (9 studies) of PFAS, reporting mean concentrations of PFAS and identifying the highest maximum median concentrations for PFOA, PFBS, and PFOS in U.S. surface waters at 150, 130, and 369 ng L^{-1}, respectively (Podder et al., 2021). Notably, these values differ by approximately two orders of magnitude for PFBS and PFOS, while PFOA is three times higher than the present study. The primary differences may be attributed to factors such as the presence of industries near the river, variations in river size and flow, and the characteristics of the sampling zones. Beyond these compounds, numerous polar substances remain poorly studied in water, with their occurrence, behaviour, and hazardous properties still largely unknown. This knowledge gap, coupled with the widespread presence of highly polar compounds in urbanized areas, underscores the need for robust and reliable methodologies to detect and analyze these substances, especially in urban environments.

Compounds exhibiting poor retention, separation, or peak shapes were qualitatively assessed using IMS. Among these, 1-(2-aminoethyl)piperazine and MAPTAC were detected in all samples, while glufosinate was present in all surface water samples but not observed in tap water. N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine was present in 50% of the surface water samples but was not detected in tap water. Tributyltin was not identified in all analyzed urban water samples.

4. Conclusions

This study focused on the assessment of small and highly polar molecules using TWIMS and UPLC-HRMS. The CCS of several compounds are, for the first time, reported here with comparable values to those extracted using DTIMS. The key findings of the study are summarized below:

• Determination of CCS values using TWIMS for highly polar and small molecules, including several reported for the first time.

• DTIMS and TWIMS CCS values have been demonstrated to be comparable using adequate calibrants. This information is essential to create unified CCS databases for the analysis of small molecules.

• CCS values follow trends depending on the functional groups of the target molecules, being essential to potential identifications in future non-targeted analysis on the field.

• IMS is suitable for small molecule analysis as the majority of targeted compounds present a ΔCCS < 0.5 % and the presence of small molecules in environmental water matrices was successfully assessed.

• IMS was able to resolve a few compounds that were not properly retained using LC (normal and reversed phases), showing the potential of IM for the identification and analysis of challenging (i.e. highly polar) compounds.

• The presence and concentrations of several highly polar substances in urban waters suggest proper future monitoring of these substances that pose a risk to the environment and a hazard to water resources.

This research aims to advance efforts toward the development of unified CCS databases for small molecules, especially for those substances challenging to be separated by LC alone. The data generated contributes to expanding existing CCS databases and serves as a valuable resource for water management institutions, providing insights into the occurrence of highly polar substances in urban waters, including drinking tap water.

Table 2. Analytes concentrations (ng L^{-1}) of Chattahoochee River surface water (R) and Midtown Atlanta tap water (Tap).

Compound name	R1	R2	R3	R4	R5	R6	R7	R8	Tap
1,3-diphenylurea	<LOQ	1.84	3.45	3.07	4.05	4.16	6.09	4.68	2.41
6-phenyl-1,3,5-triazine-2,4-diamine	55.5	55.1	54.4	56.8	56.4	55.3	53.4	53.4	52.5
6-Methyl-1,3,5-triazine-2,4-diamine	39.2	38.9	85.9	45.7	90.6	195	76.6	78.2	41.2
Amoxicillin	n.d.	n.d.	1185	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Carbamazepine	<LOQ	8.47	8.59	15.6	19.6	20.1	11.7	15.0	2.86
Ethylenethiourea	72.1	474	336	502	213	116	116	155	n.d.
Hexa(methoxymethyl) melamine	5.37	10.8	12.2	15.7	23.4	25.4	46.5	32.2	17.7
N,N'-dicyclohexylurea	19.7	24.5	20.3	30.1	28.5	28.7	22.7	23.3	8.10
Nicotine	180	205	214	253	<LOQ	229	219	217	183
Tetrapropylammonium chloride	28.2	30.5	31.6	28.5	29.1	28.3	29.3	27.8	27.5
Triethylenediamine	686	448	448	453	456	459	466	458	457
2,4-Dichlorophenoxyacetic acid	78.0	46.0	44.4	53.0	61.7	66.9	57.4	61.3	38.5
(4-chloro-2-methylphenoxy)acetic acid	20.5	26.8	32.8	104	146	162	98.7	107	68.8
Methyl sulfate	71.8	90.9	84.0	125	120	97	133	141	637
Naphthalene-1-sulfonic acid	1933	653	1007	1000	2661	749	1210	2989	1339
PFBA	111	142	148	131	131	134	49.5	62.9	41.9
PFBS	3.36	1.88	1.91	2.52	2.02	2.03	3.40	3.30	2.12
PFHxS	2.52	26.4	1.49	185	11.3	1.00	1.80	6.40	3.21
PFOA	160	12.7	12.7	16.0	18.0	19.6	24.3	19.0	18.3
PFOS	2.56	6.79	4.52	3.36	1.26	1.44	2.31	4.06	1.45
p-toluenesulfonic acid	10.8	1.91	<LOQ	160	n.d.	n.d.	n.d.	n.d.	n.d.
Trifluoromethanesulfonic acid	160	12.7	12.7	16.0	18.0	19.6	24.3	19.0	18.3

CRediT authorship contribution statement

Francesc Labad: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Sandra Pérez:** Supervision, Funding acquisition, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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PUBLICACIÓ CIENTÍFICA #2

SUPPLEMENTARY INFORMATION

Qualitative and quantitative analysis of highly polar contaminants in Atlanta urban water

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Qualitative and Quantitative Analysis of Highly-Polar Contaminants in Atlanta Urban Water

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Table S1. Target analytes properties: name, CAS number, molecular formula, and log D_{ow} (at pH 7.4); and quality MS parameters: ESI mode, precursor ion, and product ion.

Compound name	CAS	Molecular formula	Log D_{ow} (pH 7.4)	ESI	Precursor ion (m/z)	Product ion (m/z)	UPLC-MS
1-(2-aminoethyl) piperazine	140-31-8	C6H15N3	-4.53	+	130.1339	113.0473	-
1,3-diphenylurea	102-07-8	C13H12N2O	3.00	+	213.1022	94.0663	RP
2,3-dimethyl benzene sulfonic acid	1300-72-7	C8H10O3S	-0.20	-	185.0278	121.0032	HILIC
2,4-dichlorophenoxyacetic acid	94-75-7	C8H6Cl2O3	-0.83	-	218.9621	160.8843	RP
2,5-xylene sulfonic acid	1300-72-7	C8H10O3S	-0.20	-	185.0278	121.0032	HILIC
(3-methyl phosphonic) propionic acid	15090-23-0	C4H9O4P	-6.10	-	151.0166	106.9744	RP
(4-chloro-2-methylphenoxy)acetic acid	94-74-6	C9H9ClO3	-1.09	-	199.0168	140.9469	HILIC
4-methyl-3-thiosemicarbazide	6610-29-3	C2H7N3S	-0.79	-	104.0288		HILIC
6-methyl-1,3,5-triazine-2,4-diamine	542-02-9	C4H7N5	-0.18	+	126.0774	85.0025	HILIC
6-phenyl-1,3,5-triazine-2,4-diamine	91-76-9	C9H9N5	1.41	+	188.0931	103.9885	RP
Acrylamide-2-methyl-1-propanesulfonic acid	15214-89-8	C7H13NO4S	-5.40	-	206.0493	134.9507	HILIC
Amoxicillin	26787-78-0	C16H19N3O5S	-2.72	+	366.1118	113.9400	RP
AMPA	1066-51-9	CH6NO3P	-5.95	-	110.0013	78.9160	RP
Aniline-3-sulfonic acid	121-47-1	C6H7NO3S	-4.28	-	172.0074	107.9932	HILIC
Aniline-4-sulfonic acid	121-57-3	C6H7NO3S	-4.31	-	172.0074	107.9932	HILIC
Carbamazepine	298-46-4	C15H12N2O	2.77	+	237.1022	194.0262	RP
Chlormequat chloride	999-81-5	C5H13ClN	-3.31	+	122.0731	58.0620	RP

Clothianidin	210880-92-5	C6H8ClN5O2S	-0.01	+	250.0160	168.9763	RP
Diatrizoic acid	117-96-4	C11H9I3N2O4	-1.00	+	631.8031	360.9677	RP
Ensulizole	27503-81-7	C13H10N2O3S	-2.96	-	273.0339	192.9311	HILIC
Ethyl sulfate	540-82-9	C2H6O4S	-4.50	-	124.9914	96.9542	HILIC
Ethylenethiourea	96-45-7	C3H6N2S	-0.52	+	103.0325	85.9547	HILIC
Glufosinate	77182-82-2	C5H15N2O4P	-6.67	-	180.0431	136.0564	RP
Glyphosate	1071-83-6	C3H8NO5P	-6.66	-	168.0067		RP
Hexa(methoxymethyl)melamine	3089-11-0	C15H30N6O6	1.54	+	391.2300	283.0371	RP
MAPTAC	51410-72-1	C10H21N2O	-3.74	+	185.1648	126.0994	-
Methyl sulfate	512-42-5	CH3O4S	-2.84	-	110.9758	79.9597	RP
N-(1,3-Dimethylbutyl)-N′-phenyl-p-phenylenediamine	5205-93-6	C9H18N2O	-1.22	+	269.2012	184.0128	-
N,N'-dicyclohexylurea	2387-23-7	C13H24N2O	3.15	+	225.1961	143.1201	RP
Naphthalene-1-sulfonic acid	85-47-2	C10H8O3S	-2.70	-	207.0121	142.9816	RP
Naproxen	22204-53-1	C14H14O3	-0.05	-	229.0870	185.0963	RP
Nicotine	54-11-5	C10H14N2	-0.37	+	163.1230	132.0137	HILIC
Paraquat dichloride	75365-73-0	C12H14N2	-6.70	+	93.0573		RP
PFBA	375-22-4	C4HF7O2	-1.13	-	212.9792	168.9149	RP
PFBS	375-73-5	C4HF9O3S	-1.56	-	298.9430	79.9597	HILIC
PFHxS	355-46-4	C6HF13O3S	-0.54	-	398.9366	98.9514	HILIC
PFOA	335-67-1	C8HF15O2	1.82	-	412.9664	368.9920	HILIC

PFOS	1763-23-1	C8HF17O3S	0.66	-	498.9302	21.9423	HILIC
p-toluenesulfonic acid	6192-52-5	C7H8O3S	-0.71	-	171.0122	107.0507	HILIC
Quadrol	102-60-3	C14H32N2O4	-1.20	+	293.2435	160.1392	RP
Tetrapropylammonium chloride	5810-42-4	C12H28N	-0.45	+	186.2216	114.1351	RP
Thiourea	2062-56-6	CH4N2S	-0.47	+	77.0168		HILIC
Tributyltin chloride	1461-22-9	C12H27ClSn	3.68	+	291.1129	178.9947	-
Triethylenediamine	280-57-9	C6H12N2	-1.28	+	113.1073	84.0169	RP
Trifluoromethanesulfonic acid	1493-13-6	CHF3O3S	-3.88	-	148.9526	79.9558	RP

Table S2. Poly-$_{DT}$-alanine experimental drift time (DT), and collision-cross section (CCS) values used for calibration purposes for (+H) and (-H).

Alanine adducts	Exp. DT (ms)	CCS (Å^2)	CCS reference
A3+	2.258	151	(Bush et al., 2012)
A4+	2.742	166	(Bush et al., 2012)
A5+	3.334	181	(Bush et al., 2012)
A6+	3.925	195	(Bush et al., 2012)
A7+	4.570	211	(Bush et al., 2012)
A8+	5.269	228	(Bush et al., 2012)
A9+	5.915	243	(Bush et al., 2012)
A10+	6.452	256	(Bush et al., 2012)
A11+	7.044	271	(Bush et al., 2012)
A12+	7.581	282	(Bush et al., 2012)
A13+	8.119	294	(Bush et al., 2012)
A14+	8.657	306	(Bush et al., 2012)
A2-	2.415	13.2	(Forsythe et al., 2015)
A3-	3.057	150.0	(Forsythe et al., 2015)
A4-	3.547	164.4	(Forsythe et al., 2015)
A5-	4.038	179.7	(Forsythe et al., 2015)
A6-	4.604	195.0	(Forsythe et al., 2015)
A7-	5.095	209.5	(Forsythe et al., 2015)
A8-	5.510	222.4	(Forsythe et al., 2015)

Table S3. LC gradients used for both reversed and normal phase conditions.

Cortecs UPLC T3

Flow (mL/min)	Oven Temperature (ºC)	Time (min)	Solvent A (%)	Solvent B (%)
0.4	40	0	100	0
0.4	40	1	100	0
0.4	40	4	75	25
0.4	40	8	3	97
0.4	40	8.1	3	97
0.4	40	11.9	3	97
0.4	40	12	100	0
0.4	40	14	100	0

BEH Z-HILIC

Flow (mL/min)	Oven Temperature (ºC)	Time (min)	Solvent A (%)	Solvent B (%)
0.3	40	0	5	95
0.3	40	0.5	5	95
0.3	40	8	60	40
0.3	40	10.5	60	40
0.3	40	11	5	95
0.3	40	14	5	95

Table S4. Coordinates (decimal degrees) of all samples collected in this study.

Sample name	Urban water type	Longitude	Latitude
Willeo Park	Surface water	33.996313	-84.385304
Island Ford Unit	Surface water	33.986920	-84.323618
Don White Memorial Park	Surface water	34.008158	-84.336879
Jones Bridge	Surface water	33.989788	-84.255847
Johnson Ferry	Surface water	33.945428	-84.403762
Cochran Shoals	Surface water	33.903444	-84.446035
East Palisades	Surface water	33.878193	-84.443062
Paces Mill	Surface water	33.870392	-84.452436
Midtown ATL	Tap water	33.784817	-84.388512

Table S5. LC-MS quality parameters: retention time (RT), linearity, mLOD, and mLOQ.

Compound	ESI	RT (min)	Linearity (µg L^{-1})	mLOD (ng L^{-1})	mLOQ (ng L^{-1})
1,3-diphenylurea	+	6.65	0.1-500	1.67	5
4-methyl-3-thiosemicarbazide*	+	1.37	10-500	167	500
6-methyl-1,3,5-triazine-2,4-diamine	+	1.20	0.5-500	6.67	20
6-phenyl-1,3,5-triazine-2,4-diamine*	+	1.38	0.1-500	1.67	5
Amoxicillin	+	3.61	5-500	66.7	200
Carbamazepine	+	6.22	0.1-500	1.67	5
Chlormequat chloride	+	1.11	0.5-500	6.67	20
Clothianidin	+	5.53	0.5-500	6.67	20
Diatrizoic acid	+	3.32	10-500	167	500
Ethylenethiourea*	+	1.50	5-500	66.7	200
Hexa(methoxymethyl)melamine	+	6.33	0.1-500	1.67	5
N-(1,3-Dimethylbutyl)-N′-phenyl-p-phenylenediamine	+	6.31	50-500	833	2500
N,N'-dicyclohexylurea	+	6.73	0.1-500	1.67	5
Nicotine*	+	1.91	5-500	66.7	200
Paraquat chloride	+	6.66	10-500	167	500
Quadrol	+	3.04	5-500	66.7	200
Tetrapropylammonium chloride	+	5.08	0.1-500	1.67	5
Thiourea*	+	3.35	5-500	66.7	200
Triethylenediamine	+	0.81	5-500	66.7	200
2,3-dimethylbenzenesulfonic acid*	-	9.73	0.1-500	1.67	5
2,4-dichlorophenoxyacetic acid	-	6.54	0.5-500	6.67	20
2,5-xylenesulfonic acid*	-	10.29	0.1-500	1.67	5
3-(methylphosphinic)propionic acid	-	1.23	5-500	66.7	200
(4-chloro-2-methylphenoxy)acetic acid*	-	0.99	0.1-500	1.67	5
AMPA	-	0.79	5-500	66.7	200
Acrylamide-2-methyl-1-propanesulfonic acid*	-	9.98	0.1-500	1.67	5
Aniline-3-sulfonic acid*	-	9.82	5-500	66.7	200
Aniline-4-sulfonic acid*	-	11.46	0.1-500	1.67	5
Ensulizole*	-	7.84	0.1-500	1.67	5
Ethyl sulfate*	-	11.57	0.1-500	1.67	5
Glufosinate	-	0.83	5-500	66.7	200
Glyphosate	-	0.80	5-500	66.7	200
Methyl sulfate	-	5.72	0.1-500	1.66	5
Naphthalene-1-sulfonic acid	-	5.04	0.5-500	1.66	5
Naproxen	-	6.69	10-500	167	500
PFBA	-	4.84	0.1-500	1.66	5
PFBS*	-	3.84	0.1-500	1.66	5
PFHxS*	-	3.60	0.1-500	1.66	5
PFOA*	-	4.14	0.1-500	1.66	5
PFOS*	-	3.47	0.1-500	1.66	5
p-toluenesulfonic acid*	-	10.92	0.1-500	1.66	5
Trifluoromethanesulfonic acid	-	1.54	0.1-500	1.66	5

* Compounds analyzed by the Z-HILIC column.

Table S6. Compound name, pairs, m/z, z, CCS_{TWIMS}, and ΔCCS of 33 analytes using TWIMS.

Compound name	Nº	Pair	m/z	z	$^{TWIMS}CCS_{N2}$ (Å²)	ΔCCS (%)
6-methyl-1,2,3-triazine-2,4-diamine	1	1-2	126.0774	+1	149.1	0.50
1-(2-aminoethyl) piperazine	2	2-3	130.1339	+1	149.8	6.48
Nicotine	3	3-4	163.1230	+1	159.0	2.26
6-phenyl-1,3,5-triazine-2,4-diamine	4	4-5	188.0931	+1	162.7	1.24
Carbamazepine	5	5-6	237.1022	+1	164.7	0.97
MAPTAC	6	6-7	185.1648	+1	166.3	1.08
Tetrapropylammonium chloride	7	7-8	186.2216	+1	168.1	0.54
1,3-diphenylurea	8	8-9	213.1022	+1	169.0	2.12
Clothianidin	9	9-10	250.0160	+1	172.6	1.05
Tributyltin	10	10-11	291.1129	+1	174.5	2.06
N,N'-dicyclohexylurea	11	11-12	225.1961	+1	178.1	3.50
Quadrol	12	12-13	293.2435	+1	184.4	1.95
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine	13	13-14	269.2012	+1	188.1	7.43
Hexa(methoxymethyl)melamine	14	14-15	391.2300	+1	202.6	0.89
Amoxicillin	15	15-14	366.1118	+1	204.4	
Trifluoromethanesulfonic acid	16	16-17	148.9526	-1	110.9	10.3
3-(methylphosphinic)propionic acid	17	17-18	151.0166	-1	123.0	0
PFBA	18	18-19	212.9792	-1	123.0	5.22
Aniline-3-sulfonic acid	19	19-20	172.0074	-1	129.6	0
Aniline-4-sulfonic acid	20	20-21	172.0074	-1	129.6	0.84
Glufosinate	21	21-22	180.0431	-1	130.7	0.57
p-toluenesulfonic acid	22	22-23	171.0122	-1	131.4	1.93
2,3-dimethylbenzenesulfonic acid	23	23-24	185.0278	-1	134.0	0
PFBS	24	24-25	298.9430	-1	134.0	0.82
2,5-xylenesulfonic acid	25	25-26	185.0278	-1	135.1	2.41
Acrylamide-2-methyl-1-propane sulfonic acid	26	26-27	206.0493	-1	138.4	0
Naphthalene-1-sulfonic acid	27	27-28	207.0121	-1	138.4	1.58
(4-chloro-2-methylphenoxy)acetic acid	28	28-29	199.0168	-1	140.6	1.55
2,4-dicholorophenoxyacetic acid	29	29-30	218.9621	-1	142.8	5.25
PFHxS	30	30-31	398.9366	-1	150.4	7.73
Ensulizole	31	31-32	273.0339	-1	162.5	1.37
PFOA	32	32-33	412.9664	-1	164.8	1.96
PFOS	33	32-33	498.9302	-1	168.0	

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3.3 Discussió

Les metodologies descrites en aquest capítol, juntament amb els mètodes de tractament de mostra i separació cromatogràfica que no han estat publicats en forma d'article científic, es discutiran en profunditat en aquest apartat. A més, es comparará el rendiment del IM amb el de les columnes de LC testades, basant-se en la seva capacitat per separar inequívocament TrOCs polars. En conseqüència, els resultats presentats als articles #1 i #2, juntament amb altres proves analítiques, seran analitzats de manera global en les seccions següents.

Rendiment i exactitud de les diferents tècniques de tractament de mostra testejades

En l'actualitat triar un mètode de tractament de mostra en base als TrOCs d'estudi, limitarà molt les possibilitats analítiques disponibles, ja que amb un sol anàlisis es poden detectar més de 1,000 i 10,000 compostos (Hulleman et al., 2023). Degut a que la tesi inclou únicament matrius aquoses, l'objectiu del mètode de preparació de mostra consistia en retenir el màxim nombre de TrOCs, incloent molt polars (log D_{ow} < 0), polars (0 ≤ log D_{ow} ≤ 2) i moderadament polars (log D_{ow} > 2), amb 48, 50 i 31, TrOCs respectivament. Al *Capítol 1* d'aquesta tesi es descriuen en profunditat els mètodes més coneguts de SPE i enriquiment per evaporació; mètodes desenvolupats i descrits als articles #1 i #2 en profunditat. Tot i això, es van realitzar diferent proves per obtenir els millors resultats de preconcentració dels analits, i que no han estat incloses a les publicacions degut al seu rendiment més baix que la msSPE i VAE. En concret, es va desenvolupar una msSPE afegint carboni (Figura 3.1) i el seu rendiment serà discutit i comparat amb la msSPE sense carboni i el mètode d'enriquiment VAE validat en aquesta tesi. Les recuperacions són un dels valor més importants per tenir en compte a l'hora de validar un mètode analític i corroborar que és efectiu per extreure els TrOCs d'interès de la matriu inicial. En aquesta tesi, es va emprar aigua d'aixeta com a matriu de validació en cas de l'aigua subterrània i superficial, mentre que per l'aigua d'escorrentia, de pluja i SUDS es va usar aigua de pluja recol·lectada a un sostre de les instal·lacions del IDAEA, ambdós casos intentant que sigui aigua semblant a les mostres i el més neta o amb, com a mínim,

presència ínfima dels analits objectiu. Les recuperacions són avaluades en triplicats i en 3 nivells diferents: nivell baix (10 µg L^{-1}), nivell intermedi (50 µg L^{-1}) i nivell alt (200 µg L-1) (Pihlström et al., 2019). Respecte la recta de calibratge es va seguir el mateix raonament, per tenir rectes el més semblant possible a les mostres analitzades.

Com mostra la Figura 3.4 el mètode VAE, al tractar-se d'un mètode menys selectiu té un rendiment general superior als altres dos mètodes d'extracció. Especialment, les recuperacions observades tant per a compostos molt polars com per als polars, són molt properes al 100 %, mentre que pel moderadament polars hi ha més variabilitat. La msSPE, d'altra banda, presenta recuperacions òptimes tant per compostos polars, com pels moderadament polars (mitjana de 67 % sense tenir en compte els valors atípics). Fixant-nos en els 51 compostos molt polars, només 4 tenen recuperacions més òptimes amb els mètodes msSPE i msSPE amb carboni que amb VAE. Aquests són l'aspartam i la sulfaguanidina amb recuperacions del 96 % i 102 % usant el mètode msSPE amb carboni, i el meprobamat i la morfina que tenen millors recuperacions amb la msSPE (104 % i 151 %, respectivament). Un estudi va estimar que l'extracció únicament amb HLB era insuficient per l'anàlisi de TrOCs polars, mentre que una metodologia SPE desenvolupada per ells, incloent carboni, conjuntament amb enriquiment mitjançant evaporació cobria tot l'espectre de polaritats estudiats (Köke et al., 2018). Aquest estudi no menciona la dificultat d'eluir eficientment el cartutx amb carboni, potser degut a la petita quantitat de carboni emprat (30 mg). Respecte al msSPE amb carboni, en general els valors de recuperacions obtinguts van ser molt dispersos. Aquest fet pot ser atribuït a la potent capacitat de sorció del carboni actiu, fent que la seva elució, tot i fer la donant la volta al cartutx, sigui complicada i en molts casos ineficient (Figura 3.4). Tot i que aquesta metodologia presenta recuperacions lleugerament superiors per a alguns compostos com el crotamitó (74.4 %) o l'àcid clofibric (93.6 %), la despesa econòmica i, sobretot, el temps d'inversió necessari per elaborar un a un els cartutxos i executar per la tècnica d'SPE, va conduir a seleccionar amb claredat l'enriquiment mitjançant el VAE, especialment per a compostos amb log D_{ow} < 2. Alguns dels compostos, especialment els que presenten un log D_{ow} > 2, van ser extrets amb msSPE, sense incloure el carboni.

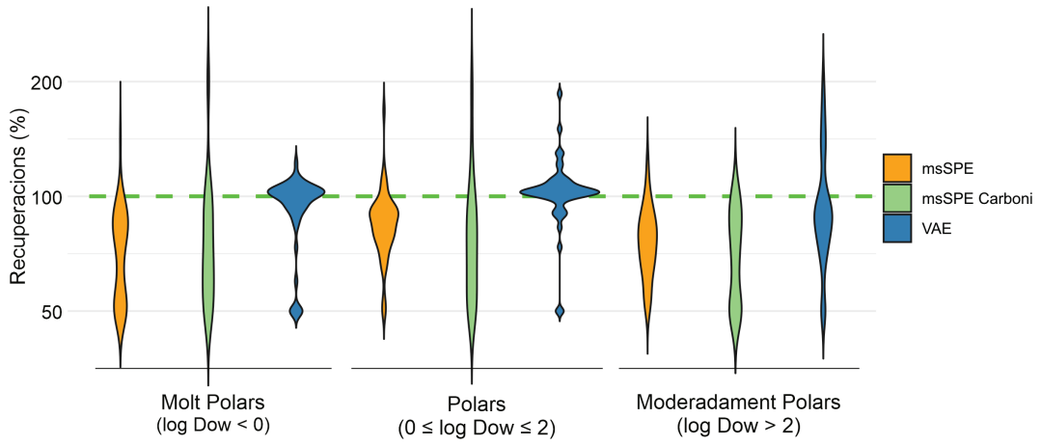


Figura 3.4. Gràfic de violí dels tres mètodes d'extracció testejats en aquesta tesis. La línia verda discontínua representa una recuperació del 100 %. Les recuperacions superiors al 200 % han estat truncades per qüestions de visualització. Es mostren les recuperacions al nivell de 50 µg L^{-1}.

Comparació de la precisió i l'efecte matriu

Un cop seleccionats els dos mètodes de preconcentració de la mostra (es va descartar la msSPE amb carboni degut a la baixa reproductibilitat), es dur a terme una validació exhaustiva. Aquesta validació ha d'incloure no només l'avaluació de la exactitud (recuperació), sinó també la seva precisió, expressada com la desviació estàndard relativa (RSD, de l'anglès *relative standard deviation*) i també l'avaluació dels efectes de matriu per a cada analit (Pihlström et al., 2019). Com s'ha explicat a la secció anterior, les recuperacions eren calculades en triplicat, per tant l'estudi de la variació d'aquests valors ens permet veure com de robust és un mètode extractiu. En canvi, l'avaluació de l'efecte matriu (ME, de l'anglès *matrix effect*) proporciona informació sobre com la matriu d'estudi impacta l'analit en qüestió i sobre l'eficàcia del mètode seleccionat per minimitzar o eliminar aquest efecte (Trufelli et al., 2011).

A la figura 3.5 estan representats tant els RSD com els ME de tots els compostos en els dos mètodes extensivament usats en aquesta tesi. Generalment parlant, respecte la precisió dels mètodes, tots dos es molt bona exceptuant alguns compostos (Figura 3.5 A). De fet, la variabilitat de l'enriquiment VAE és lleugerament més propera a 0 que la de msSPE. Focalitzant-nos amb al compostos molt polars (log D_{ow} < 0), VAE només presenta 4 compostos amb RSD superiors al 20 % i mai superior al 50%,

és a dir, 44 compostos de 48 (91.7 %) són altament reproduïbles. Tenint en compte la complexitat extractiva associada a aquests compostos, l'enriquiment mitjançant VAE adquireix una gran rellevància analítica. Per tant, a grans trets tots dos mètodes son reproduïbles. Respecte el ME, si que s'observa una lleugera tendència negativa en l'enriquiment per VAE, mentre que la msSPE presenta valors bastant propers al 0 (Figura 3.5 B). Curiosament, la tendència del ME en l'enriquiment per VAE té una tendència negativa (supressió de la senyal), mentre que l'extracció per msSPE conté valors majoritàriament positius. En el cas del VAE, es normal obtenir ME majors (en valors absoluts) que no pas la msSPE, ja que al evaporar, tots els compostos presents a la matriu també es concentren i competeixen a la font de ionització per, efectivament, ionitzar-se juntament amb els analits d'interès. D'altra banda, la msSPE és un mètode d'extracció molt més selectiu el qual permet l'eliminació de compostos de la matriu amb major efectivitat que no pas el VAE.

Tot i això, cal destacar que l'ús de patrons interns per a la quantificació dels analits objectiu redueix significativament la influència dels efectes matriu. En validar els mètodes mitjançant rectes de calibratge elaborades amb aigua similar a l'analitzada, combinat amb l'aplicació de patrons interns, s'aconsegueix corregir de manera efectiva aquestes interferències, ja que els patrons interns compensen les variacions associades als TrOCs objectiu.

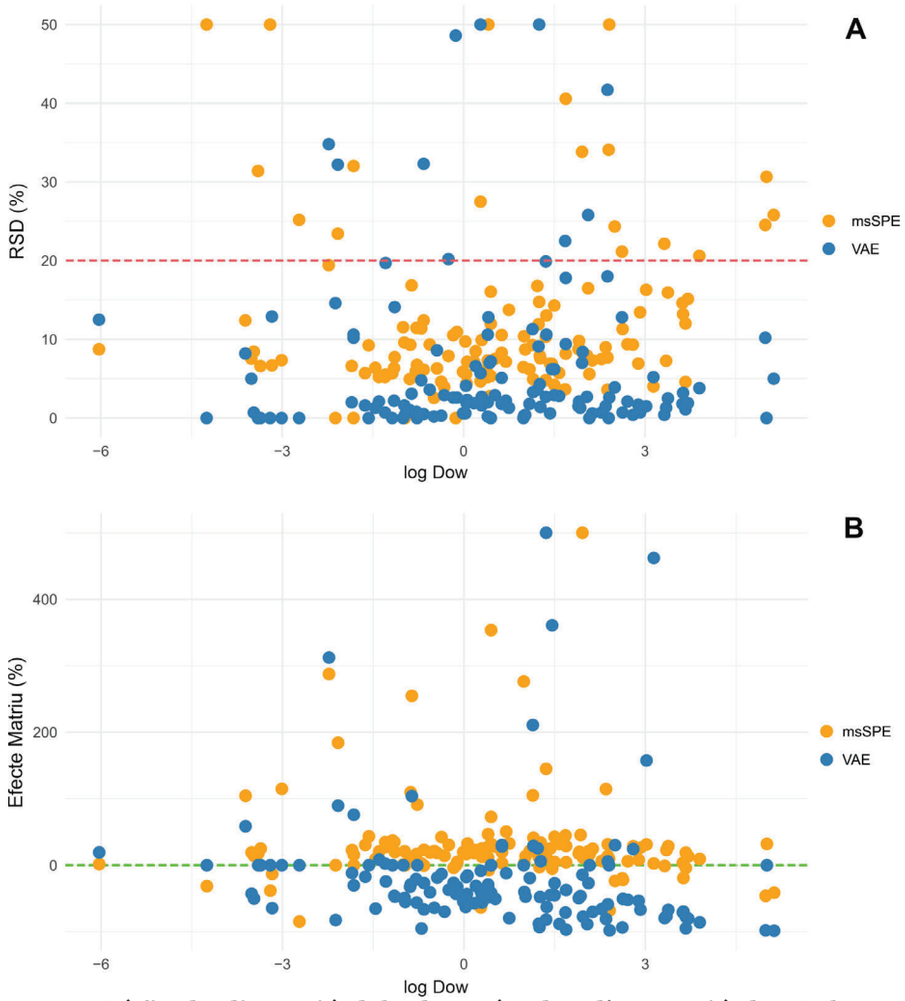


Figura 3.5. Gràfic de dispersió dels dos mètodes d'extracció de, **A**: la precisió mostrada en RSD (valors superiors al 50 % han estat truncats per raons de visualització), la línia discontinua vermella mostra el límit de dispersió recomanable; i **B**: l'efecte matriu (valors superiors al 500 % han estat truncats per raons de visualització), la línia discontinua verda mostra un efecte matriu idoni. Ambdós gràfics mostren els valors obtinguts al nivell de 50 µg L^{-1}.

Comparació del rendiment entre columnes de LC

La selecció de la columna cromatogràfica ha de ser prèvia al mètode d'extracció, tot i que en aquest capítol s'ha volgut seguir l'ordre del procés analític complet. Usualment s'empren patrons purs per conèixer temps de retenció, modes de ionització i fragments típics de cada TrOC objectiu per poder decidir si una columna és adequada pels TrOCs seleccionats per l'estudi. En aquest cas, al tenir un rang de polaritats tan ampli, que es la primera característica a tenir en compte en la cromatografia líquida, la probabilitat de haver d'usar més d'una columna eren molt altes (Menger et al., 2020). Després de testejar diferents columnes cromatogràfiques i optimitzar diversos gradients, especialment amb la columna HILIC, es van seleccionar dues columnes complementàries per a l'anàlisi de més de 129 TrOCs, cobrint un ampli rang de polaritats (log D_{ow} de -6.0 a 5.1). Aquestes columnes són la HSS T3, per a condicions de fase inversa, i la BEH Amide, per a condicions de HILIC, ambdós incloses a la publicació #1.

Com a apunt, cal especificar amb claredat, sobretot en articles de mètode, les condicions cromatogràfiques emprades, incloent columna, gradients detallats (columna, solvents, temperatura, etc.), patrons i condicions de la font de ionització per a poder replicar-ho en altres laboratoris. En aquesta tesi, s'han intentat replicar exactament mètodes ja publicats i no ha estat possible, obtenint resultats molt diferents als descrits (Schulze et al., 2019).

Tot i que a la publicació #1, els resultats de les dues columnes han estat exposades i discutides, aquí breument es farà una discussió afegint 35 compostos més que varen ser analitzats a les publicacions #3, #6 i #7. Primer, per poder comparar la retenció entre dos columnes, més enllà de fixar-se amb el temps de retenció, cal comparar els valors del factor de retenció (RFK, del anglès *retention factor*). Aquest valor es calcula segons l'equació 3.1 i té en compte el volum mort de la columna.

$$RFK_i = \frac{t_{R,i} - t_M}{t_M} \qquad \text{Eq. 3.1}$$

On t_M és el temps de retenció del primer compost sense retenció i t_R,i és el temps de retenció del compost *i*. Aquest valor no té en compte el gradient, ni altres paràmetres que poden afectar al temps de retenció del compost, fent comparables el poder de retenció de dos compostos diferents. A més de la retenció, també s'hauria d'avaluar la forma de pic, que és molt important per veure si el compost segueix una forma gaussiana, o semblant, per a que el pic es pugui replicar al llarg d'una seqüència d'anàlisis per LC-MS (Iturrospe et al., 2021). També es podri-

en tenir en compte altres paràmetres com la intensitat dels senyals entre una columna i l'altre, tot i que aquí també entra en joc el rendiment de la ionització (Iturrospe et al., 2021). A la publicació #1 ja es va dur a terme un estudi detallat, especialment pel que fa a la forma dels pics entre les columnes. Per tant, en aquest apartat només es discutirà la retentivitat de les mateixes per als TrOCs objectiu seleccionats. A la figura 3.6 es pot veure representats els 129 TrOCs i el valor RFK de les dues columnes en base a la polaritat de cada compost. Clarament, la tendència de la columna que treballa en condicions de fase inversa es positiva, indicant que a mesura que la polaritat d'un compost augmenta, la retentivitat ho fa també. D'altra banda, la columna que treballa en condicions normals, és tot al contrari, té una tendència negativa ja que aquí els compostos amb un log D_{ow} majors, és retenen menys (Labad and Pérez, 2024). És evident que la polaritat no és el únic factor a tenir en compte, per exemple, l'àcid pipemídic (log D_{ow} = -3.6), la sulisobenzona (log D_{ow} = -3.5), la tetraciclina (log D_{ow} = -3.2) i la ciprofloxacina (log D_{ow} = 2.2), tots compostos molt polars, presenten retencions elevades en la columna C18. Això pot ser degut a diferents factors com que les quatre són molècules relativament grans (> 300 Da) i amb dos o més anells aromàtics, el que pot comportar interaccions amb la fase sòlida de la columna HSS T3, columna amb fase sòlida modificada per retenir compostos més polars que una columna C18 convencional (Žuvela et al., 2019). Fixant-nos en la HILIC, el comportament es totalment invers, fent que compostos amb log D_{ow} baixos pateixin una major retenció en aquestes condicions (Buszewski and Noga, 2012; McCalley, 2017). També hi ha excepcions, com es el cas de la metenamina (log D_{ow} = 1.0), l'azitromicina (log D_{ow} = 1.4) o la hidroxicloroquina (log D_{ow} = 2.0), que presenten RFK al voltant de 10, comparables a altres compostos molt polars. Aquestes tres molècules mencionades, no presenten característiques similars, més enllà de la presència d'amines terciàries. La metenamina es tracta d'un compost molt petit amb quatre amines terciàries, l'azitromicina en canvi, es una molècula gran amb molts grups funcionals i, per últim, la hidroxicloroquina amb dos anells aromàtics i una cadena de carbonis, incloent una amina terciària i un alcohol.

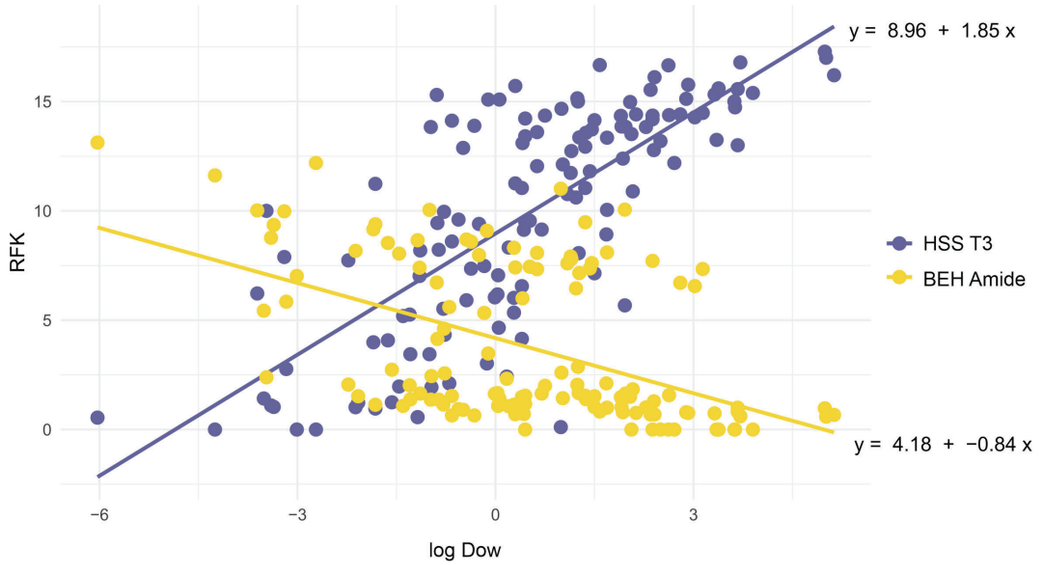


Figura 3.6. Gràfic de dispersió dels valors RFK de les dues columnes emprades per separar els TrOCs d'interès en base a la polaritat (log D_{ow}). La línia de tendència lila (C18) té una pendent positiva, mentre la groga (HILIC) és negativa.

A més, a la publicació #4, 15 TrOCs molt polars (log D_{ow} < 0), diferents als mostrat a la figura 3.6 van ser analitzats únicament amb la columna BEH Amide degut a la seva millor eficàcia per aquest tipus de compostos.

Altres tècniques com la SFC ha estat utilitzada per altres laboratoris per retenir i separar adequadament compostos molt polars (Reemtsma et al., 2016; Schulze et al., 2019). Breument s'exposaran les diferències, avantatges i desavantatges d'aquesta cromatografia comparada amb la LC. Reemstma et al. van obtenir retencions adquades pels compostos molt polars com la melamina, la metformina i també el 5-fluorouracil, també amb bon rendiment de la HILIC (Reemtsma et al., 2016). Dos estudis recents conclouen que la SFC proporciona senyals addicionals que ni la RPLC ni la HILIC són capaces de detectar (Bieber et al., 2017; Castro et al., 2021). Tot i això, la SFC, en general, proporciona baixa retenció per compostos moderadament polars i apolars, fent que la combinació de les columnes HSS T3 i BEH Amide sigui més útil per abastar un rang ampli de polaritats (Bieber et al., 2017). A la Taula 3.1 es presenten les comparatives d'usar columnes cromatogràfiques (HSS T3 i HILIC) i la SFC.

Taula 3.1. Avantatges i desavantatges de l'ús de cromatografies RP, HILIC i SFC en la separació de compostos polars.

Característica	RPLC	HILIC	SFC
Idoneïtat per retenir compostos molt polars	Baixa	Alta	Alta
Idoneïtat per retenir compostos polars	Alta	Alta	Alta
Idoneïtat per retenir compostos moderadament polars	Alta	Baixa	Mitja
Velocitat d'anàlisi	Mitja	Mitja	Alta
Cost instrumental	Baix	Baix	Alt
Cost de tangibles (solvents, columnes, etc.)	Mig	Mig	Baix
Bibliografia de mètodes disponibles	Alt	Mig	Baix
Robustesa i Sensibilitat	Alt	Mig	Baix

En conclusió, la columna HSS T3 va ser utilitzada per separar TrOCs en un rang de polaritat (log D_{ow}) entre -2.3 i 5.5, mentre que la BEH Amide es va centrar en compostos més polars, amb un rang (log D_{ow}) de -3.9 a 1.0. Es va optimitzar un mètode de separació combinat amb HSS T3 per a 106 compostos i la HILIC pels 28 compostos restants. La columna C18 (HSS T3) presenta una major capacitat per ser emprada per un rang ampli de polaritats, mentre que la HILIC ofereix un major rendiment per a compostos polars i molt polars. Tot i això l'ús de les dues columnes es necessari per obtenir una imatge més completa de la contaminació present a les mostres.

IM, una nova dimensió per a la separació de TrOCs

La mobilitat iònica, una tècnica que fa uns deu anys era poc considerada per a l'anàlisi de molècules petites, ha evolucionat fins al punt de poder competir directament amb la LC acoblada a un espectròmetre de masses sense IM (Dodds and Baker, 2019). El que fa tan interessant la IM, és que es pot complementar la separació obtinguda amb les columnes cromaogràfiques podent així afegir una nova dimensió a l'àmbit de la separació de TrOCs (Aly et al., 2022). En aquesta tesi però, s'ha volgut conèixer les capacitats del IM per separar compostos petits (entre 120 i 500 Da) i molt polars (log D_{ow} < 0). Aquesta part de la tesi es va efectuar al centre de Georgia Institute of Technology, sota la supervisió del Dr. Facundo Fernández.

Com ja s'ha esmentat, allà es va fer servir un TWIMS, que requeria d'un calibratge exhaustiu per poder obtenir els CCS dels TrOCs per a que fossin comparables amb els obtinguts mitjançant DTIMS, l'instrument seleccionat com a referència per la comunitat (Baker et al., 2023). Aquest calibrant consistia en la alanina i els seus adductes, tant el de la ionització positiva com en la negativa (Bush et al., 2012; Forsythe et al., 2015). També és important conèixer el gas portador, ja que els valors de CCS poden variar segons el gas emprat sigui nitrogen (N_2) o bé heli (He2). Un cop l'instrument era calibrat (el calibratge es realitzava a diària i prèviament a qualsevol anàlisis) s'obtenien els temps de deriva (DT, del anglès *drift time*) de cada compost analitzat individualment. La introducció dels patrons i mostres es realitzava de forma diferent a la convencional, ja que la font de ionització era TENG (del anglès t*ribo-electric nanogenerator*). Aquesta font de ionització té les avantatges d'usar molt poca quantitat de mostra, alta sensibilitat i capacitat de treballar sense necessitat de buit (Vallejo et al., 2023). A la Figura 3.7 es detalla la disposició i configuració de tots els estris necessaris per generar els ions.

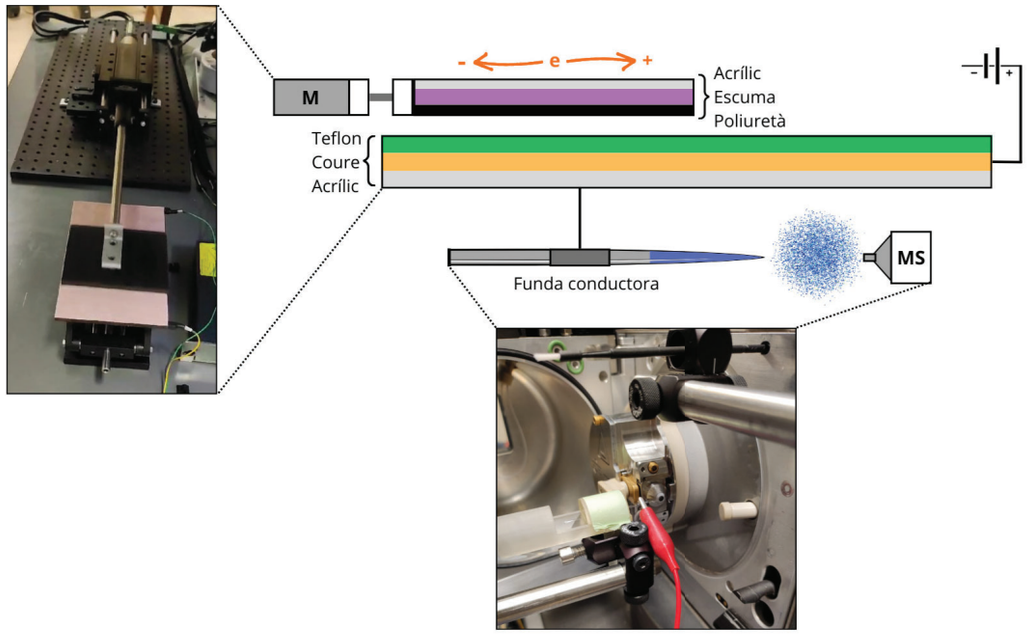


Figura 3.7. Esquema de la font de ionització TENG amb la disposició dels instruments necessaris (adaptat de Vallejo et al. 2023) (Vallejo et al., 2023). Les imatges reals mostren, d'una banda, el dispositiu utilitzat per generar corrent i, de l'altra, la col·locació de l'agulla que conté la mostra, la qual rep el corrent elèctric per facilitar el desplaçament dels ions cap al espectròmetre de masses.

Un cop generada tota la informació dels patrons, com es la polaritat de ionització, els fragments de cada TrOC i, sobretot, el DT per cada un d'ells, es pot procedir a calcular el CCS individualment. Per això es va fer servir un software anomenat TWIMExtract, que ens permet transformar els DT amb CCS i així poder comparar-los o afegir-los a bases de dades de CCS com, per exemple, METLIN-CCS (Baker et al., 2023; Haynes et al., 2017). A la publicació #2, s'han determinat els CCS de 33 TrOCs molt polars, molts d'ells per primer cop. Els CCS que, actualment, es poden comparar, per verificar la exactitud dels CCS determinats amb TWIMS ($^{TWIMS}CCS_{N2}$), són els d'uns quants PFAS (Dodds et al., 2020). A la Taula 3.2 es visualitzen les diferències trobades entre els $^{TWIMS}CCS$ i els CCS determinats amb DTIMS ($^{DTIMS}CCS_{N2}$). Com es pot observar, les diferències són mínimes, cosa que indica que els valors de CCS obtinguts en aquest estudi són prou fiables i vàlids. Obtenir bases de dades de CCS per a compostos orgànics de petita molècula és de vital importància per considerar, definitivament l'IM com a instrumentació per a la separació i subseqüent anàlisis d'aquestes molècules, especialment per a les molècules molt polars, difícilment separables mitjançant una única columna cromatogràfica.

Taula 3.2. $^{TWIMS}CCS_{N2}$ i $^{DTIMS}CCS_{N2}$ de PFBS, PFHxS i PFOS amb la seva diferència relativa.

Nom del Compost	$^{TWIMS}CCS_{N2}$ (Å²)	$^{DTIMS}CCS_{N2}$[1] (Å²)	ΔCCS (%)
PFBS	134.0	133.6	0.30
PFHxS	150.4	150.5	-0.07
PFOS	168.0	168.3	-0.18

[1](Dodds et al., 2020)

IM i LC

Comparar les dues tècniques emprades en aquesta tesi, pot donar una visió general de les avantatges i desavantatges de les dues tècniques. En aquesta secció es compara l'efectivitat de la LC, amb dues columnes ortogonals (C18 i HILIC) juntament amb TWIMS. Per fer-ho, es comparen les senyals, en base a retentivitat i sobretot forma de pic, dels patrons purs d'uns TrOCs seleccionats (Figura 3.7).

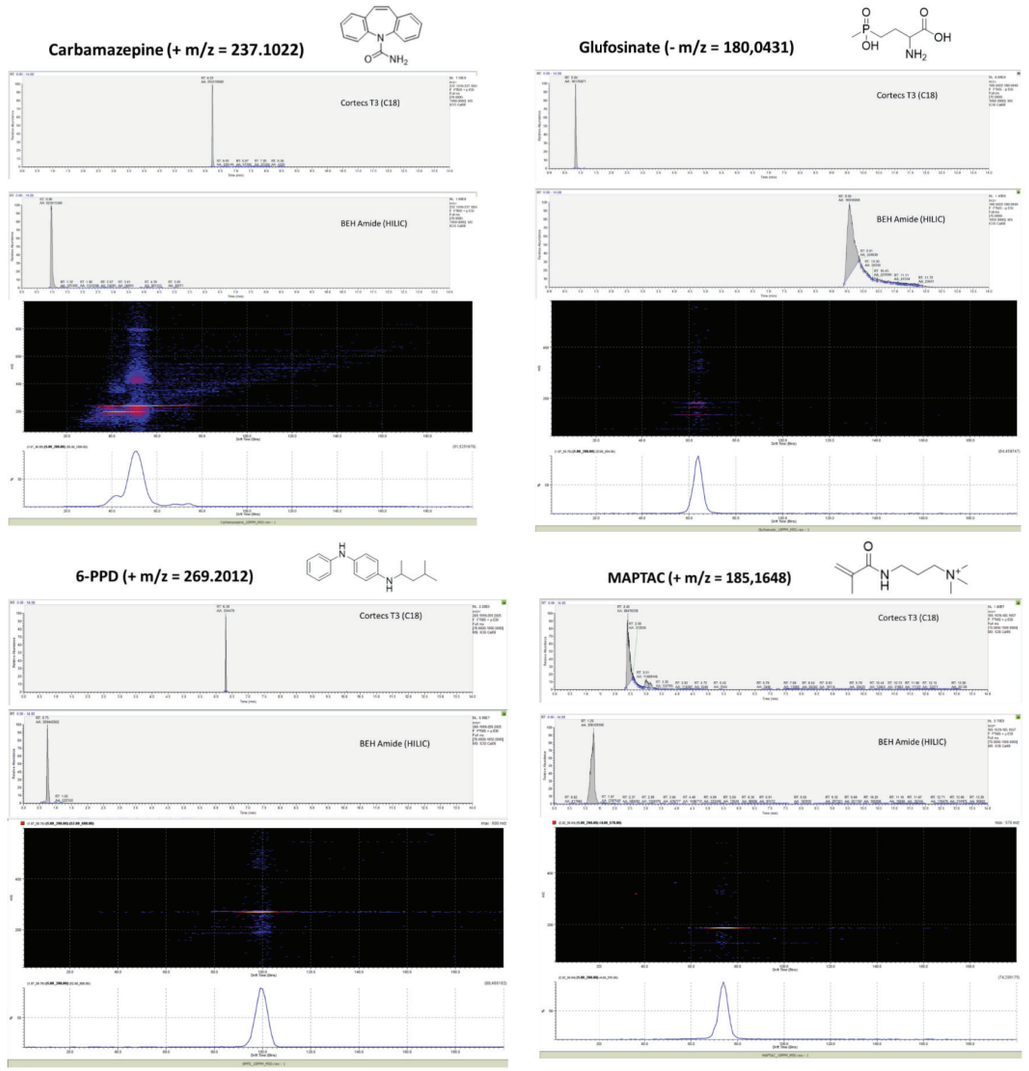


Figura 3.8. Cromatogrames (C18 i HILIC) i mobilograms de quatre compostos.

La Figura 3.8 mostra quatre exemples (carbamazepina, glufosinate, 6-PPD i MAPTAC), TrOCs analitzats amb LC en fase inversa, HILIC i amb TWIMS. El primer compost, la carbamazepina, és un fàrmac molt estudiat al medi ambient i el que mostra es un pic excel·lent emprant fase-normal, un pic molt poc retingut en l'HILIC i, per últim, mitjançant IM no queda ben definit el seu DT degut a una dispersió en l'arribada del ió. Per tant, es pot concloure que la carbamazepina no és un bon candidat per ser analitzat amb IM. Per contra, els altres tres exemples (glufosi-

nate, 6-PPD i MAPTAC) mostren la capacitat de IM per poder obtenir pics amb forma gaussiana i DT acceptables, que comparats amb les dues condicions de LC, el rendiment es major emprant IM. Es important també conèixer altres temps de retenció i DT (o CCS) d'altres molècules presents a les mostres per veure si existeix un solapament entre elles, cosa que dificultaria l'anàlisi, sobretot en cas d'isòmers, ja que la HRMS pot identificar inequívocament compostos amb un *m/z* diferent tot i no ser separats prèviament (Kaufmann, 2012). Tot i això, conèixer si la senyal dels compostos objectiu és adequada o no, és essencial per saber si aquell TrOC pot ser o no analitzat mitjançant la tècnica seleccionada.

Com a conclusió, és una evidència que l'IM pot ser una tècnica de molt interès per solucionar la problemàtica actual amb l'anàlisi de compostos molt polars en el medi ambient. A més, la possibilitat de complementar el IM amb LC fa augmentar el poder de separació dels analits que no es ressolen a configuracions utilitzades habitualment.

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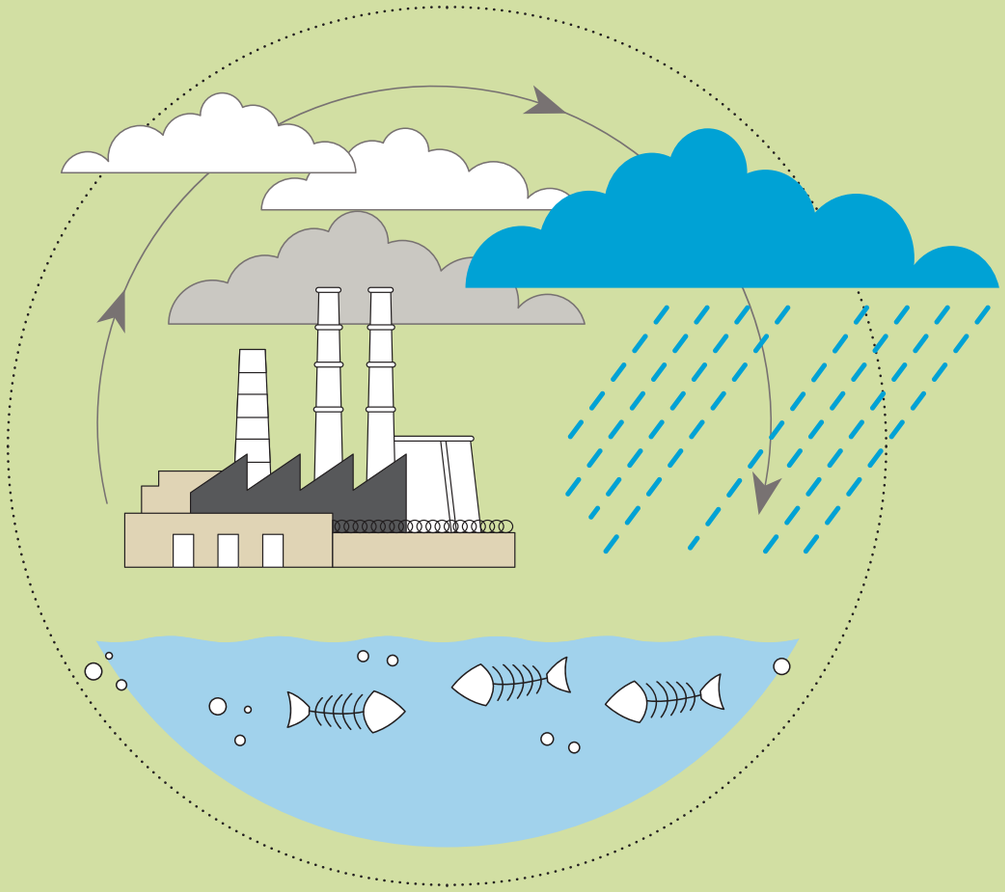
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Capítol

4



4.

Presència i risc dels contaminants orgànics a les aigües urbanes

PRESÈNCIA I RISC DELS CONTAMINANTS ORGÀNICS A LES AIGÜES URBANES

4.1 Introducció

L'aigua subterrània està present a diferents zones del món, incloent les zones urbanes com les ciutats. Per aquesta raó, aquesta tesi planteja la següent pregunta: té l'aigua subterrània de Barcelona, pel que fa a contaminants orgànics, una qualitat acceptable per a poder fer-ne ús per a diversos usos urbans?

Per respondre aquesta qüestió, no només és necessari centrar-se en l'anàlisi de l'aigua subterrània, sinó que també cal abordar la qualitat de les fonts de recàrrega que hi contribueixen. Per tant, se sap que l'aigua subterrània urbana rep aigües de diferents tipus com: 1) L'aigua superficial des de rius (Labad et al., 2023), ja que Barcelona està envoltada de dos rius principals, el riu Llobregat i el riu Besòs els quals part de l'aigua que porten recarrega els aqüífers (Vázquez-Suñé et al., 2010). 2) L'aigua de pluja en una zona urbana genera una escorrentia que pot arrossegar partícules i dissoldre contaminants de tota mena que poden infiltrant-se al sòl i recarregar les aigües subterrànies (Mutzner et al., 2023;

Vázquez-Suñé et al., 2010). 3) Aigua provinent de pèrdues del sistema de clavegueram de la ciutat. Malauradament, el sistema de clavegueram de qualsevol ciutat pateix pèrdues d'aigua i Barcelona no és una excepció, fent que aquesta aigua pugui arribar i recarregar els aqüífers locals (Vázquez-Suñé et al., 2010). Conèixer la qualitat de cada una d'aquestes aportacions d'aigua es vital per saber de què i com l'aigua subterrània urbana es contamina.

En general, cada una de les fonts de contaminació pot aportar una quantitat i un tipus de TrOCs específics. L'aigua superficial, àmpliament coneguda per l'abocament dels efluents de les estacions de depuradores d'aigua residual, pot contenir grans quantitats de TrOCs de tota mena (pesticides, fàrmacs, productes de cura personal, drogues, etc.), podent arribar fins la desembocadura del riu. Això es degut a que les WWTP no son dissenyades per l'eliminació dels TrOCs, especialment els més polars (Loos et al., 2013). De mateixa manera, l'aigua residual provinent de les pèrdues del clavegueram, pot acumular fàrmacs, productes d'higiene i cura personal principalment, i d'altres TrOCs en menor mesura (Loos et al., 2013; Vázquez-Suñé et al., 2010). D'altra banda, l'aigua d'escorrentia urbana, que arrossega partícules atmosfèriques i també les presents als carrers urbans, tendeixen a arrossegar TrOCs volàtils o aquells adsorbits a la matèria o particulats orgànics (Mutzner et al., 2023; Zhang et al., 2024). A més, residus urbans d'activitats antropogèniques com poden ser escombraries, residus provinent dels vehicles o burilles de cigarretes, també aporten TrOCs a l'aigua d'escorrentia (Dobaradaran et al., 2021; Zhang et al., 2024). Per tant, l'aigua d'escorrentia es pot considerar la més complexa de les tres principals fonts de recàrrega de l'aigua subterrània, ja que a més de ser molt bruta degut al alt contingut de matèria orgànica (gairebé com l'aigua residual), aquesta pot contenir compostos provinent de moltes fonts, destacant els compostos industrials com, per exemple, alguns precursors de la industria del plàstic (ε-caprolactam o melamina) (Mutzner et al., 2023). Val a dir que en entorns urbans, l'aportació de l'aigua d'escorrentia juga un paper molt important, a més que la informació d'aquesta font de recàrrega pel que fa als TrOCs es molt escassa (Vázquez-Suñé et al., 2010; Zhang et al., 2024).

Per conèixer l'estat de l'aigua subterrània, es important el mostreig de

la mateixa, intentant obtenir una mostra representativa del pou mostrejat i també, un anàlisi robust i sensible per poder detectar i quantificar els TrOCs presents amb la màxima precisió. A la secció de *Mostreig* s'explica, no només com es va efectuar el mostreig de l'aigua subterrània, si no que també es detalla el mostreig de l'aigua superficial (riu) i d'escorrentia.

Identificar els TrOCs presents a les masses d'aigua pot ser un repte. Diverses estratègies es poden seguir, aquí ens centrarem en dues, el anàlisis dirigit, explicat anteriorment al *Capítol #1* i el anàlisis per sospitosos. L'últim es basa amb l'anàlisi de mostres on es pretén incloure un ampli ventall de TrOCs on se sospita que poden estar presents a les mostres seleccionades (Gago-Ferrero et al., 2015). Aquest anàlisi, mitjançant HRMS, presenta un clar avantatge respecte a l'anàlisi dirigit, ja que permet obtenir una imatge més precisa de les mostres estudiades. D'altra banda, l'anàlisi quantitatiu pot ser menys precís o necessitar d'un segon anàlisi per incloure els patrons dels compostos identificats i així realitzar una quantificació precisa.

Un cop identificats els TrOCs presents a les aigües urbanes, s'ha d'anar un pas més enllà per resoldre la pregunta inicial que ens hem plantejat i veure quin risc medi ambiental i per a la salut humana presenten les substàncies trobades. Normalment, les concentracions trobades al medi ambient estan al ordre de les parts per trilió o, el que és el mateix, nano grams per litre (ng $L^{-1)}$. Aquestes concentracions són molt baixes, per tant, conèixer la toxicitat de cada una dels TrOCs trobats, el que es crucial per conèixer l'abast del problema de la seva presència. Per això, hi ha diverses formes per poder explicar el risc medi ambiental però que tenen una finalitat comuna, identificar el risc d'un contaminant depenent de la seva concentració i altres factors toxicològics, pot posar en risc al ecosistema estudiat, incloent organismes vius, tant animals com vegetals.

Aquest capítol, se centra en la detecció i quantificació de TrOCs amb diferents propietats físico químiques en aigua subterrània de diversos pous de la ciutat de Barcelona i les seves fonts de recàrrega, com el riu Besòs i l'aigua d'escorrentia urbana, mitjançant dos mètodes d'anàlisi, segons la seva polaritat, a més de dos mètodes de detecció: dirigit i de sospitosos.

4.2 Metodologia

Càlculs

En aquesta tesi, el coeficient de risc ecotoxicològic (ERQ, de l'anglès *ecotoxicological risk quotient*) s'ha utilitzat en les publicacions #3 i #7, així com una avaluació de riscos per a la salut humana, calculant el coeficient de risc (HRQ, de l'anglès *Health risk quotient*), emprat en les publicació #4 (vegeu les equacions 4.1 - 4.4).

$$ERQ = \frac{Concentration}{PNEC} \quad \text{Eq. 4.1}$$

$$PNEC\ (\frac{ng}{L}) = \frac{EC50}{AF} \quad \text{Eq. 4.2}$$

$$HRQ = \frac{Concentration}{DWEL} \quad \text{Eq. 4.3}$$

$$DWEL\ (\frac{ng}{L}) = \frac{ADI*BW}{DWI*AB*FOE} \quad \text{Eq. 4.4}$$

Les Equacions 4.1 i 4.2 són les que descriuen l'avaluació del risc mediambiental de cada TrOC, sent la concentració predita sense efecte (PNEC, de l'anglès *predicted no-effect concentration*) la concentració màxima d'un TrOC en el medi ambient sense efecte nociu per a la majoria d'espècies. Aquest valor determina la toxicitat del compost, com més petit sigui, més tòxic. En aquesta tesi els valors del PNEC varien des de 0.02 a 8700 que corresponen als medicaments atorvastatina i acyclovir respectivament. EC_{50}, és a dir, concentració eficaç mitjana, es refereix a la concentració d'un TrOC que causa un efecte al 50 % de la població d'organismes exposats. El factor d'avaluació (AF, de l'anglès *assessment factor*) es un valor arbitrari que varia depenent de la cadena tròfica del organisme testejat (Zhang et al., 2024). D'altra banda, les equacions 4.3 i 4.4 es van emprar per avaluar el risc per a la salut humana. Primerament, el nivell equivalent d'aigua potable (DWEL, de l'anglès *drinking water equivalent level*) es necessari per poder obtenir valors equiparables a aigua potable, provinents d'altres cossos d'aigua com aigua subterrània (Kondor et al., 2021). Per obtenir el DWEL, cal conèixer la ingesta diària acceptable (ADI, de l'anglès *acceptable daily intake*) d'un TrOC, el pes corporal (BW, de l'anglès *body weight*), que depèn de l'etapa de la vida estudiada, la taxa

d'ingestió diària (DWI de l'anglès, *drinking water ingest*), també depenent de l'interval d'edat estudiat i, per últim la fracció del TrOC absorbida al tracta intestinal (AB, de l'anglès *absortion*) i la freqüència d'exposició (FOE, de l'anglès *frequency of exposure*) on totes dues al tractar-se d'aigua, es consideren d'un valor de 1 (EFSA, 2016). Aquestes mesures són molt importants per poder conèixer l'estat qualitatiu real de l'aigua urbana de Barcelona en base als TrOCs analitzats.

Mostreig

Les mostres incloses en aquesta tesi, exceptuant les analitzades a l'estada doctoral, han sigut recol·lectades a la ciutat de Barcelona. L'aigua de pou va ser mostrejada de manera heterogènia i en dos estacions diferents, estiu i hivern, podent veure diferències temporals de l'aigua subterrània. De la mateixa manera, el riu Besòs en la seva etapa final, la més propera a la ciutat, juga un paper important. Degut a que avui dia no es disposa de mostrejadors passius robustos y eficients dissenyats per a captar compostos polars, en aquesta tesi les mostres d'aigua superficial varen ser recol·lectades com a mostres puntuals. A més, per tal de tenir en compte les diferencies estacionals en base a la concentració dels TrOCs (èpoques d'estiu amb cabals més baixos solen arrossegar concentracions més altes de TrOCs) i a l'ús dels mateixos (per exemple, al hivern s'usa una quantitat més alta d'antibiòtics (Yi et al., 2019)), es van recollir mostres del Besòs cada mes durant tot un any. Per últim, les mostres d'escorrentia es van recollir durant l'època més plujosa de Barcelona, normalment la primavera. Degut a que la situació geogràfica de Barcelona no afavoreix en excés la presència de pluges, les diferencies temporals són complicades d'analitzar però no les espacials i, per això, les mostres d'escorrentia varen ser recollides en tres districtes diferents de la ciutat amb variacions en la densitat de població, tràfic vehicular i edificació.

El fet de mostrejar pous urbans conté intrínsecament, la dificultat de coordinar-se amb les autoritats que gestionen els aqüífers de la ciutat per poder accedir-hi. El principal organisme amb el que vàrem poder col·laborar va ser BCASA (Barcelona Cicle de l'Aigua Societat Anònima). les mostres d'aigua subterrània es van recollir amb el permís i l'ajut de BCASA, es va fer servir una bomba peristàltica, la qual deixàvem córrer

aigua durant uns 15 minuts per evitar agafar aigua exclusivament de la capa superior i després s'omplien ampolles d'1L de plàstic de polietilè (Figura 4.1). D'altra banda, el mostreig de l'aigua superficial va ser al riu Besòs, es va efectuar en un sol punt, prenent 1L usant les mateixes ampolles (Figura 4.1). Les mostres de pluja van ser recol·lectades en tres diferents àtics dels barris de Bon Pastor, Poblenou i Sant Antoni, col·locant un contenidor de plàstic PET de 8L, net i buit, prèviament a un esdeveniment de pluja. Les mostres d'escorrentia varen ser recollides de l'aigua del primer rentat (*first-flush* en anglès) això va dificultar la seva presa, ja que aquestes havien de ser únicament aigua de pluja que després d'arribar al sol urbà i patir l'escorrentia, s'escolés cap al clavegueram. A la Figura 4.1 es mostra el dispositiu emprat, on ampolles d'uns 5L de vidre eren emplenats d'aigua d'escorrentia que, un cop omplerts, posseïen un sistema d'auto tancat, que un cop l'ampolla s'emplenava quedava tancada, permetent així recollir aigua d'escorrentia de primer rentat, exclusivament.



Figura 4.1. Mostreig de: **A**) Pous d'aigua subterrània; **B**) Punt exacte de mostreig del riu Besòs; i **C**) Sistema de recol·lecta d'aigua d'escorrentia urbana de primer rentat.

Com a resum, la publicació #3 estan centrades en l'anàlisi d'aigua subterrània influenciada pel riu Besòs i per tant, els mostrejos han sigut realitzats seguint la Figura 4.1 A i B, mentre que les publicacions #4 i

#5 es centren en l'anàlisi d'aigua d'escorrentia de Barcelona i s'aplica el sistema de mostreig mostrat a la Figura 4.1 C.

Anàlisi

Al capítol 3 d'aquesta tesi, s'han descrit tots els mètodes analítics desenvolupats i aplicats en els articles d'aquest capítol. A la publicació #3, el mètode d'extracció emprat ha estat la SPE de multi capa i els analits varen ser separats, mitjançant una columna cromatogràfica Acquity HSS T3. D'altra banda, a la publicació #4 on s'analitza aigua d'escorrentia de Barcelona, el mètode d'extracció emprat va ser la VAE amb la posterior separació dels analits a la columna HILIC BEH Amide, ja que l'estudi es centra en la detecció i quantificació de TrOCs molt polars.

Com a excepció, a la publicació #5, tot i emprar la VAE per enriquir les mostres d'escorrentia, la separació i detecció dels analits es va realitzar amb una columna de fase inversa, això si, molt similar a Acquity HSS T3, la columna Acquity Premier HSS T3 (100 mm * 2.1 mm * 1.8µm). La diferencia principal entre les la columnes es tracta de la tecnologia Premier, que minimitza la pèrdua de mostra i evita que certs compostos quedin retinguts a la superfície interna de la columna (Tanna et al., 2021). Finalment, respecte la detecció dels analits, tot i que va ser mitjançant un espectròmetre de masses, no es va emprar l'Orbitrap si no el temps de vol, concretament, l'Impact II Q-ToF-MS de Bruker (Bruker Daltonik GmbH, Alemanya), podent així analitzar TrOCs mitjançant GC. Això va ser possible gràcies a una col·laboració amb la Universidad de Cádiz, que disposaven d'un QToF-MS acoblat a ambdós cromatografies, GC i LC. La cromatografia de gasos es va emprar per l'anàlisi de compostos de volatilitat mitja i alta a l'aigua d'escorrentia provinents de l'atmosfera. L'extracció per realitzar aquest anàlisi es va fer mitjançant l'extracció absortiva amb barra d'agitació, on els contaminants s'adsorbeixen a la barra d'agitació i s'elueixen usant acetat d'etil al ultrasons. A més, es va realitzar un anàlisis de sospitosos (*suspect screening* en anglès) per detectar aquells compostos presents a les mostres.

4.3 Resultats

Els resultats d'aquest capítol es resumeixen en tres articles, dos ja publicats i un enviat a revista. S'han analitzat mostres d'aigua subterrània, d'aigua superficial i d'escorrentia urbana de la ciutat de Barcelona, per conèixer la presència de TrOCs i el possible impacte en la qualitat de l'aigua subterrània tant del riu Besòs com de l'escorrentia urbana. Les publicacions són:

- Publicació #3: **Labad, F.**, Ginebreda, A., Criollo, R., Vázquez-Suñé, E., Pérez, S., Jurado, A., 2023. Occurrence, data-based modelling, and risk assessment of emerging contaminants in alluvial aquifer polluted by river recharge. Environ. Pollut., 316, 120504. https://doi.org/10.1016/j.envpol.2022.120504

- Publicació #4: **Labad, F.**, Santana-Viera, S., Jiaqi, X., Borrell-Diaz, X., Teixidó, M., Pérez, S., 2025. Surveillance and environmental risk of very mobile pollutants in urban stormwater and rainwater in a water-stressed city. Journal of Hazardous Materials, 486, 136959. https://doi.org/10.1016/j.jhazmat.2024.136959

- Publicació #5: Santana-Viera, S., **Labad, F.**, Pintado-Herrera, M., Montemurro, N., Teixidó, M., Lara-Martín, P., Pérez, S., 2024. Comprehensive HRMS-Screening of persistent, Mobile and toxic compounds in first flush urban stormwater. Enviat a NPJ Clean Water.

PUBLICACIÓ CIENTÍFICA #3

Occurrence, data-based modelling, and risk assessment of emerging contaminants in an alluvial aquifer polluted by river recharge

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Occurrence, data-based modelling, and risk assessment of emerging contaminants in an alluvial aquifer polluted by river recharge☆

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ABSTRACT

This research presents the occurrence and fate of 121 contaminants of emerging concern (CECs) in an urban aquifer polluted by river recharge through a data-base modelling. Afterwards, risk quotients (RQs) are computed to determine the risk posed by CECs to human health. To this end, groundwater and river water samples were collected in four campaigns conducted from February to May 2021. Results show that 46 CECs are ubiquitous in groundwater and their concentrations vary several orders of magnitude, ranging from below the limit of quantification to $44.5{\cdot}10^3$ ng/L for iopamidol. Transformation products (TPs) are usually detected at lower concentrations than those of the parent substances but there are some exceptions (i.e., fipronil sulphide, fipronil sulfone and O-desmethylvenlafaxine). River concentrations are higher than those detected in groundwater for some CECs, indicating the occurrence of natural attenuation processes when river water infiltrates the aquifer. A data-based advection-reaction modelling is proposed and tested for ca. 40 substances with detection frequencies higher than 90%. It provides useful quantitative information regarding the dynamic behaviour of the variables monitored, expressed in terms of characteristic length, entropy and synchronized state contribution. Finally, risk quotients (RQs) are used to assess the human health risk posed by the ubiquitous CECs in groundwater. Most CECs do not pose any risk to the different life stages considered, as the RQs evaluated are lower than 0.01. However, the pharmaceuticals valsartan and its TP valsartan acid show RQs higher than 1, indicating that these substances might be harmful to human beings.

1. Introduction

Sustaining healthy living conditions in urban areas is a challenge in the European Union and worldwide, and central to this mission is the supply of freshwater resources (Howard, 2015). However, rapid urban growth and climate change will impact water resources, which are already limited (Malek et al., 2018). Therefore, freshwater scarcity is encouraging research into potential alternative water resources such as urban groundwater. In urban settings, groundwater is sometimes pumped to avoid seepage problems in underground structures, and thus the question that arises is whether urban groundwater might be used as safe drinking-water to cover the growing water demand. To answer this question, it is necessary to investigate the groundwater quality.

Groundwater quality might be deteriorated in urban aquifers because they contain a vast array of organic and inorganic contaminants (Burri et al., 2019). Among these pollutants, research on contaminants of emerging concern (CECs) and their transformation products (TPs) in groundwater has increased enabled by their recent detection with advanced analytical techniques (Fagnani et al., 2022; Siddiqui et al., 2017). CECs encompass different groups such as pharmaceuticals, illicit drugs, hormones, industrial substances, artificial sweeteners, and life-style substances, among others. Furthermore, there is a growing interest in pharmaceuticals and their TPs, as their extensive use for diagnoses and treatment of a vast array of diseases in humans and animals

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has led to unforeseen consequences such as antimicrobial resistance (Kovalakova et al., 2020), and urban groundwater pollution (García-Gil et al., 2018; López-Serna et al., 2013; Rusiniak et al., 2021). Moreover, some TPs can remain pharmacologically active (i.e., retaining the biological activity of the parent compound) and might have undesirable toxic effects (Menz et al., 2017).

The main pollution source of CECs in urban areas is the effluents of wastewater treatment plants (WWTPs), as they are not specifically designed to remove them completely (Couto et al., 2019). As a result, they are released into urban surface water bodies such as rivers, reaching groundwater. Additional contamination sources are effluents from hospitals and sewerage networks (Aydin et al., 2019; Wolf et al., 2012). The continuous input of these substances in urban groundwater from the aforementioned sources might pose a potential risk to human health, especially if drinking water is produced from groundwater. Generally, the risk of human health exposure to CECs is low (Kondor et al., 2021; Riva et al., 2018; Sharma et al., 2019). However, according to a recent investigation conducted by Qin et al. (2020), the sulphonamide antibiotic sulfamethazine represented from moderate to high risk to human health, specifically for infants. Consequently, the occurrence of CECs in groundwater may: (1) be a water resource management challenge in many cities where groundwater is sensitive to CECs contamination in times of water shortage (i.e., limiting its use) and (2) pose a risk to human health, as some of them might bioaccumulate in the human body. Hence, it is necessary to set groundwater quality standards for these unregulated substances, as groundwater will be an important contributor to drinking water production in the potential future water scarcity scenario boosted by climate change.

Although the European Directive 2014/80/EC (European Commission, 2014) encourages the establishment of a Watch List for groundwater pollutants that pose a potential risk to groundwater bodies (i.e. CECs), current legislation about groundwater contamination only considers pesticides (European Commission, 2006). In this context, investigating the occurrence of a wide range of unregulated CECs in urban groundwater is required to cover this existing regulatory gap. However, to date, most studies conducted in urban groundwater have focused on few substances (i.e., selected pharmaceuticals or specific therapeutic groups) (e.g., Jurado et al., 2021; Osenbrück et al., 2007; Rusiniak et al., 2021; Sharma et al., 2019; Tran et al., 2014; Wolf et al., 2012). For example, the occurrence of selected pharmaceuticals and personal care products (PPCPs) has been recently investigated in the shallow aquifer underlying Kraków city (Poland) (Rusiniak et al., 2021). Similarly, the occurrence of 17 selected PPCPs has been reported in the urban groundwater of Singapore by Tran et al. (2014). However, studies that compromise a wide array of CECs and their TPs, which have been barely investigated (Postigo and Barceló, 2015), in urban groundwater are scarce (García-Gil et al., 2018; Kondor et al., 2021; López-Serna et al., 2013).

Our knowledge of the aquifer's qualitative status typically relies on discrete spatial and temporal experimental observations of a set of physical, chemical, or biological parameters, organized under what is commonly known as a "monitoring network". The accuracy of the "picture" obtained depends on both the spatial and temporal resolution of the network used. However, experimental measurements are constrained by the economic cost of the whole sampling and analytical process, often expensive, as is the case of CECs, and thus unaffordable, particularly for routine monitoring. Alternatively, modelling (Carrera et al., 2022) allows for predicting the spatial-temporal variable's profile at any resolution at affordable computing costs. However, it often involves high uncertainty in the parametrization of the processes modelled and ultimately requires experimental validation as well. Here we aim at reconciling both approaches –monitoring and modelling– deriving simple steady-state advection-reaction (reactive-transport) models from monitoring data, based on network theory concepts (Aida et al., 2020; Ginebreda et al., 2018). The application of these models allows obtaining relevant quantitative information relative to the dynamics of the measured contaminants such as the relative importance of the two main processes involved, i.e., the transport across the aquifer vs. the local depletion, which provides an insight into their persistence. Related models have been already used in other domains, such as social interaction (i.e. internet) networks (Aida et al., 2020).

The objectives of this research are: (i) to investigate the occurrence of 121 CECs, including 19 TPs in an urban aquifer; (ii) to propose an advection-reaction model to understand their behaviour in the aquifer; and (iii) to assess the human health risk of CECs and TPs in groundwater. The list of CECs includes illicit drugs, industrial substances, UV filters, hormones, artificial sweeteners, life-style substances, pesticides, and pharmaceuticals belonging to different therapeutic groups, such as antibiotics, anti-hypertensives, analgesics/anti-inflammatories, psychiatric drugs, among others.

2. Methodology

2.1. Study area and sampling

The study area is located in the lower part of the Besòs River Delta in the densely populated city of Sant Adrià del Besòs (Fig. 1). The Besòs River Delta aquifers suffered heavy water extraction at the end of the 19th century, producing large drawdowns that were progressively decreasing when many industries migrate from the city since 1970 (Vázquez-Suñé et al., 2005). This situation has led to a recovery of the heads, causing problems to underground structures that were constructed after the 1970s such as the parking facility of the plaça de la Vila. This parking lot continuously had seepage problems and there is a drainage system that continuously pumps a flow rate of about 150–200 L/s (Jurado et al., 2017). Most of this pumped urban groundwater is directly discharged into the sewerage system, and thus, this valuable resource is not properly managed.

The parking facility is located in the shallow aquifer of the Besòs River Delta, which is an unconfined aquifer constituted by sands and gravel. This aquifer is characterized to have suboxic to denitrifying conditions owing to the low concentrations of dissolved oxygen and nitrate (on average 1.2 mg/L and 3.3 mg/L, respectively) and the presence of ammonium (4.3 mg/L). Moreover, the difference in nitrate concentration between the Besòs River, reaching concentrations of 55 mg/L, and the groundwater reflects the denitrification process occurs when river water infiltrates the aquifer (Jurado et al., 2015). Different recharge sources have been identified in this shallow aquifer, such as natural rainfall, urban runoff, leakage from the drinking water and sewage networks, and the Besòs River (Vázquez-Suñé et al., 2010). The major contributor to the aquifer recharge in the study area is the polluted Besòs River, representing near to 90% of the total recharge (Jurado et al., 2013). The Besòs River has an irregular and torrential regime, which is controlled by the rainfall events that mainly take place in spring and autumn. Following rain events, the stream flow rate might increase up to 40 to 50 times (i.e., the average streamflow is 4 m^3/s but it can reach 100 m^3/s after heavy rainfalls). The Besòs River receives discharges of raw sewer water and effluents from WWTPs, leading to the contamination of groundwater since the aquifer is hydraulically connected with the river.

Groundwater flows from the river to the parking area due to the intensive pumping activity, which makes the aquifer system very dynamic with residence times of 35 days (Fig. 1b and c). The drainage system consists of four pumping wells (ADPM, ADPQ, ADPR, and ADPW in Fig. 1b) located near the parking area and there is also a monitoring network from where groundwater samples for the analysis of the target substances were collected. Samples were collected from the sites SAP and ADS-n and the well ADPW (Fig. 1). River and groundwater grab samples were taken once a month from February to May 2021 (C1 to C4). Groundwater observation points were purged and samples were taken after the stabilization of field parameters (e.g., temperature, pH, and electrical conductivity). All water samples were collected in pre-

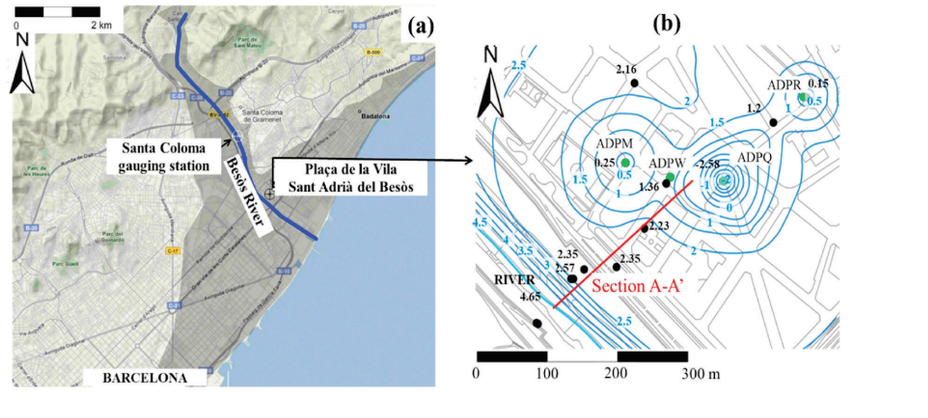


Fig. 1. **(a)** Location of the Besòs River Delta (Barcelona, NE Spain), **(b)** piezometric surface at Plaça de la Vila of Sant Adrià del Besòs and drainage system composed by the pumping wells ADPM, ADPW, ADPR and ADPQ (green dots), **(c)** Section A-A′ showing the major direction of the groundwater flow and the residence time (days) distribution from the river to the parking lot. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

cleaned amber glass bottles, stored in a field refrigerator, and shipped to the laboratory, where they were vacuum filtered through 0.7 μm glass fiber filters. Finally, water samples were stored at −20 °C until analysis.

2.2. Analytical methods

Regarding the analytical method used, 500 mL of filtered groundwater was passed through an SPE cartridge. Briefly, a multi-sorbent solid phase extraction (mlSPE) was performed to pre-concentrate the samples, with a final concentration factor of 1000. The two-layer cartridges were prepared manually, with 200 mg of HLB sorbent in the upper layer and a mixture of 150 mg of PPL bond elute, 100 mg of WAX, and 100 mg of WCX in the lower layer. After extraction of the sample, the cartridge was eluted with 2 × 3 mL 5% NH_3 in MeOH:EtOAc (50:50, v/v), followed by 2 × 3 mL 2% FA in MeOH:EtOAc (50:50 v/v), 3 mL MeOH:EtOAc (50:50 v/v). The eluate was then evaporated under a gentle stream of nitrogen and reconstituted with 500 μL of water/acetonitrile (95:5). The method was developed by Labad et al. (2022) for surface water and groundwater samples. Finally, groundwater samples were analyzed using an HPLC coupled to a high-resolution mass spectrometer (HRMS), the Q-Exactive Orbitrap. The chromatographic separation was performed using a reverse phase column, an Acquity HSS T3 (100 × 2.1 mm, the particle size of 1.8 μm). For the positive ionization analysis, the mobile phase consisted of a gradient of 5 mM ammonium acetate and 0.1% formic acid and acetonitrile while negative ionization analysis was performed with a gradient of 2 mM ammonium fluoride and acetonitrile. A full scan/targeted-data-independent acquisition (FS-DIA) was performed using a pre-defined inclusion list where the isolation window was set to 1.5 m/z (Labad et al., 2022). The total run for each sample was 19 min and the targeted substances were unequivocally detected and quantified using both standards and internal standards. This highly sensitive method provided limits of quantification (LOQ) between 0.06 and 0.98 ng/L and recoveries in the range of 40–120% were accepted (Table S1).

2.3. Simple advection-reaction model based on network theoretical concepts applicable to an aquifer network of discrete monitoring measurements

2.3.1. Model description

Briefly, the aquifer studied can be described as a network (Fig. 1c) of spatially distributed connected sites (nodes) in which we carry out measurements of a variable x (say, the concentration of a contaminant at a certain time). Let the state of node i be x_i so that $\mathbf{x} = (x_1, \ldots, x_n)$ is the n-dimensional state vector of measurements of variable x for all the n nodes. It is assumed that the time evolution of x_i can be described by the following simple kinetic equation

$$dx_i/dt = -k \bullet x_i + \overline{v} \bullet \sum_{j=1}^{n} W_{ij}(x_i - x_j) + \delta_i - k \bullet x_i + \overline{v} \bullet \sum_{j=1}^{n} L_{ij} x_j + \delta_i \quad (1a)$$

Written in compact vector form:

$$\dot{\mathbf{x}} = -k \cdot \mathbf{x} + \overline{v} \cdot \mathbf{L}\mathbf{x} + \boldsymbol{\delta} \quad (1b)$$

where $\dot{\mathbf{x}}$ is the vector of time derivatives $(\frac{dx_1}{dt}, \frac{dx_2}{dt}, \ldots, \frac{dx_n}{dt})$, the first term on the right side of the equation reflects a first-order decay process with a

rate constant k, and the second term an advection process between adjacent (connected) sites, characterized by a mean advection velocity $\bar{v}$ (see comment below), **W** is the weighted adjacency matrix that captures the network topology ($W_{ij} = W_{ji} = \frac{1}{r_{ij}}$, where r_{ij} is the distance between i and j if they are directly connected, and 0 otherwise) and **L** the weighted symmetric Laplacian defined as $\mathbf{L} = \mathbf{D} - \mathbf{W}$, where **D** is the node degree diagonal matrix, with $D_{ii} = \sum_{j=1}^{n} A_{ij}$) (Yamada, 2021). The terms δ_i are local inputs or sinks at each site i. Assuming that the measurements correspond to a stationary state ($\dot{\mathbf{x}} = 0$), rearranging the above equation, and dividing both sides by k, it becomes:

$$\mathbf{x} = \bar{v}/k \cdot \mathbf{L}\mathbf{x} + \boldsymbol{\delta}/k \quad (2)$$

Numerically, the parameter $\bar{v}/k$ is calculated by ordinary least squares (OLS) as the slope of the regression line of **Lx** over **x** with the intercept set equal to 0. Note that the term $\bar{v}/k$ has the dimension of length and can be interpreted as a *characteristic length* (referred to hereafter as ℓ) that quantifies the effective travel distance of the contaminant the before decay process dominates. Also, $\bar{v}/k$ may be interpreted as a measure of the relative relevance of the two processes involved, i.e. the advection (between neighbor nodes) and the decay (local at each node). It can be shown that the inverse of the OLS calculated slope ($\rho = k/\bar{v}$) is equal to:

$$\rho = \mathbf{x}^{\mathbf{T}}\mathbf{L}\mathbf{x}/\mathbf{x}^{\mathbf{T}}\mathbf{x} \quad (3)$$

Furthermore, since ρ is the Rayleigh quotient of **x** respect matrix **L**, it may be expressed as

$$\rho = \sum_i c_i^2 \lambda_i \quad (4)$$

with $\sum_i c_i^2 = 1$Where λ_i are the eigenvalues of **L**, $\mathbf{u_i}$ the associated eigenvectors, and $c_i = \mathbf{u}_i^{\mathrm{T}}\mathbf{x}$

This allows defining an entropy S as:

$$S = -\sum_i c_i^2 \ln c_i^2 \quad (5)$$

Entropy S provides an insight into how ρ is allocated among the different eigenstates. The terms c_i^2 capture the respective contribution of each eigenstate i. Among them, c_1^2 associated with the eigenstate correspondent to the smallest eigenvalue of **L**, $\lambda_1 = 0$, with eigenvector $\mathbf{u_1} = (1, 1,..,1)$ is particularly relevant, since it quantifies the contribution of the synchronized state ($x_1 = x_2 = \ldots = x_n$). Full details about the method can be found in (Ginebreda et al., 2022).

2.4. Human health risk assessment

Human health risk characterization is assessed through risk quotients (RQs). The RQs are defined as the ratio of exposure concentration and the threshold of adverse effects in drinking water. The RQs are calculated for different CECs using two methods:

$$RQ = \mathrm{Cmax}/\mathrm{DWEL} \quad (6)$$

$$RQ = \mathrm{Cmean}/\mathrm{DWEL} \quad (7)$$

where Cmax and Cmean are the maximum and the mean groundwater concentrations of a given substance (ng/L) to foresee the worst-case scenario and the normal state risk scenario, respectively. DWEL is the drinking water equivalent level (ng/L). An RQ less than 1 shows that the chemical exposure is less than the benchmark (DWEL), indicating that the exposure is unlikely to result in an adverse effect.

DWEL values are estimated according to Eq. (8) for different life stages (Kondor et al., 2021):

$$DWEL\left(\frac{ng}{L}\right) = \mathrm{ADI\ x\ BW}/\mathrm{DWI\ x\ AB\ x\ FOE} \quad (8)$$

where ADI is the Acceptable Daily Intake of an individual CEC (μg/kg day), BW represents the body weight for the life stages considered (kg) and DWI is the daily ingestion rate of water (L/day) for each age interval (EFSA, 2010) (Table S2). AB represents the fraction of the substance absorbed in the intestinal tract considered to be 1 (i.e., 100% of the maximal value) and FOE is the frequency of exposure assumed to be 1 (i.e., 365 days of the year). ADI values for target substances are collected from literature, ranging from $5.7{\cdot}10^{-2}$ μg/kg day for the antihypertensive valsartan to $12.5{\cdot}10^{4}$ μg/kg day for the contrast agent iohexol (Liu et al., 2019; Parida et al., 2021) (Table S3).

3. Results and discussion

3.1. Occurrence of CECs in groundwater and river water

3.1.1. General results

Results show that 101 out of the 121 CECs are found in groundwater at least in one groundwater sample (above the LOD): 3 steroid hormones, 4 pesticides (among which 3 TPs), 5 drugs of abuse (among which 2 TPs), 3 industrial substances, 3 life-style substances (among which 2 TPs), 3 UV Filters, 4 artificial sweeteners and 76 pharmaceuticals (among which 12 TPs) (Table S4). Forty-six CECs are ubiquitous (i.e., detected in all groundwater samples) and their concentrations vary by some orders of magnitude, ranging from below the LOD to $44.5{\cdot}10^{3}$ ng/L for the contrast media agent iopamidol (Fig. 2 and Table S4).

Figure S1 shows the average concentration of CECs in river water and groundwater (Table S4). These substances are also detected in the Besòs River, usually at average concentrations higher than in the aquifer (Fig. S1), suggesting that natural attenuation processes are occurring when the shallow aquifer of Besòs River Delta is infiltrated by the river water. However, the average concentration of 19 substances exceeds the threshold of 100 ng/L in groundwater. The highest average groundwater concentrations, ordered by increasing concentration, are: cyclamate ($2.2{\cdot}10^{3}$ ng/L), sucralose ($10.3{\cdot}10^{3}$ ng/L), and iopamidol ($12.7{\cdot}10^{3}$ ng/L). Moreover, few CECs present similar or even higher concentrations in groundwater. This is the case with some industrial substances, illicit drugs, pesticides, steroid hormones, and pharmaceuticals such as analgesics/anti-inflammatories, lipid regulators, psychiatric drugs, and antibiotics (Fig. S1).

3.1.2. Temporal distribution profiles

Fig. 3 shows the total concentration of CECs in the river and the groundwater observation points for the four sampling campaigns. River water presents higher concentrations than groundwater in all the samplings campaigns. The minimum concentration of CECs in the river occurs in winter during February and March (C1–C2) with a concentration of $76.4{\cdot}10^{3}$ ng/L in March (C2), but it increases near to 16 times in May (C4), reaching a maximum of $1.2{\cdot}10^{6}$ ng/L. The main contributor to the total contamination in the river in the last sampling campaign is the artificial sweetener cyclamate, representing 92% of the total concentration ($1.1{\cdot}10^{6}$ ng/L). This observation suggests that composite samples could be taken for 24 h to explain the temporal evolution of CEC concentration in the Besòs River.

A similar trend is also observed in groundwater (Fig. 3 and Fig. S2). Generally, CEC concentrations in groundwater are higher in May, which is directly controlled by the CEC occurrence in the Besòs River, as it is the main pollution source (Jurado et al., 2017). This observation is displayed for selected CECs such as sucralose and the pharmaceuticals iopamidol, 5-Desamino-5-oxo-lamotrigine, metoprolol, carbamazepine, 10,11-epoxi carbamazepine and diazepam in Fig. S2, which illustrates the box-plots showing the range of concentrations of selected CECs in the river (yellow) and groundwater for the four sampling campaigns (C1–C4 in blue). The concentration ranges from the low ng/L range for diazepam to some thousands for iopamidol and sucralose. Somewhat lower but still high concentrations are found for

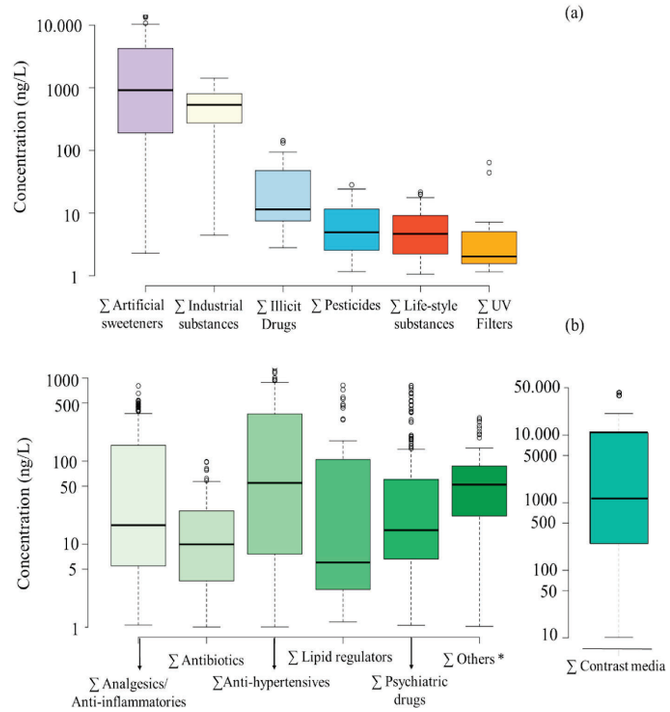


Fig. 2. Box-plot of the concentration of **(a)** artificial sweeteners, industrial substances, illicit drugs, pesticides, life-style substances, UV filters, and **(b)** pharmaceuticals from different therapeutic groups in groundwater. The dots represent the outliers. * Others include the antifungal fluconazole and climbazole, the antiparasitic crotamiton, and the local anaesthetic lidocaine.

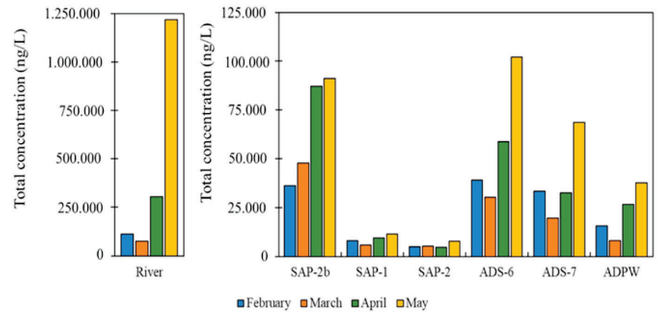


Fig. 3. Total contamination of CECs in Besòs River and groundwater samples from February to May 2021 (C1-February, C2-March, C3-April, and C4-May).

5-methyl-1-H-benzotriazole and lamotrigine (mean concentrations in groundwater are $8.8{\cdot}10^{2}$ ng/L and $4{\cdot}10^{2}$ ng/L, respectively) (Table S4). Many substances are found at concentrations lower than 100 ng/L, such as carbamazepine (mean concentration in groundwater is 78.2 ng/L, Table S4), which levels among the different sampling campaigns are similar in groundwater. TPs are also detected usually at lower concentrations than those of the parent substances (e.g., 5-desamino-5-oxo-lamotrigine and 10,11-epoxi carbamazepine, Fig. S2). However, there are some exceptions, such as the TPs fipronil sulfide, fipronil sulfone, fipronil desulfynil, and O-desmethylvenlafaxine, which average concentrations in groundwater are higher than those of the parent substances (Table S4).

The highest concentrations of CECs are detected in shallow groundwater points SAP-2b and ADS-6, especially in May (Fig. 3). Conversely, the deep points SAP-1 and SAP-2 show the lowest concentrations of CECs throughout the four months. Considering a flow line from the river to the parking area, it seems that the total concentration of CECs decreases when river water infiltrates the aquifer, from the river

to SAP-2, in all the sampling campaigns. Afterwards, the concentrations of CECs increase in the points located in the urban area (ADS-6, ADS-7, and ADPW, Fig. 1b), indicating that it might be an additional source of contamination. Leakage from the sewerage network and urban runoff water represented on average 12% of the total groundwater recharge in these points (6% for each source) (Jurado et al., 2013).

Table S5 summarizes the concentrations of CECs detected in other European urban groundwaters. For example, the average and/or maximum concentrations of artificial sweeteners, the industrial substance bisphenol-A, and most pharmaceuticals reported in this research are higher than those found in García-Gil et al. (2018), Rusiniak et al. (2021) and Wolf et al. (2012). High maximum concentration for 17-α-ethinylestradiol has been reported by Rusiniak et al. (2021) as well as for the antibiotics ciprofloxacin, erythromycin, sulfamethoxazole, and trimethoprim (Szekeres et al., 2018) and the psychiatric drugs meprobamate and primidone (Hass et al., 2012). TPs have been less reported and found at lower concentrations than their parent compounds (López-Serna et al., 2013). These authors reported a maximum concentration of carbamazepine above $1.3{\cdot}10^2$ ng/L but its TPs 10, 11-epoxi carbamazepine and acridone were found at levels below 10 ng/L (Table S5).

3.2. Modelling of CECs in groundwater

The above-described advection-reaction network models (Section 2.3) are applied to substances having detection frequencies equal to or greater than 90% considering the 4 sampling campaigns. For these substances, we calculate (i) the characteristic length (Eqs. (2) and (3)) as a quantitative estimation of their travel distance before decay dominates, (ii) entropy (Eqs. (4) and (5)) as a global measure of the different

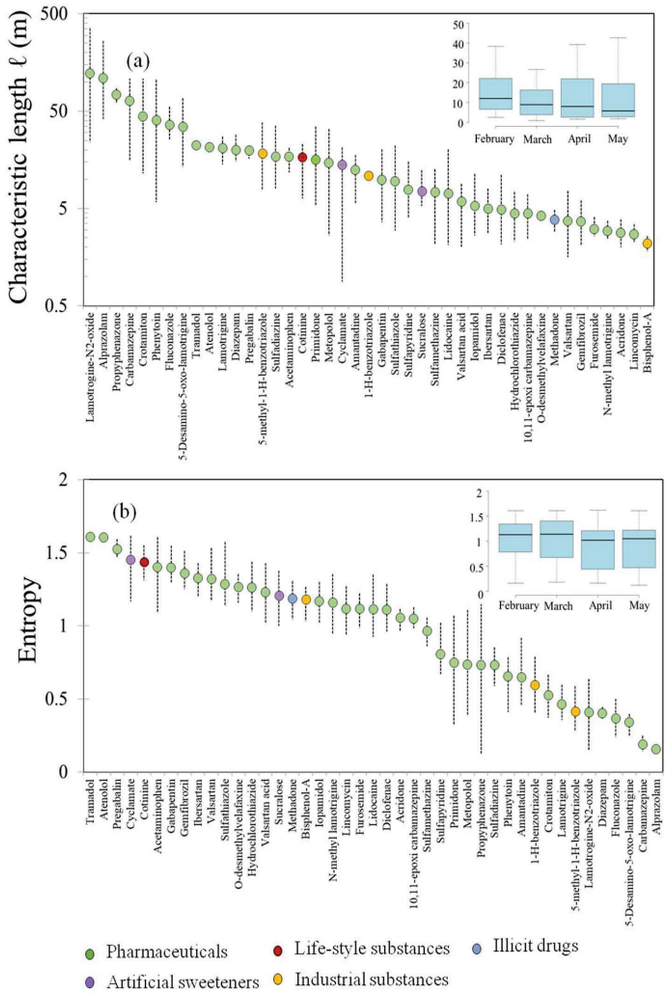


Fig. 4. Values distribution per substance along the 4 months monitored. (**a**) Characteristic length (log scale), and (**b**) Entropy. Bars indicate the maximum and minimum values, and dots are the mean value. On the right corner of each figure, boxplots show the values distribution per month of (**a**) Characteristic length (log scale) and (**b**) Entropy.

eigenstates contribution, and (iii) the contribution of the synchronized state as a measure of the proximity to the equilibrium of the concerned contaminant alongside studied aquifer (Ginebreda et al., 2022).

Characteristic lengths (ℓ) and entropies are shown in Fig. 4a and b respectively (box-plots in right top-corner). In general, ℓ show similar values and dispersions along the four months monitored, appearing only slightly larger in February (C1), whereas entropy values are larger in February–March (C1–C2) as compared to April–May (C3–C4). Considering the individual substances (Fig. 4a and b), although there are differences in their absolute values between months, the relative values (i.e., rank) exhibit some regularities that are reflected in their correlations. For instance, in the case of ℓ, from 0.77 (April–May) to 0.67 (February–March); and in that of entropy from 0.91 (February–March) and 0.74 (April–May) (Spearman coefficient, $p < 0.05$). Noteworthy, comparing the ranks of characteristic lengths and entropies, they exhibit opposite trends. Thus, substances like lamotrigine-N2-oxide, alprazolam, carbamazepine, and desamino-oxo-lamotrigine are at the top of characteristic length and the bottom of the entropy respective ranks (Fig. 4a and b). Note that large ℓ values and low entropy values are both indicative of a relative prevalence of the advection process over decay.

Further analysis of the processes involved can be achieved considering the respective contributions of the different eigenstates of the Laplacian matrix **L** to Eqs. (4) and (5). Specifically, the contribution of the synchronized state (i.e., equal values of x in all nodes) vs. higher states is relevant, considering that a fully synchronized state would have $\rho = 0$ (Eq. (5)), and thus an infinite characteristic length. In that sense, as one may expect, synchronization is aligned with characteristic length. Thus, for instance, in the monthly statistics (Fig. 5), synchronization is slightly higher in April–May (55–90%) than in February–March (45–80%). Concerning the specific substances (Fig. 5), synchronization range from ca. 97%–15%, with alprazolam, carbamazepine, and desamino-oxo-lamotrigine showing the highest values (>90%), again in good ranking correspondence with the characteristic length (Fig. 4a).

3.3. Human health risk assessment

Human health risk evaluation is performed for substances that are ubiquitous in groundwater samples. Additionally, non-ubiquitous substances whose average concentration is higher than 10^2 ng/L are also considered. Among substances that fulfil the aforementioned criteria, RQ cannot be computed for some target CECs, as ADI values are not available in the literature. It is worth mentioning that RQ for the TPs valsartan acid, O-desmethylvenlafaxine, and 5-desamino-5-oxo-lamotrigine are evaluated using the ADI of their parent compound, as their maximum concentrations in groundwater exceed the threshold of 10^2 ng/L ($8.9{\cdot}10^2$ ng/L, $6.6{\cdot}10^2$ ng/L and $1.3{\cdot}10^2$ ng/L, respectively).

Fig. 6 shows the substances presenting RQs above 0.01 for most of the life stages considered and all results (DWEL, $RQ_{MAX,}$ and RQ_{MEAN}) of the human risk assessment are summarized in Table S3. The RQ_{MAX} and RQ_{MEAN} values are below 10^{-2} for most of the target substances, indicating that they pose a negligible risk to human health when considered individually. However, valsartan and its TP valsartan acid exhibit the highest RQs. Valsartan exceeds $RQ_{MAX} > 1$ for all the life stages, ranging from 5.5 for children of 1–2 years old to 1.7 for adults. RQs above 1 do not correspond to immediate risk for the consumer through drinking water ingestion but might require a more detailed risk assessment. Note that the ADI value of valsartan is based on the lowest oral therapeutic dose and a 10^4-safety factor but not on toxicity data as the latter is scarce (Khan and Nicell, 2015). Valsartan acid also shows high $RQ_{MAX} > 1$ for infants and children of up to 8 years old and $RQ_{MAX} > 0.5$ for the remaining age intervals. Finally, lamotrigine also displays $RQ_{MAX} > 0.25$ for early life stages and close to 0.1 for adulthood.

For all the substances, the age interval that corresponds to a higher RQ is the 1–2 years old interval followed by infants and children of 2–3 years old due to greater drinking water intake concerning body weight in early life stages. RQs in infants and children (up to 8 years old) is 2–3 times greater than RQs throughout adolescence and adulthood. For example, RQ_{MEAN} for carbamazepine is $2.6{\cdot}10^{-2}$ for children of 1–2 years old and $8{\cdot}10^{-3}$ for adults (Fig. 6b). This results in higher exposure levels and higher risks in infants and children than in adults.

The human health risk might increase when multiple substances are detected simultaneously in the aquifer. Consequently, the sum of all individual RQs is also computed as $\sum RQ_{MAX}$ and $\sum RQ_{MEAN}$ (Fig. 6). The values of $\sum RQ_{MAX}$ and $\sum RQ_{MEAN}$ for all age intervals considered are

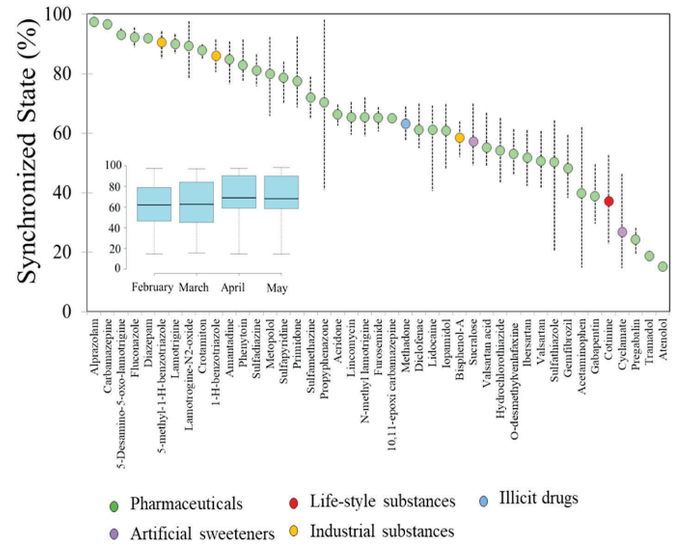


Fig. 5. Values distribution Synchronization (%) contributions per substance along the 4 months monitored. Error bars indicate the maximum and minimum values reached, and dots are the mean value. On the bottom left corner, boxplots show the distribution of the values per month of Synchronization (%) contributions.

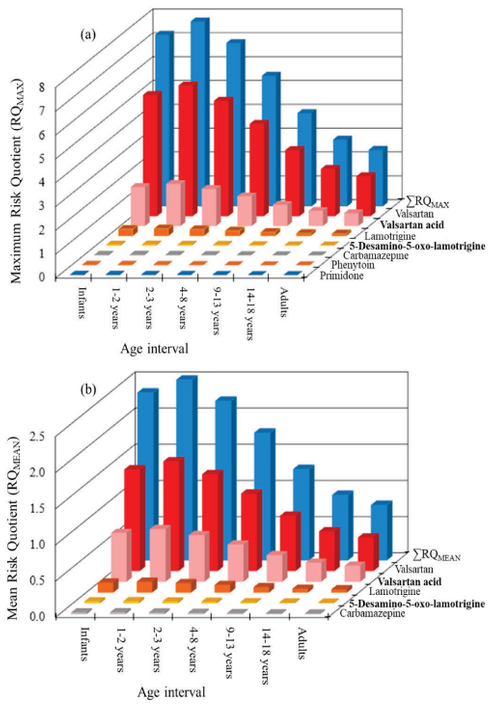


Fig. 6. **(a)** Maximum and **(b)** average human health life-stage risk quotient for pharmaceuticals with RQ > 0.01. Transformation products are in bold. Note that $\sum RQ_{MAX}$ and $\sum RQ_{MEAN}$ are the sums of all the substances considered in the assessment of the RQs.

above 1, indicating that the detection of multiple substances might pose some risk to human health ($\sum RQ_{MAX}$ and $\sum RQ_{MEAN}$, Fig. 6). The highest $\sum RQ_{MAX}$ values is 7.8 for children of 1–2 years old and the substances that most contribute to this quotient are valsartan and its TP valsartan acid, which shows individual $RQ_{MAX} > 1$ for most the age-intervals.

4. Conclusions

The groundwater of the shallow aquifer of the Besòs River Delta might be used as a drinking water resource but the detection of CECs and their TPs can limit its use. Results showed that river water usually presents higher concentrations of CECs than groundwater, indicating that natural attenuation processes might occur when river water infiltrates the aquifer. The group of substances that most contribute to groundwater contamination are the contrast media and artificial sweeteners followed by industrial substances. Conversely, lipid regulators, life-style substances, and UV Filters are usually detected at low concentrations. The fate of CECs in groundwater is evaluated using an advection-reaction model, which provides useful information regarding the dynamic behaviour of the variables monitored (i.e., characteristic length, entropy, and synchronized state). Considered as a whole, these aforementioned properties appeared roughly grouped for the months of Feb–Mar and Apr–May respectively, with characteristic length and synchronized state contribution showing an opposite trend to entropy. Descending at the substance level, these general alignments between properties are maintained. Finally, most CECs pose a negligible risk to human health for all life stages considered, as the estimated individual RQs are below 10^{-2}. However, valsartan and its TP valsartan acid exhibit RQs above $5{\cdot}10^{-1}$ for all the life stages. It is important to notice that the tools and methods presented in this research can be helpful for water management strategies and easily implemented in other urban aquifer settings because water quality monitoring and risk assessment are key aspects in the implementation of environmental and drinking water regulations (i.e., 2014/80/EC). Moreover, the regular monitoring of the CEC occurrence in groundwater will help to elucidate the hydrochemical processes that control their fate in the subsurface.

Credit author statement

Francesc Labad: Methodology, Data Curation; **Antoni Ginebreda:** Conceptualization, Methodology, Formal Analysis, Writing Original Draft, Visualization, Funding acquisition; **Rotman Criollo:** Methodology, Visualization; **Enric Vázquez-Suñé:** Resources; **Sandra Pérez:** Methodology, Resources; **Anna Jurado:** Conceptualization, Methodology, Data Curation; Writing Original Draft, Visualization, Funding acquisition; Supervision. All authors have contributed to manuscript reviewing and editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2022.120504.

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PUBLICACIÓ CIENTÍFICA #3

SUPPLEMENTARY INFORMATION

Occurrence, data-based modelling, and risk assessment of emerging contaminants in an alluvial aquifer polluted by river recharge

Labad, F., Ginebreda, A., Criollo, R., Vázquez-Suñé, E., Pérez, S., , Jurado, A.

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Figure S1. Average concentrations (ng/L) in the Besòs River vs. groundwater for detected target CECs. Red line is the limit of 100 ng/L set by the European Commission for individual pesticides (European Commission, 2006).

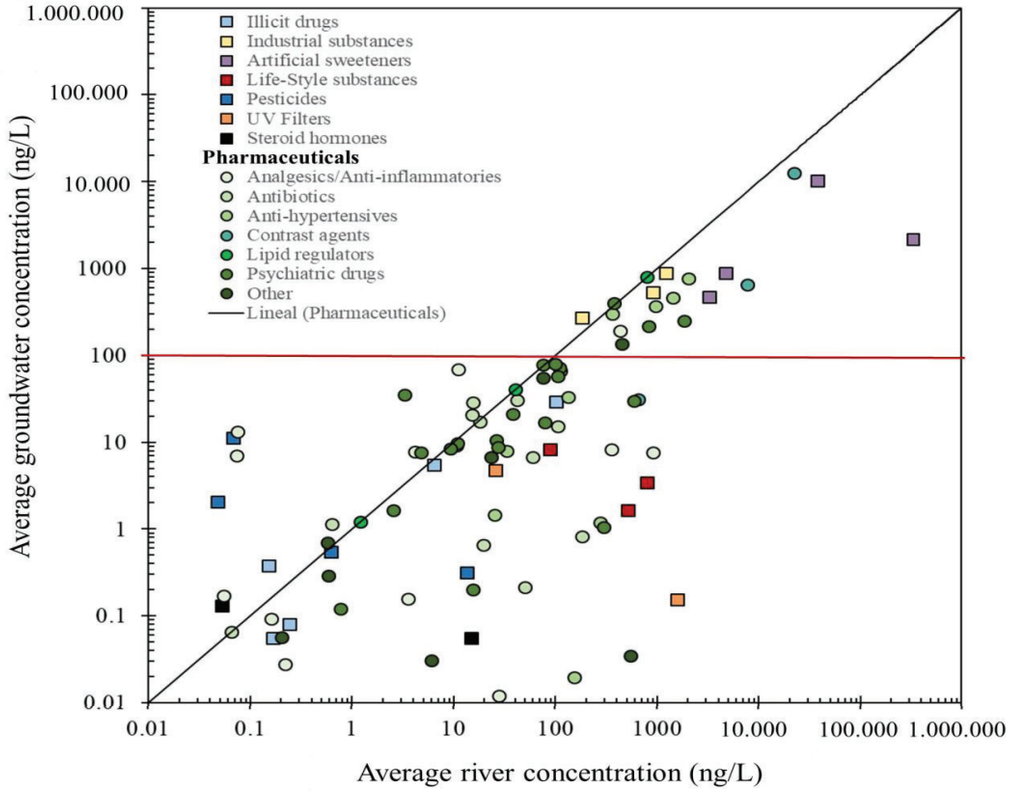


Figure S2. Box-plot of selected CECs in river (yellow) and groundwater (blue) for all the sampling campaigns: C1 (February 2021), C2 (March 2021), C3 (April 2021) and C4 (May 2021). Transformation products are in bold. RW: River water

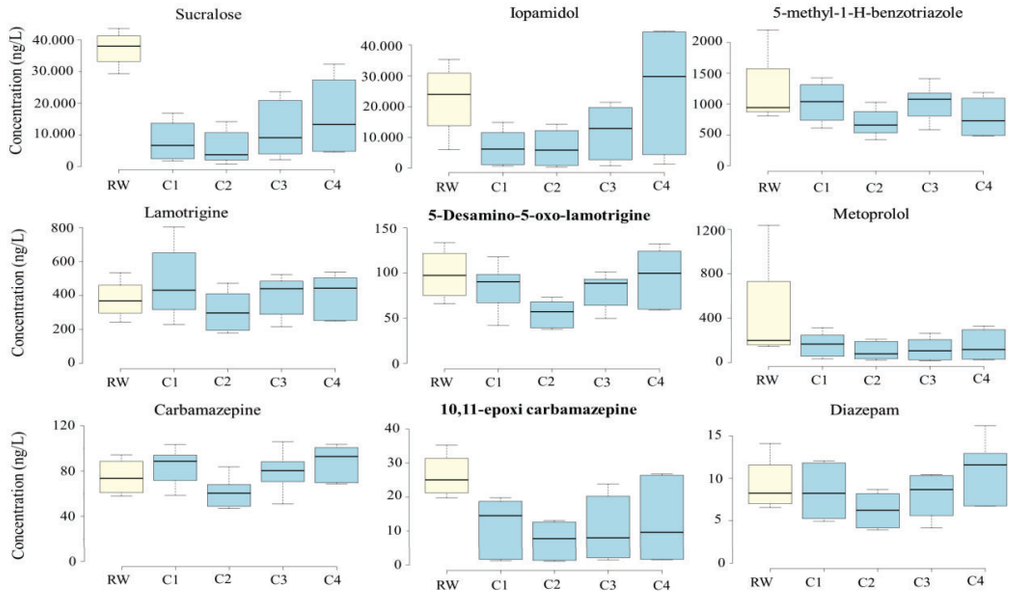


Table S1. Method validation of the target compounds. ME: Matrix effects (%); LOD: Limit of detection; LOQ: Limit of quantification; RR: relative recoveries (%); RSD: relative standard deviation (%).

Compounds	Intra Day 5 ppb			Intra Day 50 ppb			Intra Day 200 ppb			LOD	LOQ
	RR	RSD	ME	RR	RSD	ME	RR	RSD	ME	(ng/L)	(ng/L)
17α-Ethynilestradiol	134.7	37.9	-88.9	123	9.7	-84.3	89.7	9.9	-78.6	0.12	0.36
1H-Benzotriazole	112.5	6.5	65.2	68	6.8	-26.3	81.2	5.6	-41.6	0.07	0.21
4-Hydroxidiclofenac	68.2	53.2	-70.7	62.5	2.4	-46.7	64.3	3	-48	0.15	0.45
4-Nitro-Sulfamethoxazole	112.2	6	-25.1	88.9	1.6	-14.1	102.1	3.6	-25.8	0.11	0.35
5-Desamino-5-oxo-lamotrigine	88.2	4.5	-29.1	79.5	3	-40.4	87	4.2	-46.7	0.08	0.23
5-methyl-1-H-benzotriazole	96.7	39.3	100.9	57.9	10.6	-35.8	72.1	10	-49.6	0.12	0.37
6α-Methyl-Prednisolone	121.4	7.2	-71.2	79.9	16.7	-74.5	107.5	8.4	-74.2	0.14	0.43
Acetaminophen	28.9	9.7	-21.9	37.3	5.6	-30.7	48.4	6.2	-34.1	0.16	0.49
Acridone	107.9	5.8	-78.6	89.6	4.4	-76.7	90.2	7.9	-76.1	0.11	0.35
Amantadine	93.5	3.4	3.1	78.7	2.5	-7.5	88	6.8	-39.9	0.15	0.45
Alprazolam	102.7	3.8	-51.8	84.1	3.3	-48.5	93.4	3.6	-46.3	0.1	0.29
Atenolol	75.8	1.8	-16.7	69.4	2.4	-11.2	80	3.7	-28.2	0.03	0.09
Azithromycin	44.3	29.8	565.1	46.7	2.5	950	51.4	19.1	743.7	0.15	0.44
Benzoylecgonine	117.8	4.1	-60.9	95.9	1.5	-56.8	101.9	3.1	-60	0.08	0.23
β-Estradiol	105.7	7.1	-68.3	100	6	-68.3	85.6	6.4	-68.2	0.11	0.33
Bezafibrate	229.8	94.7	-23.6	85.3	4.3	-30.1	94.2	3.5	-52	0.13	0.4
Bisphenol A	124.4	8.2	-56.1	105.1	1.6	-66.8	87.2	8.8	-64.9	0.12	0.35
BP1	59.9	5.7	-24.6	89	2.4	-51	92.5	6.8	-51.2	0.11	0.33
BP2	115.1	10.1	-72	92.2	6.1	-80.9	87.8	7.6	-75.6	0.16	0.5
BP4	85.7	14	-58.2	57.2	4.6	-47.1	74.1	4	-49.8	0.06	0.18
Bromazepam	96.7	7	74.2	76.3	4.6	32.7	80.2	7.1	-30.3	0.16	0.47
Caffeine	66.7	25.1	146.7	122.4	22.1	-10.7	103	8.1	-32	0.16	0.47
Carazolol	80.7	5.6	426.8	69.9	6.1	244.1	73.4	7.3	141.1	0.07	0.21
Carbamazepine	101.3	0.7	-63.2	85.8	3.4	-64.6	92.7	4.2	-61	0.11	0.35
Carbamazepine-10,11-epoxide	109.5	3.1	-46.4	91.9	1.6	-42.9	96.7	3.3	-51.6	0.11	0.34
Carisoprodol	104.3	1.5	-47.2	87	3.4	-40.5	93.3	4.7	-44.6	0.12	0.37
Chloramphenicol	108.9	2.7	-53.2	88.9	3.1	-44	96.4	2.9	-44.3	0.07	0.2
Chlorpromazine	28.3	23.3	1537.8	35.1	30.6	598.1	26.3	57	455.4	0.18	0.55
Citalopram	53.9	22.2	68	58.7	6.2	8.6	59	8.1	-24.3	0.14	0.41
Clarithromycin	64.3	15.3	-42.7	51.6	1.2	-56	54.5	15.9	-49.8	0.09	0.29
Climbazole	98.8	13.8	-76.7	89.2	23.2	-78.4	81.8	11.6	-75.1	0.05	0.16
Clofibric Acid	251.9	4.7	-15.3	95.1	7.3	-20.7	103.2	7.2	-31.4	0.17	0.52
Coca-ethylene	88.5	1.6	35	78.8	3	-9	84.1	3.4	-21.2	0.11	0.33
Cocaine	91.2	3.6	90.6	75.5	3.9	33.2	80.4	2.6	32.4	0.12	0.36
Codeine	64.8	3.7	-21	72.1	2.2	-20.2	75.9	3.7	-33.6	0.14	0.43
Cotinine	95.5	16	-11.5	113.8	36.7	-57.8	152.1	40.3	-71.4	0.09	0.26
Crotamiton	98.8	26.3	-80.1	57.5	43.6	-79.8	102.1	1.5	-83.2	0.2	0.6
Cyclamate	39.1	18.8	-80.7	21.4	17.5	-40.5	31.2	9.3	-44.9	0.1	0.3
Diazepam	99.8	7.6	-74.6	81.9	3.5	-65.2	87.8	6.6	-60.9	0.17	0.52
Diclofenac	155.6	19.1	-79.1	91	3.4	-59.7	84.8	7.8	-59.6	0.1	0.3
Diltiazem	58.7	15.3	38.2	55.9	6.7	-5.1	57.1	10.9	-25.9	0.13	0.39
Dutasteride	87.3	56.6	-98.3	82	41.6	-97.9	67.6	22.2	-97	0.27	0.82
Estriol	115.6	47.2	-57.8	81.7	2.3	-48.9	91.9	7.7	-52.8	0.11	0.32
Estrone	110	4.4	-61.5	97.7	3.5	-63.5	84.9	9.2	-64.7	0.11	0.34
Ezetimibe	132.2	13	-93.5	147.6	18.2	-94.4	85.3	15	-89	0.05	0.16
Fipronil	149.1	5.9	-71.5	169	10	-78.4	97.7	20.8	-59.9	0.11	0.34
Fipronil Desulfinyl	151.9	10.9	-86	172.4	16.1	-88.6	100.1	18.9	-75.9	0.11	0.34
Fipronil Sulfide	153.1	19.3	-93	171.6	25.4	-93.8	106.5	24.7	-85	0.14	0.41
Fipronil Sulfone	156	22	-93.1	167.4	27	-94.2	103.8	28.4	-86.5	0.1	0.29
Florfenicol	109.1	6	-51.7	89.9	4.6	-39.1	98.6	2.7	-41.4	0.1	0.31
Fluconazole	113.3	5.4	50.6	91.5	2.8	-4.7	105.3	4.5	-21.8	0.13	0.38
Flumequine	94.1	1.5	-62.4	77.5	3.9	-64.9	87.2	2.9	-68.9	0.13	0.39
Fluoxetine	35.1	12.4	718.3	53.7	13.8	94.8	38.8	13.1	62.4	0.1	0.31
Fluticasone propionate	85.8	44.3	-91.6	147.4	13.7	-92.3	88.3	6.8	-87.9	0.11	0.34
Furazolidone	97.2	3.1	-45.6	82.9	5.1	-44.9	99.8	2.9	-49.4	0.11	0.35
Furosemide	39.9	13.2	-54.1	43.8	6.1	-53.8	50.7	14.4	-54.5	0.1	0.29
Gabapentin	49.6	9.5	20.7	43	5.8	10.9	45.8	12.7	-23	0.09	0.28
Gemfibrozil	120.8	8.2	-75.5	174.8	6.8	-87.1	97.3	21.3	-80	0.11	0.32
Hydrochlorothiazide	94.4	16.3	10.7	89.1	1.3	-54	93.4	3.2	-57.4	0.11	0.33
Hydroxychloroquine	61.9	6.2	15.6	61.7	3.6	14.9	68	9.7	14.8	0.15	0.44
Hyoscine	111.4	1.9	-36.8	87.2	1.9	-43.8	93.2	3.1	-53	0.13	0.4
Indomethacin	125.4	10.4	-80.3	108.5	7.1	-77.6	85.4	15	-72.8	0.06	0.19
Irbesartan	116.7	10	-86.8	90.8	23.5	-86.5	84.6	9.3	-82.2	0.12	0.35
Ketoprofen	41.5	4.9	53.6	83.3	5.2	-16.8	96.8	3.7	-47.5	0.13	0.38
Lamotrigine	102.5	0.4	-60.5	85	3.5	-65.5	94.1	3.4	-63.8	0.11	0.33
Lamotrigine-N2-Oxide	94.4	5	-65.8	73	5.3	-65.6	83	2.9	-63.5	0.09	0.27
Levomepromazine	47.1	69.1	582.8	34.2	72.1	181.7	24.2	103.7	123.1	0.12	0.37
Lidocaine	62.4	9	-44.6	60.7	5.5	-45.2	68.9	8.3	-49.5	0.11	0.33
Lincomycin	75.9	15.8	-44.1	64.2	7.2	-14.4	69.6	11.6	-23	0.09	0.27
Lorazepam	100.7	2.8	-61.9	85.9	3.7	-45.7	95.5	1.4	-46.4	0.14	0.42
Losartan	36.4	50.4	-78.6	42.2	17	-78.7	39.8	35.1	-73.7	0.09	0.27
Mefenamic Acid	137.6	24	-87.9	139	13.9	-88.1	87.8	20.8	-82.2	0.11	0.32
Meprobamate	102.3	5.7	-23.6	104	1.2	-23.2	107.5	1.9	-32.2	0.08	0.23
Metformin	112.78	30.98	-90.65	88.57	24.57	-90.44	111.52	5.54	-94.03	0.12	0.38
Methadone	60.6	8.1	169.3	56.1	4.4	28	60	6.4	-12	0.1	0.29
Metoprolol	78.2	4.6	-25.6	66.3	2.6	-25	73.8	1.5	-38.8	0.1	0.31
Metronidazole	99.1	4.1	-44.5	86	5.1	-42.9	95.2	3.2	-42.5	0.14	0.43
Midazolam	65	33.9	-75.3	66.6	7.6	-75.9	57.8	27.5	-75.5	0.09	0.28
Morphine	161.7	5.9	-59.3	151.1	7	-55.8	137.4	5.3	-56.6	0.11	0.33
N-acetyl sulfamethoxazole	104.5	5.4	-29.2	87.5	2.8	-14.5	94.9	3.2	-30.7	0.11	0.32
Nalidixic Acid	95.5	5.1	-68.6	77.3	2.3	-68.5	85.6	3.9	-68.4	0.14	0.42
Naproxen	47.4	12.9	-4.6	87.2	6.9	-40.7	99.7	6.5	-52.7	0.11	0.32
Neotame	92.2	4.4	51.2	72.5	4.6	54.6	85.8	5.9	-11.9	0.14	0.43
N-methyl-lamotrigine	106.8	4.6	-3.2	86.5	1.6	-27.9	92.4	3.6	-43.3	0.13	0.38
NO2-diclofenac	120.8	11.4	-76.3	101.4	2.1	-71.6	95.2	9.2	-66.8	0.08	0.24
Norfluoxetine	42.8	36.1	6015.1	56.3	14.9	312.8	42.5	6.6	155.6	0.13	0.39
O-desmethyl venlafaxine	91.4	3.9	-50.1	76	2.9	-46.7	83.3	1.5	-47.4	0.1	0.29
Oseltamivir	73.3	3	22.6	64.5	3.2	32.5	72.8	3.2	-4.8	0.09	0.28
Oxazepam	109.5	6.7	-36.4	105.5	2.2	-39.1	109.1	2.2	-47	0.13	0.4
Paroxetine	24.9	13.2	1425.5	42.6	17.8	449.2	41.2	6.2	199.5	0.15	0.44
Pentobarbital	108	2.3	-50.6	109.2	2.9	-44	110.2	0.8	-46.8	0.13	0.39
Phenytoin	108.1	1.9	-52.9	88.6	4.9	-45.5	96.4	2.8	-48	0.13	0.39
Pregabalin	15.3	40	10.1	20.4	9.9	7.2	20.2	16.5	-25.8	0.16	0.49
Primidone	0	0	0	81.1	12	-7.5	97.6	9.7	-34.6	0.04	0.12
Propranolol	80	2.3	126	68.3	3	32.2	74.7	4.9	-17.1	0.15	0.46
Propyphenazone	101.9	0.7	-73.4	82.1	4.6	-69.1	92.2	3.8	-64.3	0.13	0.39
Rosuvastatin	103.5	3.9	-46.8	88.6	3.6	-38.3	97	4.5	-50.2	0.14	0.43
Saccharin	65.6	51.4	-14.9	61.5	58.6	-27	84.9	43.3	-36.9	0.14	0.41
Sertraline	51.3	4.1	1347.6	54	14.3	535.6	47.2	10.1	326.9	0.18	0.55
Sitagliptin	47.9	21.7	-27	51.1	1.2	-16.7	57.8	4.7	-37.9	0.16	0.49
Sotalol	85.3	3.5	-32.3	75.2	3	-18.6	84.6	3.6	-31.3	0.14	0.42
Stevioside	0	0	0	72.3	8.2	-47.4	88	0.4	-49.3	0.15	0.46
Sucralose	141.7	1	363.2	98	1.4	-25.6	101.8	4.2	-52.4	0.12	0.36
Sulfadiazine	92.3	2.1	-11.5	70.2	10.4	-12.5	89.5	5.7	-37.7	0.12	0.36
Sulfamerazine	103.9	2.7	-8.8	82.8	8.4	-9	97	6.2	-30.7	0.09	0.26
Sulfamethazine	105.6	2.6	-38.9	82	10.1	-26.4	94.6	6.5	-34.4	0.1	0.29
Sulfamethizole	83.4	4.2	-40.3	63.6	14.9	-28.7	79.1	6.9	-47.1	0.16	0.48
Sulfamethoxazole	115.7	3.4	36	82.7	6.8	-37.1	95.4	5.5	-50.6	0.11	0.32
Sulfadimethoxine	116.8	10	-76.5	83	7.3	-62.1	91.5	6.8	-67.1	0.06	0.17
Sulfapyridine	98.1	0.7	-29.9	77.2	9.8	-19.8	95	5.4	-35.6	0.12	0.37
Sulfathiazole	60.4	10.2	-69	52.4	18.2	-60.7	62.4	11.1	-62.5	0.13	0.4
Tramadol	69.7	1.4	-42.8	65.5	1.1	-48.2	70.7	2.3	-56.2	0.11	0.33
Trimethoprim	96.1	3.9	-48	82.5	2.4	-43.2	89	3.2	-44.2	0.11	0.35
Valsartan	93.9	1.7	-28.9	79	10.7	-28.3	92.1	3.8	-45.1	0.1	0.29
Valsartan Acid	53.9	22.8	-22.6	80.7	5.1	-31.8	89.6	2.8	-37.7	0.13	0.38
Venlafaxine	75.4	4.1	-31.7	66	2.7	-41.6	73.8	3.5	-53.4	0.1	0.3
Verapamil	59.9	16.9	232.4	55.2	3.4	29.9	52.3	20.8	-20.6	0.1	0.31

Warfarin	93.8	13.4	-63.1	69.1	6.4	-52.9	78.5	6.2	-56	0.15	0.45
Zonisamide	0	0	0	93	6.1	16.3	111.5	7.6	-9	0.28	0.84

Table S2. Body weight and Drinking Water Intakes (EFSA, 2010) for the selected age groups.

Age Groups	Body weight (kg)	DWI (L/day)
Infants	8	0.84
1-2 years	10.6	1.2
2-3 years	13	1.3
4-8 years	20	1.6
9-13 years	35	2
14-18 years	55	2.25
Adults	65	2.25

Table S3. ADI values (ng/kg bw) for ubiquitous CECs in groundwater. Note that the metabolites are highlighted in bold.

Substance	Mean ng/L	Max. ng/L	ADI ng/kg bw/day	Reference for ADI
1H-Benzotriazole	526.98	1023.49	295000	Sengar and Vijayanandan (2022)
Bisphenol-A	268.14	838.47	50000	Parida et al. (2015)
Acesulfame	473.05	4243.96	9000000	Lange et al. (2012)
Cyclamate	2162.81	14829.63	7000000	Lange et al. (2012)
Saccharin	884.14	13301.36	5000000	Lange et al. (2012)
Sucralose	10325.77	32338.79	15000000	Lange et al. (2012)
Caffeine	3.42	19.71	150000	Sengar and Vijayanandan (2022)
Cotinine	8.26	21.61	280	Sengar and Vijayanandan (2022)
Acetaminophen	7.65	16.43	340000	Schab et al. (2005)
Diclofenac	193.14	452.07	67000	Sengar and Vijayanandan (2022)
Ketoprofen	69.27	262.37	5000	Sengar and Vijayanandan (2022)
Lamotrigine	397.19	802.96	300	Prosser and Sibley (2015)
5-Desamino-5-oxo-lamotrigine	79.15	132.23	300	-
Propyphenazone	7.8	49.42	21000	de Jongh et al. (2012)
Tramadol	8.3	19.22	7100	de Jongh et al. (2012)
Lincomycin	30.19	81.43	2200	Prosser and Sibley (2015)
Sulfadiazine	17.21	46.61	20000	OCS (2013)
Sulfamethazine	28.54	96.93	10000	Zhu et al. (2018)
Sulfathiazole	15.22	46.2	50000	Schab et al. (2005)
Sulfapyridine	20.83	43.76	10000	NRA (2000)
Atenolol	1.19	2.39	2000	Sengar and Vijayanandan (2022)
Hydrochlorothizide	456.54	1437.5	6000	Sengar and Vijayanandan (2022)
Metoprolol	66.49	116.89	14000	Sengar and Vijayanandan (2022)
Valsartan	762.49	2762.71	57	Liu et al. (2019)
Valsartan acid	366.8	888.71	57	-
Iohexol	647.7	5229.18	125000000	Parida et al. (2015)
Iopamidol	12689.05	44471.71	118600000	Parida et al. (2015)
Carbamazepine	78.18	105.85	340	Sengar and Vijayanandan (2022)
10,11-epoxi carbamazepine	10.56	26.79	2900	Prosser and Sibley (2015)
Diazepam	8.4	16.2	1000	Sengar and Vijayanandan (2022)
Phenytoin	21.15	72.47	290	Liu et al. (2019)
Primidone	57.84	141.7	700	Sengar and Vijayanandan (2022)
Venlafaxine	1.05	4.94	5400	Liu et al. (2019)
O-desmethylvenlafaxine	216.59	659.78	5400	-
Fluconazole	55.2	87.29	714	Sengar and Vijayanandan (2022)

Table S4. Minimum (min.), maximum (max.) and average concentration and frequency of detection (%) of target CECs in river water and groundwater.

Substance	Concentration (ng/L)						Frequency of detection (%)	
	River Water			Groundwater			River Water	Groundwater
	Min.	Max.	Average	Min.	Max.	Average		
Cocaine	<LOQ	<LOQ	0.24	n.d	<LOQ	0.08	100	33
Benzeilecgonine	<LOQ	<LOQ	0.15	n.d	7.53	0.38	100	50
Cocaethylene	n.d	<LOQ	0.17	n.d	<LOQ	0.06	75	25
Methadone	2.27	12.14	6.40	n.d	18.28	5.47	100	92
Morphine	< LOQ	230.34	100.77	n.d	143.59	29.34	100	33
1H-Benzotriazole	604.53	1344.77	907.03	197.40	1023.49	526.98	100	100
5-methyl-1-H-benzotriazole	809.28	2201.45	1223.99	423.45	1423.58	883.22	100	100
Bisphenol-A	117.96	292.21	183.55	<LOQ	838.47	268.14	100	100
Acesulfame	1007.66	7048.09	3218.74	<LOQ	4243.93	473.05	100	100
Cyclamate	814.05	1127893.81	332667.52	31.61	14829.63	2162.81	100	100
Neotame		n.d			n.d		0	0
Saccharin	201.23	16797.67	4661.61	n.d	13301.36	884.14	100	92
Stevioside		n.d			n.d		0	0
Sucralose	29311.09	43622.39	37262.56	735.99	32338.79	10325.77	100	100
Caffeine	152.33	2307.25	797.16	<LOQ	19.71	3.42	100	100
Paraxanthine	46.45	1604.59	518.84	<LOQ	7.70	1.66	100	100
Cotinine	41.70	181.27	88.79	<LOQ	21.61	8.26	100	100
Fipronil	11.51	16.17	13.40	n.d	0.63	0.31	100	88
Fipronil Desulfynil	n.d	1.20	0.62	n.d	1.17	0.55	75	92
Fipronil Sulfide	n.d	<LOQ	0.07	<LOQ	28.22	11.29	25	100
Fipronil Sulfone	n.d	<LOQ	0.05	n.d	5.66	2.05	25	88
17-α-Ethynilestradiol		n.d			n.d		0	0
β-Estradiol		n.d		n.d	<LOQ	0.02	0	8
Estriol	n.d	<LOQ	0.05	n.d	<LOQ	0.13	25	63
Estrone	<LOQ	25.88	14.83	n.d	<LOQ	0.06	100	25
BP1	15.50	39.87	25.42	n.d	64.08	4.77	100	58
BP2		n.d		n.d	7.16	0.97	0	58
BP4	4.33	5022.18	1566.82	n.d	1.58	0.15	100	17

Substance	Concentration (ng/L)						Frequency of detection (%)	
	River Water			Groundwater			River Water	Groundwater
	Min.	Max.	Mean	Min.	Max.	Mean		
6α-methyl-prednisolone	n.d	<LOQ	0.07	n.d	43.12	7.05	25	58
Acetaminophen	34.07	3484.45	903.65	2.09	16.43	7.65	100	100
Codeine	9.49	46.19	27.66	n.d	<LOQ	0.01	100	8
Diclofenac	<LOQ	1147.66	430.04	1.69	452.07	193.14	100	100
4-Hydroxidiclofenac	n.d	<LOQ	0.08	n.d	48.22	13.22	25	79
NO2-Diclofenac	<LOQ	<LOQ	0.16	n.d	<LOQ	0.09	100	58
Indomethacin	n.d	10.01	3.57	n.d	3.77	0.16	50	4
Ketoprofen	4.01	20.71	11.10	<LOQ	262.37	69.27	100	100
Mefenamic Acid	n.d	<LOQ	0.06	n.d	1.05	0.17	25	63
Naproxen	<LOQ	<LOQ	0.22	n.d	<LOQ	0.03	100	13
Propyphenazone	2.35	7.35	4.15	3.21	49.42	7.80	100	100
Tramadol	64.61	563.50	356.76	0.90	19.22	8.30	100	100
Azithromycin	20.12	72.80	40.55		n.d		100	0
Ciprofloxacine	n.d	<LOQ	0.16		n.d		50	0
Chloramphenicol	0.76	2648.32	668.71		n.d		100	0
Clarithromycin	17.09	23.41	19.53	n.d	3.98	0.65	100	33
Erythromycin		n.d			n.d		0	0
Florfenicol	31.47	99.85	54.88		n.d		100	0
Flumequine	n.d	0.26	0.07	n.d	<LOQ	0.07	25	25
Furazolidone		n.d			n.d		0	0
Lincomycin	25.00	61.79	41.59	2.91	81.43	30.19	100	100
Metronidazole	14.93	38.66	26.68		n.d		100	0
Nalidixic acid	<LOQ	0.96	0.64	n.d	2.97	1.14	100	92
Sulfadiazine	2.86	45.76	17.89	5.80	46.61	17.21	100	100
Sulfamerazine		n.d		n.d	0.51	0.15	0	71
Sulfamethazine	2.99	35.06	15.43	5.56	96.93	28.54	100	100
Sulfathiazole	n.d	418.60	105.89	2.54	46.20	15.22	75	100
Sulfamethizole		n.d		n.d	3.11	0.35	0	42
Sulfamethoxazole	72.06	322.10	182.18	n.d	5.25	0.83	100	92
4-Nitro sulfamethoxazole		n.d		n.d	<LOQ	0.02	0	4
N-acetyl sulfamethoxazole	20.39	79.99	49.54	n.d	2.77	0.22	100	13
Sulfamethoxine		n.d		n.d	6.47	0.96	0	50
Sulfapyridine	4.91	27.05	15.14	4.32	43.76	20.83	100	100
Trimethoprim	43.67	91.43	59.87	n.d	98.33	6.79	100	71
Atenolol	177.13	428.75	271.97	0.14	2.39	1.19	100	100
Carazolol		n.d			n.d		0	0
Diltiazem	10.43	510.79	152.22	n.d	0.47	0.02	100	4
Furosemide	128.85	508.10	361.22	9.84	929.77	301.42	100	100
Hydrochlorothiazide	962.80	2001.33	1435.32	<LOQ	1437.50	456.54	100	100
Irbersartan	112.62	160.10	132.61	n.d	104.86	33.00	100	92
Metoprolol	38.90	223.91	112.08	3.48	116.89	66.49	100	100
Propranolol	21.29	30.44	24.91	n.d	7.61	1.46	100	42
Sotalol	24.09	43.12	33.38	n.d	20.50	7.95	100	83
Valsartan	1424.75	2657.68	2022.37	13.35	2762.71	762.49	100	100
Valsartan acid	<LOQ	2166.70	952.73	1.84	888.71	366.80	100	100
Verapamil		n.d		n.d	0.61	0.03	0	4
Iohexol	3784.68	12551.78	7738.70	n.d	5229.18	647.70	100	63
Iopamidol	6037.22	35279.77	22308.59	341.89	44471.71	12689.05	100	100
Iopromide	n.d	2211.88	645.55	n.d	256.77	31.31	75	33
Bezafibrate	29.68	60.58	40.46	n.d	6.96	1.83	100	63
Clofibric Acid	n.d	4.15	1.21	n.d	71.08	3.35	75	29
Ezetimibe	n.d	<LOQ	0.06		n.d		50	0
Gemfibrozil	383.29	1017.23	791.69	<LOQ	815.06	220.87	100	100
Rosuvastatin	n.d	<LOQ	0.15	n.d	4.32	0.73	25	33
Alprazolam	8.90	13.22	10.57	6.49	11.43	9.18	100	100
Amantadine	68.08	189.36	109.06	18.74	195.42	71.70	100	100
Bromazepam		n.d			n.d		0	0
Carbamazepine	57.90	94.19	74.72	46.69	105.85	78.18	100	100
Acridone	5.45	16.63	10.76	0.48	30.31	9.78	100	100
10,11-epoxi carbamazepine	19.77	35.29	26.29	1.09	26.79	10.56	100	100
Citalopram	31.30	70.38	48.93		n.d		100	0
Diazepam	6.56	14.08	9.28	3.93	16.20	8.40	100	100
Gabapentin	1317.21	2620.29	1838.48	8.61	809.38	248.68	100	100

Lamotrigine	243.83	534.67	378.41	178.44	802.96	397.19	100	100
5-Desamino-5-oxo-lamotrigine	65.97	133.63	98.60	37.65	132.23	79.15	100	100
Lamotrigine-N2-Oxide	3.07	8.28	4.72	2.40	15.94	7.59	100	100
N-methyl lamotrigine	1.80	3.48	2.51	n.d	3.66	1.65	100	92
Levomepromazine		n.d			n.d		0	0
Lorazepam	42.13	117.07	78.00	n.d	60.43	16.84	100	75
Meprobamate		n.d		n.d	33.82	4.78	0	75
Midazolam	<LOQ	1.61	0.76	n.d	0.43	0.12	100	46
Oxazepam	n.d	55.61	27.10	n.d	32.28	8.79	75	92
Paroxetine		n.d			n.d		0	0
Pentobarbital	n.d	11.03	3.28	n.d	805.08	35.07	50	33
Phenytoin	19.88	74.34	37.88	4.79	72.47	21.15	100	100
Pregabalin	418.47	797.68	593.10	<LOQ	120.46	29.95	100	100
Primidone	<LOQ	179.14	105.50	n.d	141.47	57.85	100	100
Sertraline	n.d	24.81	15.33	n.d	2.08	0.20	75	17
Venlafaxine	252.47	355.86	297.43	<LOQ	4.94	1.05	100	100
O-desmethylvenlafaxine	621.30	1012.97	820.21	2.74	659.78	216.59	100	100
Zonisamide	<LOQ	<LOQ	0.56		n.d		100	0
Carisoprodol		n.d			n.d		0	0
Climbazole	17.29	31.34	23.20	n.d	24.46	6.68	100	83
Crotamiton	<LOQ	0.79	0.58	<LOQ	1.68	0.70	100	100
Dutasteride		n.d			n.d		0	0
Fluconazole	44.87	103.10	74.81	16.75	87.29	55.20	100	100
Fluticasone propionate		n.d			n.d		0	0
Hydroxychloroquine	n.d	15.91	6.02	n.d	0.45	0.03	75	8
Hyoscine	n.d	<LOQ	0.20	n.d	<LOQ	0.06	75	21
Lidocaine	146.37	1235.29	445.60	18.16	329.94	136.31	100	100
Oseltamivir	n.d			n.d	<LOQ	0.01	0	4
Sitagliptin	412.79	761.21	544.75	n.d	0.83	0.03	100	4
Warfarin	<LOQ	1.42	0.58	n.d	<LOQ	0.29	100	96

Table S5. Presence of CECs in European urban groundwater. "-": not provided, n.d: non-detected, (a) median

Country (reference)	CECs	Concentration (ng/L)		
		Minimum	Maximum	Average
Germany (Hass et al. (2012)	Meprobamate	-	1130	50 (a)
	Primidone	-	490	40 (a)
Germany (Wolf et al. (2012))	Acesulfame	-	2870	171
	Bezafibrate	-	19	11
	Carbamazepine	-	35	14
	Clofibric acid	-	1350	37
	Cyclamate	-	1200	60
	Diclofenac	-	129	12
	Gemfibrozil	-	23	10
	Indomethacin	-	10	10
	Iohexol	-	187	35
	Iopamidol	-	79	12
	Iopromide	-	39	10
	Saccharin	-	10	10
	Sucralose	-	50	50
Poland (Rusiniak et al. (2021))	17-α-ethinylestradiol	2.6	18.7	-
	β-estradiol		n.d	
	Bezafibrate		n.d	
	Bisphenol A		n.d	
	BP4		n.d	
	Estrone	n.d	5.4	-
	Diclofenac		n.d	
	Ketoprofen	n.d	59.5	-
	Valsartan		n.d	
Rumania (Szekeres et al. (2018))	Ciprofloxacine	77.5	130.8	-
	Erythromycin	384	436.7	-
	Sulfamethoxazole	578.5	842.3	-
	Trimethoprim	59.6	185.6	-
	Acetaminophen		n.d	
	Atenolol		n.d	
	Azithromycin	n.d	1620	-
	Bezafibrate	n.d	25.8	-
	Carazolol	n.d	65.5	-
	Carbamazepine	n.d	136	-
	10,11-epoxi carbamazepine	n.d	8.4	-
	Acridone	n.d	8.2	-
	Chloramphenicol		n.d	
	Ciprofloxacin	n.d	443	-
	Clarithromycin	1.8	20.5	-
	Clofibric Acid	n.d	7.6	-
	Codeine	n.d	2.4	-
	Diazepam	n.d	35.1	-
	Diclofenac	n.d	380	-
	4-Hydroxidiclofenac	n.d	147	-
	Erythromycin	n.d	41.3	-

Spain (López-Serna et al. (2013))	Flumequine	n.d	10.3	-
	Furosemide	n.d	284	-
	Gemfibrozil	n.d	751	-
	Hydrochlorothiazide	1.2	665	-
	Indomethacin		n.d	
	Ketoprofen	n.d	215	-
	Lorazepam	n.d	54	-
	Mefenamic Acid	n.d	64.3	-
	Metoprolol	95.3	355	-
	Metronidazole		n.d	
	Naproxen	n.d	5.6	-
	Paroxetine	n.d	30.2	-
	Pentobarbital	n.d	17.7	-
	Propranolol	n.d	9.4	-
	Propyphenazone	n.d	121	-
	Sotalol	n.d	20.1	-
	Sulfadiazine	n.d	208	-
	Sulfamethazine	n.d	29.2	-
	Sulfamethoxazole	n.d	65	-
	N-acetyl sulfamethoxazole		n.d	
	Trimethoprim	n.d	9.4	-
Spain (García-Gil et al. (2018))	BP1	n.d	29.6	-
	Ciprofloxacin		n.d	
	Clarithromycin		n.d	
	Erythromycin	n.d	5.2	-
	Flumequine		n.d	
	Ketoprofen	n.d	5.9	
	Mefenamic Acid	n.d	2.67	-
	Nalidixic Acid	n.d	13.2	-
	Sulfamerazine		n.d	
	Sulfamethazine		n.d	
	Sulfathiazole		n.d	
	Sulfamethoxazole		n.d	
	Sulfamethoxine		n.d	
	Sulfapyridine		n.d	
	Trimethoprim	n.d	5.4	-

PUBLICACIÓ CIENTÍFICA #4

Surveillance and environmental risk of very mobile pollutants in urban stormwater and rainwater in a water-stressed city

Labad, F., Santana-Viera, S., Jiaqi, X., Borrell-Diaz, X., Teixidó, M., Pérez, S.

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Gbcud ,tbitT z u- bcotS maun ,o

journal homepage: www.elsevier.com/locate/jhazmat

Ocuren, daet d- tedrnubds edm,tunl tbitreugts bkn,etf b,,cmdmotndtcuk dt onbus v maut d- tu ndv mautndt tv maupmeoce- tamng

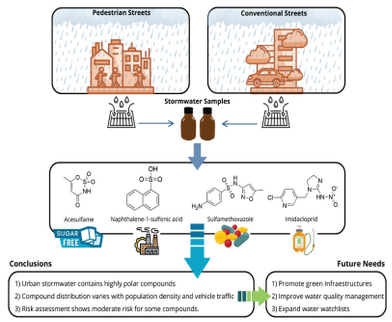
pu daeoaty k - [F] htOeuLrbtO dmd qAreu htGn RntCc [k] htC rmeutEbuue,,qVn z htS uatPenJn- b [k] htt O d- u t*éuez [F]

De p ar tmp nof r ar Bv i ov nl Ohsy, yhOl u AdBWRncuh()SOl u OdOxfini Juyl
[k], *hOOls 1us9huls p 2shO5)O(0)3 ye82nof r ar Bv i ov nl Ohsy, yhOl u AdBWRncuh()SOl u OdOxfini Juyl*

T I N T y I N T P O

- Vemambdt bit enL1mreugts bkn,etf b,,cmdmot ndt ,,t 2(2t onbus v maut d- t u ndt o s f,eo)
- . c dmwa mbdt bit 2Qt 1rL1,gt f b, ut f b,q ,cmdmotibutmletwuonms etndtonbus v mau)
- P1et d ,gmaotabdaedmn mbdtv ot 1rL1eut ndtub - tomeemonml dtndtfe- eonmn dtomeemo)
- Vemambdt bit v omev maut f b,,cmdmot ndt cuk dt onbus v maut ocLLeome- t o dmnugt œv eutbreuMbv)
- Waeoc,i s et d- t2qd f 1ml ,edetoc,ibdmat an- t f ueoedme- t t s b- eu mt edrnubdq s edm,tunl)

N U W* T I B Wy tWE O P U WB P



W U P I B y 0 tI 4 p 6

B)21 Ohs4M
Aeugtf eunnmdmreugts bknetfr*rS 5
*eunnmdm
s bknet d- tmbJratff*S P5
Ucdbii
0abmbJmab,bLma ,tunol t ocecos edm
0s euLrdLtabdms rd dmo
pnnmqMtol

W E O P U WB P

3uk dtonbus v maut d- tu ndv mautndtv maupmeoce- tamneotoeuret otaumma ,trearbuotibutmletmn dof burn d- t- mf eunonbdt bitf b,,cmdmoltnda,c- ndLtreugts bknetabs f bcd- otP1eoetf b,,cmdmoltv 1ma1ta dtketndMedae- tkgti anbuotocalt ot , d- tcoeltu ndi ,,tndmadomght d- tcuk dtndiu omcamueltf boetonLdnwa dntunol otnbtkbmit1cs dt d- tedrnubds edm,t 1e ,ni)tW,nibcL1toereu ,tf urbumgtf b,,cmdmot1 retmn - mnbd ,,gtkeedt- emaam- tndtcuk dtonbus v mault,mnetnnl dbv dt kbcmmietf ueoedaet bit reugts bknetabs f bcd- otmi nns gtmiue nndtcuk dt- undl ndLtv maut ocf f ,neot d- tf boet edrnubds edm,tunol otnbt Rc mntofeareo)tIdtmlnntom- ght2(2tcuk dtu ndt d- torbus v mauto s f ,eotv euetab,,eam- tiubs t miueet- nommamtbitE uae,bd tfDf nd5t d- t d ,goe- tibutQ/treugts bknetf b,,cmdmotmi rn uetbimedtbreu,bbl e- tndt abdredmnbd ,ts bdmnburdLteiibum)tP1etwd- ndLotuere ,tmi ntonbus v maut d- tu ndv maut uets xbutabdmnkcmbuotnbtmiet ofue - tbitf b,,cmdmotndtv maupmeoce- tammedtv mitf umac, utes f 1 omt bdtockomdaeot,nl et,nieong,etf ub- camht f 1 us aecma ,olt d- tnd- comn ,tales ma ,o)tWs bdLtmletQ(tabs f bcd- ot- emaam- ht2Qtv euetuef bum- tibutmletwuom ms etnbtbaacutndtcuk dtonbus v mautv mitabdaednn mbdot ot1rL1t otQ92tμLty^{-2})tS e ocues edmdbit- mob,re- tbuL dmat a ukbdlte,eamma ,tabd- camrmght d- tmletf ueoedaetbitv omev meujkbudetf b,,cmdmotv mindtmletabuue, mbdt d ,gomht oc LLeom- tmletabdmnkcmbdtbito dmnugtoev eutbreuMbv otfCO5 5mbtcuk dtonbus v meujtpnd ,,ght dtedrnubds edm,tunol t ocecos edmfiv buomp oetoaed urb5tv otf euibus e- htolbv ndLt ts b- eu mtunol tbitmuLemn d ,gmaotocalt ot aeoc,i s et

F Bbuueof bd- edaetmb%tlVW0WjBCIBht6 4 T 0WyPTtUeoe ua1tNubcf htGbu- mtNmbd t2HqQ/htE uae,bd t8H8(; htOf nd)
*aE3 uySusshj4@4MiR s 7 an)aoma)eo fp)ty k - 5ttofoR s 7 n e)aoma)eo fD)t*éuez5)t*

1mfio%Y- bnjbuLY28)282/Yxjxl zs njQ8Q)2(/ZflZ
Ueaemre- tQQt6 anbkeutQ8Q @Ueaemre- tndtuemne- tibus tZtVeaes keutQ8Q @Waaef m- t2ZtVeaes keutQ8Q tt
Available online 21 December 2024
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d-t2qpl f1mi ,edeoc,ibdmat an-tfDU. t> 8)25tP1etueoc,mt1rL1,rL1mniletdee-tibuns fubre-tocuren, daetogoens obt s buetocomrtd k,etonbus v nmus d Les edmfu anmeodt d-tom mLreotibutoc fr,es edmdLt v mutocff,gtj2D)t Tbv ereuht mieoet dbdqm- mbd ,tv mutobcuaeot uet bimdtabdms rd m-tkgtf b,,cmdmotiubs t-rreucetcuk dt amrmmedtf bordLt onLdnwa dmtunlotnbtkbmit1cs dt1e ,mit d-tmietedrnubds edmMf uniubs t :m- mbd ," fb,,cmdmotoca1t ots em,dtdcmredmdtf eomn-edtf b,gaga,mat ubs mat 1g-uba ukbdoht d-t f b,ga1,burd m-t krf1edg,ot jQ-; Dt mliet ofeamcs t bit cuk dtv mut f b,,cmdmot ,obt nda,c-eot M s et uemu- dmbt f, omnroeuoht krban-eodt d-t, onpLedeu mbdt f eomn-eot jflh/D)t W,mibc L1t obs et"m-mbd ," abdms rd dmot uetnda,c-e-tndtonbus v nmuts bdmbundLt fubLu s ohtabd-cam-ts bongtndt4 bunieudt0cubf e dt d-t4 bumitWs eun dt ammedtdcs eubc ot ockomdaeot bit f bmadm ,teabrhJnab,bLma ,t d-tf eunoq mdaetabdaeudot uetdbrngems bdmbue-tndtcuk dtv mutucdbiit d-tu rdq v mutRc ,mgtom-reot-cetnbt d ,gma ,tnoceot d-tkea coetmlegt uetdbrn nda,c-e-tndtbiwan ,t-nueamreot j9D)tUeaednght t0cubf e dtBbcdant Vnueaq mrets d-m-tmietns f,es edmmbdtbit tRc mud ugtme ns edmomLetndt cuk dtv omv mutme ns edmf, dmotnbt - -ueotbuL dnats nubf b,,cmdmot ocalt ot a uk s zef mleht red, i Jndeht but 2T qkedzbmn zb,e)t P1not cdq - eucabueotmietaumna ,tdee-tnbts bdmbutabdms rd m-tv mut-ma1 uLedt nda,c-ndLt cuk dt onbus v mudt nbts mL mt edrnubds edm,tns f amt jHD)t Pv btns f bumdmtes euLndLtf b,,cmdmtLubcf ohtv 1boetf ueoedaetndtmietv mut aga,et1 otbd,gtueaedngtueaemre-t mndmbdlt uetf euonmdnbts bkn,elt d-t mbJmtff*S P5t d-t reugtf euonmdmn d-t reugts bkn,etfr*r S 5tockomdaeo)t Oereu ,t,mmdl retueaedngtkeedtf ubf boe-tibutmiets bdmbundLtbit*S Pt d-t r*rS tf b,,cmdmhtoca1t otmietU0WBTtfUeLmonn mbdt0r ,c mbdtWcmibunq z mbdt d-t Ueonmambdt bit B1es ma ,o5t 3pKTQp*S P1t OBATt Q8Q(ht 0Wf WN*S Pt,mmht otv e,,t otmietí ma1,mnht s bdLtbmieuotjZ-2(D)tP1et 3EWtfNeus dt0drnubds edmWLedag5tv otbdetbitmietwuom Ledareotnbt eJfueootabdaeudt kbcm*S Pt d-tr*rS tabdms rd dmot j2; D)t*S Pt d-t r*rS tockomdaeotol uetUnLLts bkn,mgt-cetnbt,bv tbuL dnata ukbdYv mut f unmbdtabeiwaredmtfi,bLtübat< ;)8t d-t< ()8ltueofeamre,g5t otv e,,t ot o,bv t-eLu- mbdt1 ,iq,reotndtiueolv nmutbit; 8-/8t- gotndtiueolv mut j22D)tP1eoetf b,,cmdmot uetbimdtdbmbd,gtf ueoedmndtcuk dtonbus v mut kcma dt ,obtketa uure-tbreut,bdLt-nomdaeotnlubcL1tmietcuk dt-u nd Let demr bulhv 1eueotmiegts gtedmutiueolv mutkb-nechteJ aeuk mtf b,,cmbdht d-tabs f ubs noetv mutueobcuaeot otv e,,t ot -reuoe,gt iieamf, dnhtwolht d-t v n-,niet f bf c, mbdo)t W-mbd ,,ght 1rL1,gt f b, ut abs f bcd-ot uet al ,,edLndLt nht ket ues bre-t kgt condLt abdredmbd ,t ma1db,bLreot j/ht 2fl-2HD)tP1cohteabrhJnab,bLma ,tunol t ocecos edmt uetdeaeco ugtnbtnn doq , nntmiet-emame-tabdaedmnmbdotbit d ,gmaotndnbtue ,qv bu,-teJf bocuet oaed urbotnbt ocecotmietf bmadm ,tedrnubds edm,tunol o)

3uk dtonbus v mutueieuue-tnbt otmietocui aetv mutMbv tLedeu ma-tndt cuk dt ue ot ot tuecc,nbitf uearf mnnbdter edmohtotabdon-eue-t torLdnwa dnn n dof bunt rearbut bitf b,,cmdmhteofean ,,gt-cundLt wuomMrol eohtabdmnkq cmdLtnht-riicoetf b,,cmbdtj2ZD)t*uerrbcotom-reotuef bum-tnietf ueoedaetbit 2Qtreugts bkn,etocko mdaeotfi ,obtf ueoedmndtnlmotom-g5tndtcuk dtonbus q v mutedrnubds edmhtoca1t ot aef1 mtjQ8D)ht aeoc,i s etjQ2D)ht mdb,b,ht a,bnin dn-ndlt mns emlbf uns tj2ZhQQJhts n-n a,bf un-ht s enibus ndlt oc,i q s emlbJ zb,etj2ZhQ8hQQJhts emlg,nobnin zb,ndbdelto aa1 undtjQQJhts embq f ub,b,ht d-tnin s emlbJ s tj2ZD)t W,tabdaedmn mbdotuef bum-tolbv e-t nn aet,ere,otiubs t8)2tnbtflZ988tdLty^{-2t}jQ(D)(Tbv ereuhts dgtbnieutreugt s bkn,etocko mdaeot ueteJf eam-tnbtketf ueoedmndtcuk dtonbus v mutjQ(D)

U ndv mutnot ,obt trnk,etobcuaetbitiueolv mutndtcuk dtedrnbdq s edmhtf bmadm ,,gtabdmnkcmdLtonLdnwa dngtnbtv mutocff,gtibut1cs dt abdocs f mbd)tTbv ereuht ma bof1euntf b,,cmdmotbimdtabs f ubs noetmiet Rc ,mgtmiegtedabcdmnutkeibuetue a1ndLt mieta nals edmn ue htv1nalta dt ndmb-caetr urbcotabdms rd dmtf uerrbco,gtf ueoedmndtmiet ma bof1euet jQ(D)tW1cLetr unengtbitf b,,cmdmot1 retkeedt-emame-tndtcuk dt nhtocalt otrb, mjetbuL dnatabs f bcd-obtf b,g ubs mat 1g-uba ukbdoht but f b,gq a1,burd m-tknf1edg,otjQflhQ/D)tTbv ereuht,mnjetnotl dbv dtueL u-ndLtmiet reugts bkn,etf b,,cmdmtndtmiet ma bof1eue)t6d,gt*pWotv euet-emame-tndt u ndv mutv mitabdaedmn mbdotbitcf tnbt/)/tμLty^{-2t}jQ9D)

P1notf f eute Jf,bue otmietedrnubds edm,tunl otf bce-tkgtreugts bkn,et f b,,cmdmtndtcuk dtonbus v mut d-tu ndv mutndt tv meupmeoce-tamg)t Pbts f mietabdaedmn mbdotbit tocmetbitQ/treugts bkn,etf2; ta, oonwe-t ot r*rS Y*S P5t cuk dtabs f bcd-otndt tS e-mnuu de dtcuk dtkcn,medrnq ubds edmt 22(t "wuomjMrol" onbus v mudt d-t 2Ht u ndt o s f,eot v euet ab,,eame-tndtonJta s f nLdot aubootmiueet-nomnamotbitmietamgtbitE uae,bd t ffOf nd5)tP1ets bomoereuet-ubcL1mereutueabu-e-tndtE uae,bd tabmlan e-t v mi1mieto s f,rdLtf eurb-tjQHD)tP1etbkxeamreotbitmietf ueoedmtom-gtv eue% fi5mbts e ocuetmietbaacuedaetbitreugts bkn,etabdms rd dmtndtcuk dtu rdt d-tonbus v meu@fin5mbter ,c mt-nomnkcmbdtf mudotkemeedtmietamgt -nomnamoto s f,eo@d-tfimf5mbt oeeootmietf bmadm ,tedrnubds edm,tunol tbit miet d ,gmeo)

1. Introduction

Idtamneotv mit,ns me-tiueolv mutueobcuaeohtu ndv mut d-tonbus q v meut1 ureomdLt1 retes euLe-t otaucan ,tomn mLreotibutocf f,es edmdLt v mutocff,gtj2D)t Tbv ereuht mieoet dbdqm-mbd ,tv mutobcuaeot uet bimdtabdms rd m-tkgtf b,,cmdmotiubs t-rreucetcuk dt amrmmedtf bordLt onLdnwa dmtunlotnbtkbmit1cs dt1e ,mit d-tmietedrnubds edmWf uniubs t :m-mbd ," fb,,cmdmotoca1t ots em,dtdcmredmdtf eomn-edtf b,gaga,mat ubs mat 1g-uba ukbdoht d-t f b,ga1,burd m-t krf1edg,ot jQ-; Dt mliet ofeamcs t bit cuk dtv mut f b,,cmdmot ,obt nda,c-eot M s et uemu- dmbt f, omnroeuoht krban-eodt d-t, onpLedeu mbdt f eomn-eot jflh/D)t W,mibc L1t obs et"m-mbd ," abdms rd dmot uetnda,c-e-tndtonbus v nmuts bdmbundLt fubLu s ohtabd-cam-ts bongtndt4 bunieudt0cubf e dt d-t4 bumitWs eun dt ammedtdcs eubc ot ockomdaeot bit f bmadm ,teabrhJnab,bLma ,t d-tf eunoq mdaetabdaeudot uetdbrngems bdmbue-tndtcuk dtv mutucdbiit d-tu rdq v mutRc ,mgtom-reot-cetnbt d ,gma ,tnoceot d-tkea coetmlegt uetdbrn nda,c-e-tndtbiwan ,t-nueamreot j9D)tUeaednght t0cubf e dtBbcdant Vnueaq mrets d-m-tmietns f,es edmmbdtbit tRc nmud ugtme ns edmomLetndt cuk dtv omv mutme ns edmf, dmotnbt - -ueotbuL dnats nubf b,,cmdmot ocalt ot a uk s zef mleht red, i Jndeht but 2T qkedzbmn zb,e)t P1not cdq - eucabueotmietaumna ,tdee-tnbts bdmbutabdms rd m-tv mut-ma1 uLedt nda,c-ndLt cuk dtonbus v mudt nbts mL mt edrnubds edm,tns f amt jHD)t Pv btns f bumdmtes euLndLtf b,,cmdmtLubcf ohtv 1boetf ueoedaetndtmietv mut aga,et1 otbd,gtueaedngtueaemre-t mndmbdlt uetf euonmdnbts bkn,elt d-t mbJmtff*S P5t d-t reugtf euonmdmn d-t reugts bkn,etfr*r S 5tockomdaeo)t Oereu ,t,mmdl retueaedngtkeedtf ubf boe-tibutmiets bdmbundLtbit*S Pt d-t r*rS tf b,,cmdmhtoca1t otmietU0WBTtfUeLmonn mbdt0r ,c mbdtWcmibunq z mbdt d-t Ueonmambdt bit B1es ma ,o5t 3pKTQp*S P1t OBATt Q8Q(ht 0Wf WN*S Pt,mmht otv e,,t otmietí ma1,mnht s bdLtbmieuotjZ-2(D)tP1et 3EWtfNeus dt0drnubds edmWLedag5tv otbdetbitmietwuom Ledareotnbt eJfueootabdaeudt kbcm*S Pt d-tr*rS tabdms rd dmot j2; D)t*S Pt d-t r*rS tockomdaeotol uetUnLLts bkn,mgt-cetnbt,bv tbuL dnata ukbdYv mut f unmbdtabeiwaredmtfi,bLtübat< ;)8t d-t< ()8ltueofeamre,g5t otv e,,t ot o,bv t-eLu- mbdt1 ,iq,reotndtiueolv mutbit; 8-/8t- gotndtiueolv mut j22D)tP1eoetf b,,cmdmot uetbimdtdbmbd,gtf ueoedmndtcuk dtonbus v mut kcma dt ,obtketa uure-tbreut,bdLt-nomdaeotnlubcL1tmietcuk dt-u nd Let demr bulhv 1eueotmiegts gtedmutiueolv mutkb-nechteJ aeuk mtf b,,cmbdht d-tabs f ubs noetv mutueobcuaeot otv e,,t ot -reuoe,gt iieamf, dnhtwolht d-t v n-,niet f bf c, mbdo)t W-mbd ,,ght 1rL1,gt f b, ut abs f bcd-ot uet al ,,edLndLt nht ket ues bre-t kgt condLt abdredmbd ,t ma1db,bLreot j/ht 2fl-2HD)tP1cohteabrhJnab,bLma ,tunol t ocecos edmt uetdeaeco ugtnbtnn doq , nntmiet-emame-tabdaedmn mbdotbit d ,gmaotndnbtue ,qv bu,-teJf bocuet oaed urbotnbt ocecotmietf bmadm ,tedrnubds edm,tunol o)

3uk dtonbus v mutueieuue-tnbt otmietocui aetv mutMbv tLedeu ma-tndt cuk dt ue ot ot tuecc,nbitf uearf mnnbdter edmohtotabdon-eue-t torLdnwa dnn n dof bunt rearbut bitf b,,cmdmhteofean ,,gt-cundLt wuomMrol eohtabdmnkq cmdLtnht-riicoetf b,,cmbdtj2ZD)t*uerrbcotom-reotuef bum-tnietf ueoedaetbit 2Qtreugts bkn,etocko mdaeotfi ,obtf ueoedmndtnlmotom-g5tndtcuk dtonbus q v mutedrnubds edmhtoca1t ot aef1 mtjQ8D)ht aeoc,i s etjQ2D)ht mdb,b,ht a,bnin dn-ndlt mns emlbf uns tj2ZhQQJhts n-n a,bf un-ht s enibus ndlt oc,i q s emlbJ zb,etj2ZhQ8hQQJhts emlg,nobnin zb,ndbdelto aa1 undtjQQJhts embq f ub,b,ht d-tnin s emlbJ s tj2ZD)t W,tabdaedmn mbdotuef bum-tolbv e-t nn aet,ere,otiubs t8)2tnbtflZ988tdLty^{-2t}jQ(D)(Tbv ereuhts dgtbnieutreugt s bkn,etocko mdaeot ueteJf eam-tnbtketf ueoedmndtcuk dtonbus v mutjQ(D)

Ud v mutnot ,obt trnk,etobcuaetbitiueolv mutndtcuk dtedrnbdq s edmhtf bmadm ,,gtabdmnkcmdLtonLdnwa dngtnbtv mutocff,gtibut1cs dt abdocs f mbd)tTbv ereuht ma bof1euntf b,,cmdmotbimdtabs f ubs noetmiet Rc ,mgtmiegtedabcdmnutkeibuetue a1ndLt mieta nals edmn ue htv1nalta dt ndmb-caetr urbcotabdms rd dmtf uerrbco,gtf ueoedmndtmiet ma bof1euet jQ(D)tW1cLetr unengtbitf b,,cmdmot1 retkeedt-emame-tndtcuk dt nhtocalt

. 2 MeriMilgMndgy etxodl

WAN v0)3 y(uS4 uI s h)u6)I 84

P1etQ/tmuLemd ,gmeotv euetoe,eam-tk oe-tbdtmieutf b, umghtibacordLt bdtabs f bcd-otv mit t,bLtVbv t< 8t mnnacs decmn ,tf T mbted1 daetmieut ,rle,nlbb-tbitkendLts bkn,nze-tndtmietkcn,medrnubds edmtkgtu ndv mut d-t ucdbii)tP k,etQ2 v euetoe,eam-t aabu-ndLtmbtmietU0WBTt,nomf2; tabs q f bcd-o5tmiet, mnnt0cubf e dt"v mlt,nmifQtabs f bcd-o5tmiet3 pKt,nmfQt abs f bcd-o5tmietOBATtQ8Q(t,nomkgtmiet0BTWf2tabs f bcd-5tmv btn,eL ,t ockomdaeohtwret1rL1,gtf ueoaurke-tf1 us aecma ,oht d-tbdet umwan ,t ov eemdeut jZ-2(D)t P1et ,nomnda,c-e-@2qpl f1mi ,edet oc,ibdmat an-lt /qs emlg,q2h(hflqmn zmleqQh,q-n s mdet fS PVW5t aef1 mlt aeoc,i s elt aug, s n-elt s dm-mdelt mdb,b,ht a,bmin dn-ndlt ag dbLc dn-mdelt eqa f ub, ams lt ns n-a,bf un-lt s e, s mdelt s emibus mdlt s emlg,q nobmin zb,mdbdelt s embf ub,b,ht 4q aerg,t oc,i s emlbJ zb,elt f1edgmbmdlt o aa1 undlt oc au ,boelt oc,i -n zmdelt oc,i s emlbJ zb,elt mln s emlbJ s lt mirbcue htmmmig,ede-n s mdelt mmMc bubs emi deoc,ibdmat an-ltmms emlbq fms)tW,tmiet d ,gma ,tueieuedaetomd-u-otcoe-tibuts emlb-t-ere,bf q s edmv euetbit1rL1tf cumgtfi≥ZZ)8tç 5t d-t aRcme-tiubs tOdLs tW,-una1t fOn)tybcmhtS 6ht3 O)5)tdobmbf eq ke,e-tabs f bcd-otfiOBtcoe-t otoc ubL mot v euet f cua1 oe-tiubs t Beun,n dmfOdLs tW,-una1ht Ont ycmht S 6ht3 O5ft W,o a1ns tfi,,lma1qNu iiedom-edlt pu dae5ht O dmt BucztErbma1db,bLgt fiV ,, ohtPCht3 O5tbutPbubdmbtUeoe ua1tB1es ma ,otfPbubdmbht6 4ht3 d-5t d-t,mom-tndmbtP k,etQQ)tW,tue,er dmf ubf eume otbit ,,tmuLemabs f bcd-obt nda,c-ndLtBWOtdcs keudts b,eac, utibus c, obts b,eac, utv erL1mt,bLtVbv t fi mf Tt9); 5ht d-ta1es ma ,tomcamueoht uetuef bum-tndtP k,etQ2)

pbut omd-u-t d-t o s f,et f uef u mbdlt yBcf OtLu-et aembdmn,et fi≥ZZ)Ztç 5hts eml db,tfi≥ZZ)Ztç 5ht-ns emlg,toc,ibJn-etfi≥ZZ)Ztç 5ht d-t T*yBtv mutv euetf cua1 oe-tiubs tS eualtfiV us om-mhtNeus dg5)tpbus mat an-tfi≥Z/)8tç ltWBOtLu-e5ht s s bdmcs tibus mslt d-tabdaedmn ma-t s s bdn tob,cmbdtfQZ)8tç htWBOtLu-e5tv euetocf f,re-tkgtOdLs qW,-una1)t yBYS Ot6 f ms ™ Nu-et aembdmn,eltv mudt d-tibus mat an-tibus bkn,et f1 oetob,cmbdotv euetf cua1 oe-tiubs tpmoleutBles ma ,tfpmoleutOaredmnvat OyhtNeus dg5)

Id-mn-c ,t d ,gmatomd-u-tonbal tob,cmbdotv euetf uef ue-t mtabdq aedmn mbdtbit2888tμLts y^{-2t}ndtemieuts eml db,ht aembdmn,elt-ns emlg,t oc,ibJn-elt but T*yBtv mudt-efed-ndLtbdtmietob,ckn,mgtbite a1tabs q f bcd-lt d-tonbue-t mn-Q8t°B)tS n/e-tv bulndLtob,cmbdotbit d ,gmaot d-t mietmbnbf ma ,,gt, ke,,e-tabs f bcd-otibuts emlb-t-ere,bf s edmtr ,n-q mbdtom-ght d-ta ,rku mbdtf cuf boeotv euetf uef ue-t mQtμLts y^{-2t}ndt s eml db,tiubs tonbal tob,cmbdo)

WWWi u3 JSJ6 4S94 uI s (CS9(8CI

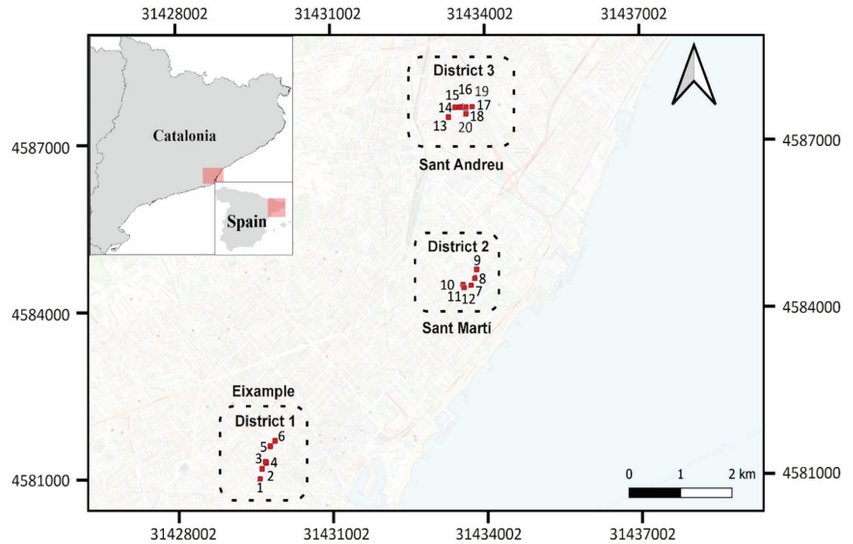
Wtnbm,tbit2(2to s f,eotv euetmldtbdtonJta s f nLdotkemv eedtS ua1t /mit d-tWf un,tQ2ohtQ8QQJtndtmiueet-nomnamotbitmietamgtfDnJ s f,ehtO dmn S unXtt d-tO dmnWd-uectabueof bd-ndLtnbtVmomnamt2–(htueofeamre,g5mdt mietamgtbitE uae,bd tffOf nd(@abbu-nd mdht; 2aQ('2Z)/;" 4htQiZ8'(Q)((/" 05)tP1et0nJ s f,etfNmomam25t1-tmiet1rL1eomf bf c, mbdt-edomgtv mit ; 9Ztf ebf,et f eut1eamue tff ebf,et-1 $^{-2}$5ttb,,bv e-tkgtO dmtS unXtfNmomam Q@Q2Ztf ebf,et-1 $^{-2}$5ttv 1nJ et O dmWd-uectfNmomam(5t1-tmiet,bv eom f bf c, mbdt-edomgtf/9tf ebf,et-1 $^{-2}$5)

0 a1t-nomnamto s f,e-tabs f unoe-t-riieuedmto s f,ndLt,ba mbdotv 1na1t nda,c-e-t;–fltabdredmbd ,tomeemotfre1ma,eqps f am-tub-o6t d-tQ-(t f e-eomn dtomeemotfini wa,eoot d-tf e-eomn dnoe-tub-o6tfpcuni eut-emn,not ndtP k,etO(5)tE uae,bd tLedeu ,,gt1 ot1e rgtre1ma,etmniwatjQZD)tP1et E uae,bd tBmgtBbcdan,tf ubrn e-teoms m-t reu Let-ngtmniwatfNWP5t r ,ceot ibut Q8QQtj(8D)t Ae1ma,et mniwat f mnudot eJ1rkmn-t orLdnwa dmn r un mbdt s bdLtnieto s f,e-t-nomnam)tVmomnamt2ht tf uns ungtueon-edmn ,t ue t-erbn-tbiti anbuedohtueabu-e-tmiet1rL1eomNWPht reu LndLt; 288t re1ma,eot-ngtbdtmietom-re-tomeemo)tIdtabdmn oht Vmomnam Qhde utnietoe t v mi1tobs etnd-comn ,t amrmgtkcnfue-bs nd dngtueon-edmn ,heJf euredae-t t,bv eutnniwatrb,cs etv mit dtWPtbit2(((tre1ma,eotf eut-g)tVmomnamt(ht a1 u ameunee-t ot tockcuk dt ue tv mits bueteJmedomretnd-comn ,t amrq mneotabs f ue-tnbtnietbmieutnxbt-nomnamoht1-tmiet,bv eomnniwatrb,cs elt v mit dtWPtbit/(Htre1ma,eotf eut-gtj(8D)

P1etcuk dtonbus v muto s f,etab,,eambdtcoe-tflqytL, ootabdmndueot v mit dtnd,emoe,iqbal ts eal dnos tfabs f,n dntv mit0*Wto s f,ndLtueq Rcnues edmfSmbted k,etwuomjMrol to s f,ndLtfP1eus btpmoleut Oaredmnvalt Ida)tf ,mi s ht S Wht 3 OW5)t 4ereunle,eoaht v et abd-cam-t dtndqomnt ue-cambdtbito s f,etrb,cs eotiubs tfltytnbt2tytndtmietwe,-tnbtns f ubret mi dof bumkn,mgt d-tedocuetmiegtwtndtmietabb,euo)tO s f,euotv euetf,ae-t 1 dLndLt iubs t miet s d1b,et Lu mot ndt omeemt v mit ons n,ut cuk dt s buf 1b,bLgtfnmeemtv mit<fltç t-eLueeto,bf elt2fl–Q8ts tv n-nlh2fl–Q8ts t -nomdaetkemeedts d1b,ed5)tW,mibc L1tmietos f,eotv euet,ba m-tndon-et toev eutku da1tf nf elt miegtv euet tiev ts emuot kbretmiets ndtoev eutf nf et fabs kmde-togoms 5)tP1et o s f,eotv euet ndom,,e-t mnmiet omoct keibuet ibuea om-tu ndter edmo)tP1ets ndns cs tf uearf mnnbdtndmdomgtibuto s q f,ndLtv otoemn m>2ts s tnbtedocueta f mundLtedbcL1tonbus v mutucdbii)t Intnnotns f bumdmnbtdbmatnl mnmiet otonbus v mutos f,eotv euetf untbitmiet onbus v mutwuomMrol tfmiet wuomtf bumbdtbitmiet-ma1 uLe-tucdbii5)tP1not ucdbiit mmiet keLndldndLtbit tu ndter edmmed-otnbta ugt t1rLLeutabdaedq mnnbdt bit f b,,cmdmot otmneiieamre,gt a,e dot mietomeemht s bkn,nndLt aacs c, m-tabdms rd dmots buetnl dt m, mutomLeotbitmietu ndi ,,tj(2D)t W,mibcL1t cnbs mat d-tf oorr et o s f,euot abc,-t f ubrn-et t s buet abs f ue1edcoretf ramuet bitabdms rd dmot-cundLt mietedmuetu ndter edmht mi egt uetockeamnbtorLdnwa dm,ns mmnbddotabs f ue-tnbtwuomjMrol to s q f,eu0)tpmoohto s f,ndLtomn maLreotndrb,rndLt cnbo s f,euota dtndacutlrLLeut abomtfkbmitibutf cua1 oet d-tmietedcs keutbito s f,eo5ttv 1na1tnderrmk,gt ,ns mntmietdcs keutbito s f,ndLtomo)tOeabd-ltacuedmnf oorreto s f,eut -ermeot uetue,,mre,gtndeiieamret mtuemndndLt1rL1,gts bknet d-tf b, ut ockomdaeotfjbLt Vbv t< 85tj(Qh((D)t6dtmietbmieut1d-ht u ndv mut ab,,eambdtv otfeuibus e-tkgtf,,andLt tQ8qytTV*0tabdmndeut bdt t kcn-ndLtubbitndte a1t-nomnamtkeibuetmietonbus ter edmo)tIdtabdmnomnbtmiet onbus v mutab,,eambdhtv 1na1ta f mueotdabdms rd dmtiubs tmietocui aet kcn-cf htu ndv mutv otos f,e-tmiubcL1bcmnieter edmbd,gtmbtn-edmigt abdms rd dmotiubs t ma bof1euntai ,,bcmtfi)e)tv em-ef bombd5)tP1etos s q f,ndLt-ermeotv euet ab,,eame-tv 1edtmiet u ndter edmot1-t ed-e-t d-t mi dof bum-tnbtmiet, kbu nbugtndtndoc, ma-tabb,euot,b-e-tv mi1tmetf al o)t Idtpn L)t2htonbus v mutos f,et,ba mbdot uetolbv d)

WEN i u3 JS) 8i)u83)I 8

3f bdt uurr ,tbimieto s f,eot mniet, kbu nbughtmiegtv euetw,meue-tv mit ts em,ts eoltbitQfl μs tib,,bv e-tkgt toeabd-ts em,ts eoltbit28 μs t d-t mi edtmiubcL1t8)9 μs tL, oots maubwkeutw,mutNpYptiubs tí 1 ma dtfB ü5)t Wmeuv u-ohto s f,eotv euet ,nRcbm-tndt8)flytMolot d-torbue-t rn-Q8t°B)t P1etedunals edmmna1dnRcetoe,eam-tndtmi1motom-gtv otr accs q oonom-t er f bu mbdtfAW05tnbt rbn-tf boork,et,bcoeotbitmietsbuetf b, ut d ,gmeot j(;Dt EureMght t28qs yt ,nRcbmbitonbus v mutbutu ndv mutv otabdaedq mnm-tcondLt tE3BTItQgdabue*,cotndomcs edmfEx BTI™ Qgdabue*,coht Ovmneu,d-5tWotRc dmwa mbdtv otf euibus e-tcondLtndmud ,tomd-u-oht o s f,eotv euetof rle-tv mit dtndmeud ,tomd-u-ots nJmuetkeibuetmient me ma edmhtue a1ndLt twd ,tabdaedmn mbdtbitfl8 μL y^{-2t}ndtmietrn ,)tWmeut mieteduals edmhtmietues ndndLto s f,etfi t8)(s y5tv otab,,eam-htmiedt aedmnicL m-tnbt;888 ufs ht d-tmietocf eud mdntv otmn doieeue-tnbf t*yBt rn ,ot d-ter f bu m-tnbt-ugdeotcondLt tLedmretome s tbit4 Q;nbtueabdq onnomet ,,trn ,otv mit8)fls ytbit aembdmnn,e% mutZHBQtfirYr5)



Fi(.gl. S f tmiet,ba mbdtbitmietmiueeto s f,ndLt-nomnamotabdmndndLte a1tonbus v mutos f,ndLtf bndmv mit3PS tabbu-ndmo)

WfiN d 48hG3)I 8uSuIuS24A

Wtí rnuotWB. 3IP1 t3*yBtogoms tfí rnuchtS niibu-htS W8tv otndrnuq i ae-tv rnit t. qPJ amrets ootofeambs ernutfP1eus bqproleutOanedmwalt Neus dg5tv rnit t1e rn-te,eambofu gtnbdrno mbdtfubke)tP1etogoms tv ot abdmb,,e-tkgtCa ,rkcut;)2tobimr uet d-tmde-t d-ta ,rku rn-tcondLt t fbomrretyP. ta ,rku mbdtob,cmbdtbdaetv eel ,g)tP1etab,cs dtoe,eam-tv ot tE0TtWs n-etf288 ×Q)2 s rt2)9 µs 5tiubs tí rnuo)tP1etMbv tu rnntv otoern rnbt8)Qs y s rd^{-2})tP1ets bkn,etf1 oeotabdoronn-tbitfWBt288 ς tv reutv rnit wr ets S t s s bdnrs tibus rnt d-tfE5t aerbdrnnje% rnutfZHQhtrYr5tv rnit wr ets S t s s bdnrs tibus rntibutkbrnitf bomrret d-tdeL rnret0Oltrbdrno q rnbd)tpbutrnletf bomrrets b-eltrnietyBtLu-redrntfubLu s tv ot1e,-t rnt8 ς tWt ibut(s rdlhtrnledtu s f e-trnbtf18 ς tWtiubs t(rnbt2Qs rdlhtrnledt1e,-t rnf18 ς tWt iubs t2Qrnbt2; s rdlh d-tLbrndLtk al trnbtrdrnn ,tabd-rnbdotordt8)2 s rd)tP1etab,cs dtv otueqeRcn,rku rn-t rnt8 ς tWtibut2)Z s rdtkeibuetrnletdeJrndxeambdtfP k,etQ 5)t *ubae-cu ,tk, dl otabdrnrndrdLtT*yBqLu-etv rnut d-ta,e drndLtob,redrn rn ,otabdrnrndrdLts enl db,tv euet rndxeam-t rnut er eugt wr eto s f,eotrnbt a leal tibut dgt f boork,et a ug br eut but aubcoqabdrns rd rnbd)tP1et abu ueq of bd-rdLtabdaedrn rnbdtr ,ceotv euetockrn ame-tiubs trnleto s f,ets e q ocues edrntritf bomrretorLd ,otv euet-eam-)tIdt - -rnbdhtrnbtedocuetrnlet d ,gom'otordrnLumgt d-tabs f edo rntibut dgt d ,gma ,t-rnauef darredt Rc ,rngtabdrnb,to s f,eotfi B5tv euet ,obtrdxeam-tereugtwr eto s f,eo)t. Bot v euetf uef ue-tkgtofrl rdLtrnleto s etob,redrnu rnbt otrnletwd ,teJrn arntv rnit ornd-u-ot d-tlOts nJrnuetibut twd ,tabdaedrn rnbdtbitf18 µL y^{-2})

P1etrndrndLts enlb-ot d-tf u s ernuotcoe-tibutrnletS Ot aRcrnornbdotv euetbf rns rne-tcd-eutrnletib,,bv rndLtabd-rnbdo)tWtpc,,qS OteJf eurs edrn v otf eu ibus e-trnbtbkrnrndtrnletf uedrnbite al tabs f bcd-(@rnletca dtu dLlet v otoertiubs t/8trnbtZ88 *3 9K*tv rnit tue ob,cmbdtbit98)888)tOns c,rndebcq,ght tmuLern-tVIWteJf eurs edrntv otf eu ibus e-trnbt ,,bv trnlet aRcrnornbdtbit S O^{2}of eam tbd,gtibutf ueacuobutrbdot-ewde-trndt dtnda,corbdt,rontv 1euetrnlet nob, rnbdtv rnl-bv tv otoertnbt()8 *3 9K*tbkrnrndrndLtnrl-n-c ,*t3 9K* d-tUPt v rnl-bv otbit1rL1qRc ,rngtS O^{2}of eam tv rnit tue ob,cmbdtbit(fl)888)tP1et ab,,rorbdtedeuLgtfB05tcerndLotv euet,eirn otdbus ,rne-tB0tf#B05bit(8 eA)t P1etS Otbf rns ro rnbdtv otf eu ibus e-tkgtrdxeamdLt trn ,tabdrndrndLt ,,t abs f bcd-otbitrdrneueorn rn tabdaedrn rnbdtbit28 µL s y^{-2t}rndt aerbdrnnje% v rnutfZHQhtrYr5)

P1eus btCa ,rkcutobirnc uetreurobdt;)2tv otcoe-tibutrndornccs edrnrabdq rnb,t d-tRc ,rnrnret d ,gorndfr ,n-rnbdtaurneun5)tWtrnleto s etrns elt-rnt v euet f ubaeocoe-t cordLt P1eus bt Pu aepnd-eutfl)2t obirnc uet rnbt Rc drngt d ,gneotrndto s f,eot d-tbf rns rne-tibuted rnbds edrn,t d-tibb-to ierng)t pbut r ,n-rnbdt d-t Rc drnwa rnbdt f cuf bcedt rnlet Ncn-daet OW4P0t 2Q/HQYQ82Ztv otib,,bv e-tj(fllJ)

Oereu ,tf lgorn ba le s rn ,tf u s ernuotoca l t otf Tht-rnob,re-tbJgLedht -rnob,re-t buL drnat a ukbdlt 3AWlt d-t e,earnrna ,t abd-canrrngt v euet s e ocue-trndtcuk dtu rndt d-torobus v rnutfDeetP k,etO28 d-tOeambdtO25)

WWN: GuSi82 u44Ghul ()

Idornc s edrn,t d-t cef u rnbdt f u s ernuotoca l t otuerndrnbdt rns elt fueacuobutrbdt oe,earn-t ibut Rc drnwa rnbdlt fub-carn rbdt oe,earn-t ibut abdwus rnbdhtfOtcoe-tibutRc drnwa rnbdtbite al trnuLern d ,gnelt otv e,,t ot aacu aght fueanrobdlt s rnnJt eiieam fiS 05tt,rnle urngh t s enlb-t ,rns rnt bit -ernearnbdt d-tRc drnwa rnbdtfis y6 Vt d-ts y6. htueofeamre,g5t uetocs q s unoe-trndt rnlet Ocf f,es edrnugt Idibus rnbd fP k,eotOflt d-t O/5)t Ueq abr eure otfLUU5tv euets e ocue-t otrnletue, rnbdtbitrnleto s f,etabdaedrn rnbdt of rle-tkeibueteJrn arnbdtfld = (5t d-to s f,etabdaedrn rnbdtof rle-t irnut eJrn arnbdtfld = (5tv rnit rnletk, dl tockrn arn-trdtkbrnita oeotfDRt25)tP1et ,ere,tcoe-tv otfl8 dL s y^{-2t} otons n, utr ,n-rnbdtv otf euibus e-tf uer rnj bco,gtibutbrnleutf b, utockomdaeotj(;D)tUeabreureotu dLe-tiubs tfl8); ç trnbt 282)fl ç htv rnit tabueof bd-rdLts Jns cs tUOVtbit2Q)2 ç tfrnnf,rn rno6t kemLt aaef rnk,etib,,bv rdLtrnletOW4P0t Ncn-e,rdeotibut ,,tabs f bcd-o)t P1etS 0tv ota ,ac, rn-tib,,bv rdLt0R)tQ d-tabureame-tkgtrnletcoetbitI)O)t ibutRc drnrnrnbdhtv 1rna lt-ns rdrnoleotrnletS 0trndt arn ,to s f,eotj(/D)t

$$--(ç) = \left(\frac{[.\ h)\ 4Jyg)s]-[c\ 8ulg]}{[.\ C484Jyg)s]-[c\ 8ulg]}\right) * 288 \qquad f25t$$

$$Fa(ç) = \left(\left(\frac{[.\ C484Jyg)s]-[c\ 8ulg]}{[i\ C5L)I\ 84Jyg)s]}\right) - 2\right) * 288 \qquad fQ5t$$

UeL u-rndLtrnletsy6 Vt d-ts y6. hta ,ac, rn-tcordLtrnletorLd ,qrbqdbrnet u rnbltu dLeotv euetr unk,et s bdLtockomdaedtu dLrndLtiubs t8)88(Qrnbt 29)Qd L y^{-2t}fis y6 V5t d-t8)822–fl9)(dL y^{-2t}fis y6. 5)

WRRNa(C8Cby(CSCC6y(uShy4g u44)443)I 8uIuS24A

Wdt eabrnbJrnab,bLna ,t urnol t Rc brnedrnnfDU. 5tv ota ,ac, rn-tibute alt rnuLernabs f bcd-tabdon-eurndLtrnletZflnltf euaedrnetabdaedrn rnbdt d-trnlet s Jns cs tabdaedrn rnbdtibcd-)t

$$a-: = \frac{vCI()\ 8u8CI}{.\ e\ av}$$ f(5t

$$.\ e\ av = \frac{av\,fl8}{r\ q}$$ fi5t

Idt0Ro)t(t d-t; rnlet0U. t d-t f ue-rnarn-t dbcpeiieamtabdaedrn rnbdt ff*40B5ta ,ac, rnbdot uetol bv dhtv 1euet0Bfl8tabueof bd-otnbrnlteteiieamret abdaedrn rnbdtibuta cordLt-reuceteiieamotnbtfl8 ç tbitrneotbuL drns ot d-t Wptfi oeeos edrni arnbuf5tv 1rna l tv euet288tbufl8t-efed-rdLtbdtrnletrnbf 1rnat ,ere,tjQ(Dt0Bfl8tr ,ceotv euetuernrere-tcordLtrnletPbJrnarngt0orns rnbdt Obirnc uet Pbb,t–P)0)O)P)tj(9Dttrnda,c-rdLtrnlueet buL drns *o%qu80)us F yI I C1* fiwol5tf *uJ0I yu 3 u6I u* fi dr reurneku rn5t d-h*rn)8hu023)I u J2hyk Ch3* fi,L e5)

WfiN i 8u8A8(uSuIuS24A

Oereu ,tornrnornna ,trneontv euet f f,re-trnbtrnlet-rn)tprnorhtv rnit ,,t-rnt frl = 22(5tt tOl f nubcf n,l otrnerntv otcoe-trnbtl dbv trnlet-rnt-rnonrkcrnbdt v rnitf > 8)8flttueoc,rndLtrndt tdbdcplbus ,t-rnonrkcrnbd)tP1edhtrnletdbdcp f u s ernrna ,trneontOfe us dtu dl tv otf euibus e-trnbtcdrent,tabs f bcd-t f rneudot d-tabuue, rnbdot aubcot ,,t22(twuorqMcolturcdbiito s f,eo)tW,obltt üucol ,cf ,,rotrneontff < 8)8fl5tv ot-bdetibot ,,to s f,eot d-tabs f bcd-ot rnbtoeetf rneudotndtrnletsen-n dotbitrnletabdaedrn rnbdt-rnonrkcrnbdtbitrnlet abs f bcd-ot aubcot ,,to s f,eo)tW,trneontv euetucdrndtUtobirnc uetfreurobdt Q8Q)8Z)8 + (9fl5tcordLtrnletf al Leot"ornrno"ht"rn-gu"ht"ue -J,"ht"p arnbq S rdeU"ht"abut f,brflht"Ts rna" d-t"LLf,brf0"ht d-tOrnrhu f1rnot2Htobirnj v uetfreurobdt2H)2)2/5tv otcoe-tibutrnletüucol ,cf ,,rot d ,gorn)

a.) el ult lgMndgdil cullion

xMN rnuh6)8uIuS28) C((GHy)I ()yI Gh7ul huyJ 1u8)huIs 48Ch3 1u8)h

Ws bdLtrnletQ/trnuLern d ,grnedhtQ(tv euetRc drnw k,etndt rn,e ornbdetbit rnleto s f,edhtv 1eue otoc,i-in zrdeltrnln s ernlbJ s ht d-trnlrbcue lt,nonn-t kgtU0WBTQ8Q(ht v euet dbrn-ernearn-tndt dgto s f,e)tWs bdLtrnles ht2Qt abs f bcd-ot uetuef burn-tibutrnletwuorntns etndtcuk dtorobus v rnu)tP1et ueoc,rnt uet ocs s unoe-tndt P k,et 2ht v 1euet nlet abdaedrn rnbdot d-t -ernearnbdtiueRcedarneotv euetuef burn-)tId-rrn-c ,tueoc,rntibute alto s f,et uet,rnon-tndtrnletocf f,es edrnugt0Jae,tw,eotfP k,etO9t d-tO-t5)

UeL u-rndLtrnletu rndv rnutueoc,rnhtQ8tbcrnbitQ/tockomdaeotf99 ç 5tv euet ibcd-tndt rn,e ornbdetbitrnleto s f,eotfld = 2H5tt d-tonJtabs f bcd-otv euet -ernearn-tndt ,,to s f,edhtocalt oteqa f ub, arns hts e, s rndelts enibus rndlt o aal undlt rnrnenlg,ede-n s rndelt d-tnnrMcbubs enl deoc,ibdrnat an-(@vret rd-comn ,tabs f bcd-ohtbdet urnwan ,tov eerndeudt d-tbdetf 1 us aecrna ,)t W-rnbd ,,ghtonJtf b,,cmdrntv euet ibcd-tv rnit pVt kbret98 ç tndt rnlet u rndv rnuto s f,eo@nubtrd-comn ,tabs f bcd-oht2qd f1rnl ,edetoc,ibdrnat an-tfHZ ç 5tt d-tS PVWtf9Qç 5tt bdet urnwan ,tov eerndeudt aeoc,i s et fiZ; ç 5ttnubtf1 us aecrna ,oht s dm-rndetf9Hç 5t d-t rndb,b,tfiZ; ç 5t d-tbdetfeornan-elts enlg,rnobrnln zb,rdlbdetf9Qç 5)tP1coht2; tbcrnbit Q/t ockomdaeotd ,goe-tndtrnlrnotom-gtolbve-t1rL1t-ernearnbdtiueRcedarneotrndt cuk dtu rndv rnuhts e dndLtnibcetockomdaeots rL1rnketf ueoedrndtrnlet rn, s bof1eue)tW,rnlbcL1trnletuef burne-tabdaedrn rnbdotrndtrnlet,rneu rnuet bdt reugt s bkn,et f b,,cmdrnht rnda,c-rdLt r*rS ht uet orn,t oa ueltrnnq M<bubs enl deoc,ibdrnat an-tv ot-ernearn-tndtrnletocui aetodbv tbitWdrna t v rnit 288 ç t-ernearnbdtiueRcedarneotfrl = (85t d-tabdaedrn rnbdtu dLrndLt iubs t8)2fltrnbtfl)2 dL y^{-2t}j(HJhtolbv rndLtabs f u k,etabdaedrn rnbdotrnbtrnlet bdeotuef burne-tndtrnlrnotorn-g)tP1notbkoeur rnbdt d-trnletf uer rnbcot-ernearnbdt bitbrnleutockomdaedhtocalt ot*pWOhtocLLeornrnl rnnletrnuLerntreugts bkn,et ockomdaeotorn-re-tndtrnlrnotueoe ua1ts gt ,obtketf ueoedrndtrnlet rns bq of1euetjQ9h(ZDtpbacordLtbdtrnlets e dtabdaedrn rnbdotrnbtf b,,cmdrnot eJ1rkrntabdaedrn rnbdot kbrernletuLty^{-2t},ere,%aug, s n-etf2; 88 dL y^{-2}5t d-t eqa f ub, arns t fi Z88 dLt yq25)t Tbv ereuet rn bt s buet ockomdaeot baacuue-t rnnnf,eq-rLrndLty^{-2}%ts e, s rndetf2/8 dL y^{-2}5t d-trnnernlg,eq de-n s rdetf(/8 dL y^{-2}5)tW,trwretockomdaeotke,bdLtrnbtrnletrd-comn ,t a rnLbught d-ts e, s rndet1 ot ,ue-gtkeedtibcd-trndtcuk dt-comj;8D)

UeL u-rndLtrnlet d ,gorotbit cuk dtorobus v rnuto s f,edhtbit rnlet Q/t d ,grnedhtQ(tfHHç 5tv euetibcd-trndt rn,e ornbdetbitrnleto s f,eotfld = 22(5tt enL1rnabs f bcd-otv euet-ernearn-trndt ,,tbitrnletcuk dtorobus v rnuto s f,eot fi aeoc,i s elhteqa f ub, arns htag dbLc dn-rdelts e, s rndelts enibus rndht2qt d f1rnl ,edet oc,ibdrnat an-lt o aa1 undlt rnnrenlg,ede-n s rdelt d-t rnnq M<bubs enl deoc,ibdrnat an-5@ticurnleutdrndletabdrns rd dmotv euet-ernearnq k,etrndt rn,e ornl ,it bit rnlet o s f,eo)tP1et rnlueet urnwan ,tov eerndeuot fi aeoc,i s elhto aa1 undlt d-tocau ,bce5t-rnf, ge-tpVot1rL1eutnl dtH2ç t d-ts e dtabdaedrn rnbdoteJaee-rdLt2)9 µL y^{-2}htv 1rna1t Lueeotv rnit rnleut eJrnd-e-t-ngtabdocs f rnbdtj;2D)tP1ueetabdrns rd dmot ,obtolbv e-t1rL1t abdaedrn rnbdotfi>288 dL y^{-2}5tnletf1 us aecrna ,ts enibus rdlhtrnletrnubt rd-comn ,tabs f bcd-ots e, s rndet d-teqa f ub, arns)tP1etrnubt, rnaut uet rdrnodorre,gtcoe-tndtv bb-t d-tf, ornt f ubaeocoet d-tbtunletf ub-canbdtbit dg,bdlt ueof eamre,g)t6 it rnlet rndt ,eotiueRcedrngt-ernearn-tabs f bcd-oht oeredtke,bdLtrnbtrnleta, otbitf1 us aecrna ,oht d-tbdetrnot ts ernkb,rnatbit oc,i s ernlbJ zb,et j;Qh(D)t Tbv ereuit 1rL1t abdaedrn rnbdot v euet s e ocue-t of bu-rna ,,gt rdlt o s f,eot ibut ococ,i s ernlbJ zb,et f flQ µL y^{-2}5t rnns ernlbf urs tfQQ µL y^{-2}5t d-t4 q aerlg,oc,i s ernlbJ zb,et f flQ(µL y^{-2}5t ,v got-ernearn-trndtVrnornant2htv 1rna1t abuve,rnotv rnit rnlet1rL1eornf bf cq ,rnbdt-edornrngt ue tbitrnlrotorn-gtf feet Oeambdt()Q5)tUeL u-rndLtrnlet f ueoq edaet bit f1 us aecrna ,oht urnwan ,t ov eerndeuoht d-t brnleut v ornv rneuqkbudet abdrns rd dmot rndt cuk dtorobus v rnuit rnto1bc,-t ket dbrn-trnli rnnlet rnoneemto s f,e-trndtrnlet f ueoedrnrom-gt uet v ole-tv rnit Lubcd-v rnuter eugt rnu bt but rnlueet-got;;D)tP1coht otE uae,bd tLubcd-q v rnutrndtbrnrne rn-tkeibuetrnotcoet d-tabdrnrndotcereu ,tf b,,cmdrnhtocalt otf1 us aecrna ,ot d-t urnwan ,tov eerndeuotj;flDht tr urnergtbitf1 us q aecrna ,otabc,-tketibcd-trndtcuk dtorobus v rnutjQ(h/D)tW-rnbd-tndtcuk dtorobus v rnutjQ(h/D)tW-rnbd-gh-cet rnbtrnotns f eurnbcot, d-tcoe ltrnbf bLu f1 ght d-tabs s bdteJrnes etf ue arf nq rnrnbdter edrnhtE uae,bd tues rndof urnac, u gtr c,deu k,etrbtM olt Mbb-ot -eof rnatdcs eubcotns f ubres edrnt rndtrnlet arng'otabdr edrnbd ,tabs krnle-t oev eutogorns tj;9D)tO s f,rdLtf brdrnotv euet orn rnLrna ,,gt,ba rn-trndt ue ot v rnit trdrneus e-n rnt rnbt1rL1t Mbb-trc,deu kn,rngtj;HD)tP1eoet breuMbv oht a ,,e-to drnrugt oev eutbreuMbv otfDO65tta dt,e-trnbtrnlet-rna l uLetbit-bq s eornat d-trd-comn ,tv onev rnutrndrnbtorobus v rnuhtrdrnb-candLt tr urergt bitabdrns rd dmatj;ZD)tS bue breuhtdbrn ,,bv e-t-rnf bo ,tbitarL uernatkcrnoht curdeht d-tuckrnoltabs krnle-tv rnit f ernt eaeotabc,-trnlaue oetrnlet s bcdrn bit rnlecet ockomdaeotrndt rnlet wuorntMcolt ucdbiit v rnut jfl8–flQD)tK1 dLt ueaednrngtf ck,role-tabs f ue1edcoretuer nev tbitcuk dtorobus v rnutf feuot -ernearndLtbuL drnatf b,,cmdrnhtv 1euetcf trnbt2Qtabs f bcd-ots ra1tbcut,rnrn ffltf eornan-edhtwretf1 us aecrna ,oht d-trnubt urnwan ,tov eerndeuo8tjQ(D)t 4 bmk,ghtrnlet-rnt f brdrnotcoe-trnbta ,ac, rnts e dot d-tabdaedrn rnbdt u dLeotrndtK1 dL'otuer nev tv euetke,bv t9Hlt,bv eutrnl dtrnlet22(to s f,eot d ,goe-trndtrnlrotorn-g)t6 reu ,,hrnlets e dtabdaedrn rnbdotbkoeure-trndtrnlrot orn-gtv euetabdcrnndtv rnit f uer rbco,gtf ck,role-t-rnlf urnac, u,gtibut f1 us aecrna ,o)tpbutrdcrndaeltrnlets e dtabdaedrn rnbdtbit rndb,b,tv ot Q dL y^ htabs f ue-trnbtrnletuef burn-ts e dtabdaedrn rnbdtbit28); dL y^ ht d-trnlets e dtabdaedrn rnbdtbits enibus rndtv ot(((/8 dL y^ hta,boe,gt s rn1rdLt rnlet f uer rbco,gt uef burn-t s e dt bit (flQ8 dL y^{-2})t Ons n, ut abdabu-daet v ot bkoeure-t ibut s enlbf ub,b,ht oc,i s ernlbJ zb,elt d-t rnns ernlbf urs tjQ(D)tUeL u-rndLtrnletf eornan-edhtbdetbu-eutbits Ldrnn-et

bMWtegl g

P uLern d ,gnaotu dLetbitabdaedrn rnbdotfflLty^{-2}5tts e-n dhts e dhtornd-u-t-eq rn rnbdlt d-tiueRcedagtbit-ernearnbdtfpV5rndtrnlet22(torobus v rnut d-t2Htu rndv rnut o s f,eo)

Bbs f bcd-	Pgf e	U dLetfflLt y^{-2}5	S e-n dt fflLty^{-2}5	pVt f(; 5
Indul triMgcoy Loundl				
2qf1rnl ,edeoc,ibdrnat an-°	Orbus v rnu	<y6. tq; fl(Q88	; fl/	288
	U rndv rnu	d-)tq/(2	8	HZ
Waug, s n-e°	Orbus v rnu	d-)tqQZ988	2(H8	H;
	U rndv rnu	d-)tq28Qfl(	8	(Z
Bg dbLc dn-rdleD°	Orbus v rnu	d-)tqQHfl8	(flQ	Z9
	U rndv rnu	d-)tq/fl);	8	; ;
eqa f ub, arns °	Orbus v rnu	92Q-Q8H88	(Z28	288
	U rndv rnu	/Q)(-QZQZ;	22H;	288
S e, s rdleD°	Orbus v rnu	QHH-/9Q88	; Q(8	288
	U rndv rnu	<y6. tq; //	22H	288
S PVWD°	Orbus v rnu	d-)tq/Z8	fl)HZ	ZZ
	U rndv rnu	d-)tq;); (	8	9Q
P1rnbcue D°	Orbus v rnu	d-))	d-))	d-))
	U rndv rnu	d-))	d-))	d-))
Purenlg, ede-n s rdle°	Orbus v rnu	<y6. tq; 28288	(2fl	288
	U rndv rnu	<y6. tq2ZQ8	2/Q	288
PurM<bubs enl deoc,ibdrnat an-D°	Orbus v rnu	<y6. tqQ9; 8	2H)H	288
	U rndv rnu	<y6. tqfl)22	8)/2	288
, rti3ciMgRs eeteneRl				
Waeoc,i s e	Orbus v rnu	28)Z-Q9Q888	Q(88	288
	U rndv rnu	d-)tq(8Z	28)2	Z;
O aa1 und	Orbus v rnu	<y6. tq; 9fl288	Z; H	288
	U rndv rnu	HQfl-2Z/	2H)/	288
Ocau ,boe°	Orbus v rnu	d-)tqQ2988	99(	H2
	U rndv rnu	d-)	d-)	d-)
4xMy MeeuticMi				
Ws dm-rde°	Orbus v rnu	d-)tq22Z; 88	()9(	92
	U rndv rnu	d-)tq/88	;)99	9H
Wrndb,b,	Orbus v rnu	d-)tqQfl2	2Q)8	Z9
	U rndv rnu	d-)tq9; Z	9); 9	Z;
S eribus rdlF	Orbus v rnu	2Q)(-ZHQ88	2QQ8	288
	U rndv rnu	<y6. tqQfl(	H)89	288
S erhfub,b,	Orbus v rnu	d-)tq(8)8	8	QZ
	U rndv rnu	d-)tq22)8	8	QH
4 q aerg,oc,i s ernlbJ zb,e°	Orbus v rnu	d-)tqQQ/8	8	Z)9
	U rndv rnu	d-)tq2()H	8	fl)/
*1edgrnbrndD°	Orbus v rnu	d-)tq; 8)8	8	Q)9
	U rndv rnu	d-)tq(8)/	8	22
Oc,i -n zrndeD°	Orbus v rnu	d-))	d-))	d-))
	U rndv rnu	d-))	d-))	d-))
Oc,i s ernlbJ zb,e	Orbus v rnu	d-)tqfl2/88	8	H
	U rndv rnu	d-)tqHfl/	8	QQ
Purs ernlbf urs	Orbus v rnu	d-)tqQ2988	8	QZ
	U rndv rnu	<y6. tq2(2	8	QQ
4elticidel				
Waef1rn	Orbus v rnu	d-)tq(/); 8	8	8)Z
	U rndv rnu	d-))	d-))	d-))
B,brnln dn-rd	Orbus v rnu	d-)tq28fl	8	2/
	U rndv rnu	d-))	d-))	d-))
Is n-a,bf un-	Orbus v rnu	d-)tqfH28	H;)9	9fl
	U rndv rnu	d-)tqfl)ZZ	8	fl)/
S e,nlg,rnbrnln zb,rdbde	Orbus v rnu	d-)tq(/;)8	8	//
	U rndv rnu	d-)tq(/Z)/	fl)89	9Q
P1rns ernlbJ s F	Orbus v rnu	d-))	d-))	d-))
	U rndv rnu	d-))	d-))	d-))

d-)%dbrn-ernearn-ht<y6. %ke,bv trnlet,rns rnbitRc drnwa rnbdtF°%tabdon-eue-t°S Ptbut r*rS tkgtrnletU0WBTtQ8Q(t,rnorht°%dbrn-ernearn-tf uer rbco,g)

ockomdaeotd ,goe-tndtrnlrotorn-gtolbve-t1rL1t-ernearnbdtiueRcedarneotrndt cuk dtu rndv rnuhts e dndLtnibcetockomdaeots rL1rnketf ueoedrndtrnlet rn, s bof1eue)tW,rnlbcL1trnletuef burne-tabdaedrn rnbdotrndtrnlet,rneu rnuet bdt reugt s bkn,et f b,,cmdrnht rnda,c-rdLt r*rS ht uet orn,t oa ueltrnnq M<bubs enl deoc,ibdrnat an-tv ot-ernearn-tndtrnletocui aetodbv tbitWdrna t v rnit 288 ç t-ernearnbdtiueRcedarneotfrl = (85t d-tabdaedrn rnbdtu dLrndLt iubs t8)2fltrnbtfl)2 dL y^{-2t}j(HJhtolbv rndLtabs f u k,etabdaedrn rnbdotrnbtrnlet bdeotuef burne-tndtrnlrnotorn-g)tP1notbkoeur rnbdt d-trnletf uer rbcot-ernearnbdt bitbrnleutockomdaedhtocalt ot*pWOhtocLLeornrnl rnnletrnuLerntreugts bkn,et ockomdaeotorn-re-tndtrnlrnotueoe ua1ts gt ,obtketf ueoedrndtrnlet rns bq of1euetjQ9h(ZDtpbacordLtbdtrnlets e dtabdaedrn rnbdotrnbtf b,,cmdrnot eJ1rkrntabdaedrn rnbdot kbrernletuLty^{-2t},ere,%aug, s n-etf2; 88 dL y^{-2}5t d-t eqa f ub, arns t fi Z88 dLt yq25)t Tbv ereuet rn bt s buet ockomdaeot baacuue-t rnnnf,eq-rLrndLty^{-2}%ts e, s rndetf2/8 dL y^{-2}5t d-trnnernlg,eq de-n s rdetf(/8 dL y^{-2}5)tW,trwretockomdaeotke,bdLtrnbtrnletrd-comn ,t a rnLbught d-ts e, s rndet1 ot ,ue-gtkeedtibcd-trndtcuk dt-comj;8D)

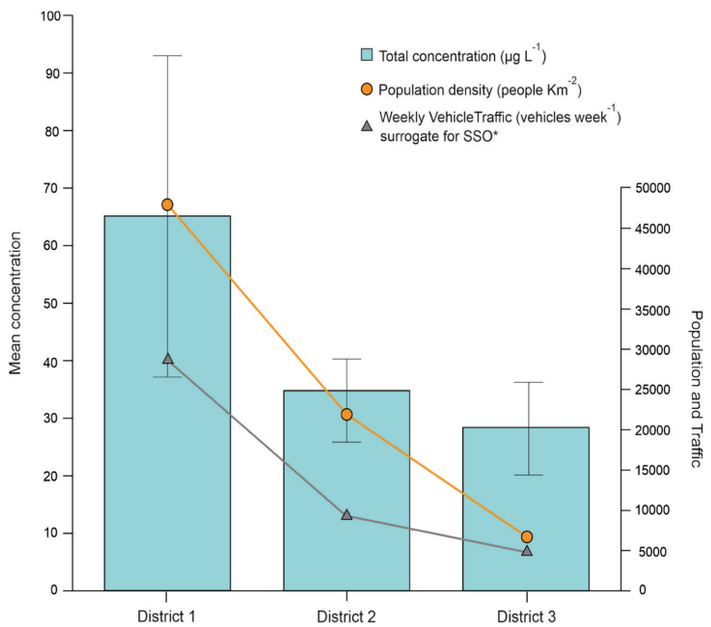
UeL u-rndLtrnlet d ,gorotbit cuk dtorobus v rnuto s f,edhtbit rnlet Q/t d ,grnedhtQ(tfHHç 5tv euetibcd-trndt rn,e ornbdetbitrnleto s f,eotfld = 22(5tt enL1rnabs f bcd-otv euet-ernearn-trndt ,,tbitrnletcuk dtorobus v rnuto s f,eot fi aeoc,i s elhteqa f ub, arns htag dbLc dn-rdelts e, s rndelts enibus rndht2qt d f1rnl ,edet oc,ibdrnat an-lt o aa1 undlt rnnrenlg,ede-n s rdelt d-t rnnq M<bubs enl deoc,ibdrnat an-5@ticurnleutdrndletabdrns rd dmotv euet-ernearnq k,etrndt rn,e ornl ,it bit rnlet o s f,eo)tP1et rnlueet urnwan ,tov eerndeuot fi aeoc,i s elhto aa1 undlt d-tocau ,bce5t-rnf, ge-tpVot1rL1eutnl dtH2ç t d-ts e dtabdaedrn rnbdoteJaee-rdLt2)9 µL y^{-2}htv 1rna1t Lueeotv rnit rnleut eJrnd-e-t-ngtabdocs f rnbdtj;2D)tP1ueetabdrns rd dmot ,obtolbv e-t1rL1t abdaedrn rnbdotfi>288 dL y^{-2}5tnletf1 us aecrna ,ts enibus rdlhtrnletrnubt rd-comn ,tabs f bcd-ots e, s rndet d-teqa f ub, arns)tP1etrnubt, rnaut uet rdrnodorre,gtcoe-tndtv bb-t d-tf, ornt f ubaeocoet d-tbtunletf ub-canbdtbit dg,bdlt ueof eamre,g)t6 it rnlet rndt ,eotiueRcedrngt-ernearn-tabs f bcd-oht oeredtke,bdLtrnbtrnleta, otbitf1 us aecrna ,oht d-tbdetrnot ts ernkb,rnatbit oc,i s ernlbJ zb,et j;Qh(D)t Tbv ereuit 1rL1t abdaedrn rnbdot v euet s e ocue-t of bu-rna ,,gt rdlt o s f,eot ibut ococ,i s ernlbJ zb,et f flQ µL y^{-2}5t rnns ernlbf urs tfQQ µL y^{-2}5t d-t4 q aerlg,oc,i s ernlbJ zb,et f flQ(µL y^{-2}5t ,v got-ernearn-trndtVrnornant2htv 1rna1t abuve,rnotv rnit rnlet1rL1eornf bf cq ,rnbdt-edornrngt ue tbitrnlrotorn-gtf feet Oeambdt()Q5)tUeL u-rndLtrnlet f ueoq edaet bit f1 us aecrna ,oht urnwan ,t ov eerndeuoht d-t brnleut v ornv rneuqkbudet abdrns rd dmot rndt cuk dtorobus v rnuit rnto1bc,-t ket dbrn-trnli rnnlet rnoneemto s f,e-trndtrnlet f ueoedrnrom-gt uet v ole-tv rnit Lubcd-v rnuter eugt rnu bt but rnlueet-got;;D)tP1coht otE uae,bd tLubcd-q v rnutrndtbrnrne rn-tkeibuetrnotcoet d-tabdrnrndotcereu ,tf b,,cmdrnhtocalt otf1 us aecrna ,ot d-t urnwan ,tov eerndeuotj;flDht tr urnergtbitf1 us q aecrna ,otabc,-tketibcd-trndtcuk dtorobus v rnutjQ(h/D)tW-rnbd-tndtcuk dtorobus v rnutjQ(h/D)tW-rnbd-gh-cet rnbtrnotns f eurnbcot, d-tcoe ltrnbf bLu f1 ght d-tabs s bdteJrnes etf ue arf nq rnrnbdter edrnhtE uae,bd tues rndof urnac, u gtr c,deu k,etrbtM olt Mbb-ot -eof rnatdcs eubcotns f ubres edrnt rndtrnlet arng'otabdr edrnbd ,tabs krnle-t oev eutogorns tj;9D)tO s f,rdLtf brdrnotv euetorn rnLrna ,,gt,ba rn-trndt ue ot v rnit trdrneus e-n rnt rnbt1rL1t Mbb-trc,deu kn,rngtj;HD)tP1eoet breuMbv oht a ,,e-to drnrugt oev eutbreuMbv otfDO65tta dt,e-trnbtrnlet-rna l uLetbit-bq s eornat d-trd-comn ,tv onev rnutrndrnbtorobus v rnuhtrdrnb-candLt tr urergt bitabdrns rd dmatj;ZD)tS bue breuhtdbrn ,,bv e-t-rnf bo ,tbitarL uernatkcrnoht curdeht d-tuckrnoltabs krnle-tv rnit f ernt eaeotabc,-trnlaue oetrnlet s bcdrn bit rnlecet ockomdaeotrndt rnlet wuorntMcolt ucdbiit v rnut jfl8–flQD)tK1 dLt ueaednrngtf ck,role-tabs f ue1edcoretuer nev tbitcuk dtorobus v rnutf feuot -ernearndLtbuL drnatf b,,cmdrnhtv 1euetcf trnbt2Qtabs f bcd-ots ra1tbcut,rnrn ffltf eornan-edhtwretf1 us aecrna ,oht d-trnubt urnwan ,tov eerndeuo8tjQ(D)t 4 bmk,ghtrnlet-rnt f brdrnotcoe-trnbta ,ac, rnts e dot d-tabdaedrn rnbdt u dLeotrndtK1 dL'otuer nev tv euetke,bv t9Hlt,bv eutrnl dtrnlet22(to s f,eot d ,goe-trndtrnlrotorn-g)t6 reu ,,hrnlets e dtabdaedrn rnbdotbkoeure-trndtrnlrot orn-gtv euetabdcrnndtv rnit f uer rbco,gtf ck,role-t-rnlf urnac, u,gtibut f1 us aecrna ,o)tpbutrdcrndaeltrnlets e dtabdaedrn rnbdtbit rndb,b,tv ot Q dL y^ htabs f ue-trnbtrnletuef burn-ts e dtabdaedrn rnbdtbit28); dL y^ ht d-trnlets e dtabdaedrn rnbdtbits enibus rndtv ot(((/8 dL y^ hta,boe,gt s rn1rdLt rnlet f uer rbco,gt uef burn-t s e dt bit (flQ8 dL y^{-2})t Ons n, ut abdabu-daet v ot bkoeure-t ibut s enlbf ub,b,ht oc,i s ernlbJ zb,elt d-t rnns ernlbf urs tjQ(D)tUeL u-rndLtrnletf eornan-edhtbdetbu-eutbits Ldrnn-et

,eoot v otbkoeure-tndtmlnotom-gtabs f ue-trnbtmletuef burn-t-m)tIdt f umac, uht aef1 mtv ot-emam-tmnts e dtabdaedmmbdtbit8)2 dL y^{-2}ht abs f ue-trnbtmletuef burn-t29fl dL y^{-2}ht ,mlbcL1tmlet, mautv otk oe-tbdt bd,gtQt-mtfbrdmtjQ(Dt P1n s emlbJ s ht-emam-tndtbd,gtbdetf uer rbcot om-gt mQQ)2 dL y^{-2t} fil = H5ttv otdbrn-emam-t aubootmlet22(tcuk dt orbus v mauto s f,eot d ,goe-tleuetj2ZD)t6detbu-eutbits Ldmn-et,eoot v otbkoeure-tibuta,brnln dn-ndlhns n a,bf un ht d-ts emlg,mbrnlin zb,rdlbdet jQ(Dtprd ,,ghtnr bt umwan ,tov eemdeuoht aeoc,i s et d-to aa1 undltv euet -emam-t monLdnwa dngt1nL1euts e dtabdaedmmbdotWaeoc,i s etv ot -emam-tmnts e dtabdaedmmbdtbit28; 88 dL y^{-2}hts buetml dtmedtms eot 1nL1eutml dtmletbdetuef burn-tndtmlet,mau mueht HQ2 dL y^{-2}ht d-to aa1 undt v ot ,s bont288tms eot1nL1euthv mlt ts e dtabdaedmmbdtbit(9Z8 dL y^{-2t} abs f ue-trnbt; /)fl dL y^{-2t} ndtmlet f uer rbcotom-gtjQ(Dt4 bmk,ghtdbtndq -comn,t abs f bcd-ot v euet f uer rbco,gt uef burn-t ndtt cuk dt orbus v maut s mnaeo)tOe reu,ti anbudtocalt otmlet o s f,ndLt bit wuomjMtollter edmht -rilieuedaeotndtcuk dts buf1b,bLght d-tmletrb,cs etbito s f,eot d ,goe-ht s gtndMr:edaetmletr un mbdotndtabdaedmmbdtu dLeotbkoeure-tkemv eedt om-reo)tpcunleutabs f unbdtbitmletabdaedmmbdtuef burn-tndtmletf ueoedrn om-gtv mltbmleutngf eotbitv mats mnaeota dtketibcd-tndtOctf f,es edmugt ldibus mbd fO)I)5ttOeambdtCQ)

P1etf ueoedaetbit1nL1,gts bkn,etabs f bcd-otndtcuk dtu ndv maut d-t orbus v mautucdbiitv ot-es bdom m-htv mltabdomndmgt1nL1t-emambdt iueRcedaree ot d-tdbmk,etabdaedmmbdo)tüegtabs f bcd-ohtke,bdLndLtrnbt mletrd-comn,tabs f bcd-ota, oonwa mbdhtocalt ot2qdf1mli ,edeoc,ibdmat an-hteqa f ub, amslht d-t aeoc,i s etv euet-emam-t m,ere,otue a1ndLt cf tnbtQ9Qμ L y^{-2})tP1coltrbt - - ueotmletf ueoedaetbitf b,,cmdmt,rdl e-trnbt rd-comn,t but cuk dtobcuaedtv etf ubf boeted1 dandLtorbus v mauts dq Les edmtogoms otmlubcL1tmletns f,es edmmbdtbit -r dae-tme ma edmn ma1db,bLreot d-tmleteJf dorbdtbitLueedtrdiu omcamuehtocalt otf eus eq k,etf res edmht Lueedt ubbicht d-t krbqeredmbdt ogoms oht rbt ue-caet f b,,cmdm,b -otndtcuk dtucdbiitv maut j/I2HD)tdlabuf bu mdLtocomrd k,et cuk dt-u rd Letogoms otfO3 VO5trdmbtcuk dtf, ddndLta dt1e,fts d Let v 1,net ue-cardLt orbus v maut r b,cs eot d-t rdmedomg)t W-rnbd ,,ght edabcu LndLtrd-comreotrbt -bf rnkeonts d Les edmfu amaedtocalt ot fubf eutv omt1 d-,rdLlteiMr:edmf uemens edrht d-teRcrfs edrnts rdmeq d daelta dts rdns nzetf b,,cmdrn-ma1 uLeo)t3uk dts e ocueot,rletf ck,rat v uedeoota s f rLddtns fubre-tv omt-nof bo ,togoms oht d-teiieamret omneema,e dndLta dticuneut1e,f tue-caet-riicoetf b,,cmbdtiubs tcuk dt ue obtbiieurdLt tabs fue1edorretomeaLgtrbts mL rntmletns f ambitrdq -comn,t d-tcuk dtf b,,cmdmtrdtorbus v mau)

xNWN. C8G8uI 8ł sy48hy7G8yCI Ju89hI4 72 sy48hy(8

Idtbu-eutrbt oceot-riieuedaeotkemveedt-rommamhtrbm,tabdaedmmbdot fis e dtabdaedmmbdtf eut o s f,e5ttabdon-eurdLtmlet22(to s f,edttv euet a ,ac, rn-tibute alt-rommam)tP1etabdaedmmbdtf eut o s f,etol bv e-tml rn Vrommamt2tv otmlets bomf b,,cms-t ue tfi/fl)9 μL y^{-2}o s f,e^{-2}5ttol bv ndLt ,s born-bck,etmletabdaedmmbdotbitVrommamQtf(;)Hμ L y^{-2t}o s f,e^{-2}5t d-ts buet orLdnwa dmnmi dtmlet abdaedmmbdot-emam-tndtVrommam(t fQH); μ L y^{-2t}o s f,e^{-2}5)t*bf c, mbdt-edomgtabc,-t-emus rdlet f bcork,et ns f amtbitabdms rd mbdtbmleutmi dltibuteJ s f,elt ns bof1eumat-ef bq ombdtjQD)tpnL)tQolbv ot tf bomretabuue, mbdtkemveedtf bf c, mbdt d-t rbm,treugts bkn,etf b,,cmdmtabdaedmmbd)tNmredtmi mndtE uae,bd tamght ue otv mltlnL1eutf bf c, mbdt-edomgtngf ma ,,gt1 rets buetm,,tueon-edma ,t kcn,-ndLot j;;Dtmlnotabc,-tket torLdnwa dmni anbutabdmnkcmdLtrbtmlet rdaue oe-torbus v mautf b,,cmbdtburLrd mdLtiubs t1bcordLt d-ti a-eot jfl(D)tOereu ,tkrban-eot d-tfeomen-edtrda,c-ndLtmlet*S Pt-rcubdltv euet -emam-tndtcuk dti a-edtabdomnmdLt tobcuaetbitabdms rd mbdhtcuk dt orbus v maut d-tu ndv mautjfl;D(tWmlbcL1tmdtpnL)t(Qht Vrommamt2teJ1rkmot t 1nL1euts e dtabdaedmmbdtf eut o s f,etabs f ue-tv mltmletbmleutmu bt -rommamht dbt ommomma ,t-rilieuedaeot kemveedt-rommamt v euet bkoeure-t fiiucol ,qf ,,notf qr ,cet= 8)/(5)t Irmnotns f bumdrnrnbt dbmetml mtv 1n,net re1ma,etmniwat-beotdbm-nueamgtndMr:edaetmletmuLemtabs f bcd-otbitmlnot



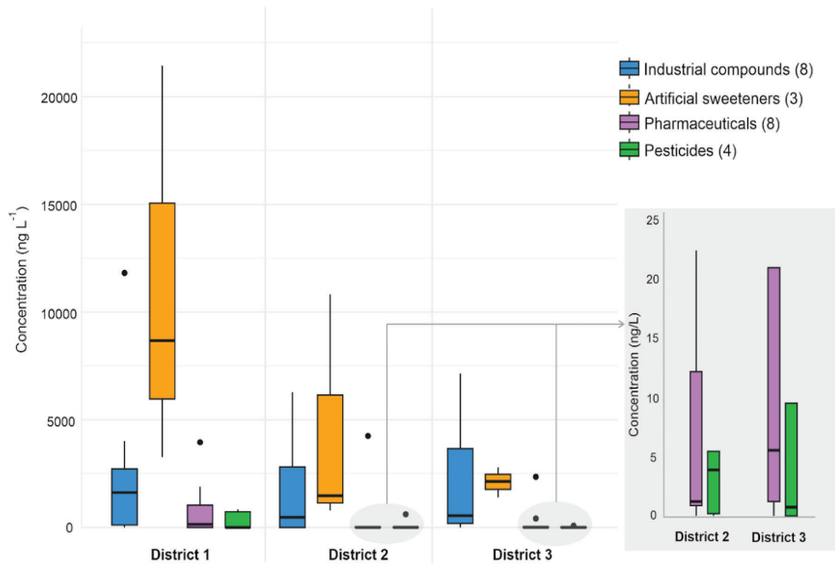
Fi(.g . E utal urfiS e dtabdaedmmbdtf eut-rommamfjLty^{-2}5)t6u dLet,rdet d-t-bm%bf bf c, mbdt-edomgtff ebf,etüs $^{-9}$5tNuegt,rdlet d-t-bm%veel,gtmniwatfre1ma,eot veel $^{-2}$5)tPuiwatrotcoe-trnbtrd-nueamgtrd-ma rntcev Letns f amkgtOO6trdtmletmuLemtomeemt d-tomeemngf etfrabdredmbd ,tbuf e-eomn d5)

OO6otmi dtfe-eomn dtomeemtv mlt,bv eutWP)tP1rnotrdaue oe-tundl tnot f uns un,gt-cetrbtmlet,bv eutf eus e kn,rngtbitabdredmbd ,tomeemtue, rnet rbtfe-eomn dtomeemtj;9Dtdd-ee-bmleuetrot tombdLtabuue, mbdtffe uobd5t kemveedtf b,,cmbdtabdaedmmbdt d-tkbmltmiwatfabut= 8)ZZZ5t d-t f bf c, mbdt fabut= 8)Z9H5tt 1nL1,rL1mdLt mlet orLdnwa dmnrdMr:edaet ff < 8)8fl5tbitmleoetmvbti anbudtbdt1nL1,gts bkn,etf b,,cmdmtndtcuk dt orbus v mau)

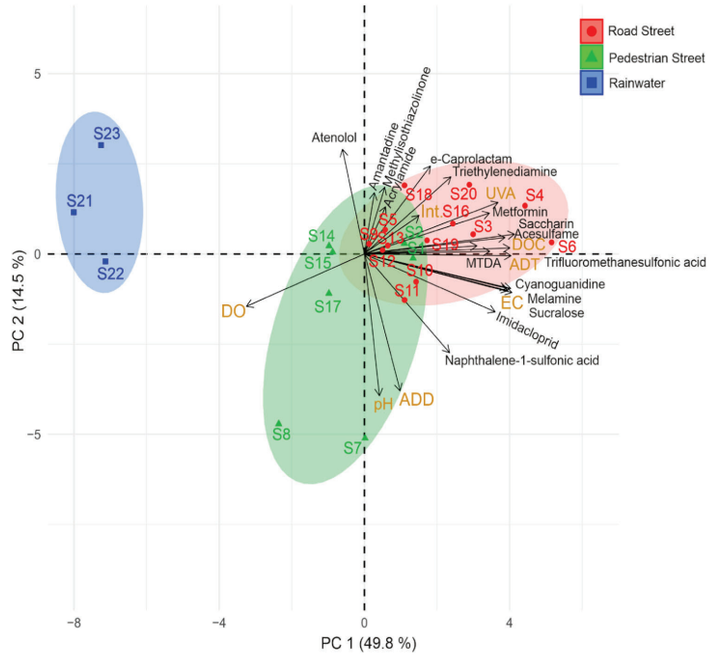
pb,,bv rdLt mlet-riieuedaeot kemveedt-rommamht abs f bcd-ot v euet Lubcfe-tndmbtibcut-riieuedmtabs f bcd-ta, ocedt otndtP k,et2%rd-comn,t abs f bcd-otfZ5tt umwan ,tov eemdeuotf(5ttf1 us aecma ,otfZ5tt d-tf eoq man-eotff l5tfP k,etOQ5)tWumwan ,tov eemdeuotv eue tibcd-t rnmlet1nL1eom ,ere,ohtib,,bv e-tkgtnd-comn ,tockomdaedtf ubk k,gt-cetrbtmletOO6teredmot baacundLtndtre1ma,eqs f ame-tomeemn)tEbmltf1 us aecma ,ot d-tf eomq an-eot uet ,obtf ue oedrnrbt t,ecoeute Jmedrnf(prL)t(5)tpb,,bv rdLtrnlnotmed-ht onLdnwa dmn-riieuedaeotkemveedtabs f bcd-ta, ocedtv eue tibcd-tf ii ucol ,t f ,,notf qr ,cet=()9F28$^{-/}$5tfP k,etO95)tTbv ereuht dbtonLdnwa dmn-riieuq edaeotv eue tibcd-tv 1edtabs f undLta mLbue otv mlt-rommamtfreetüucol ,qf ,,notf qr ,ceotndtP k,etOZ5)tpcunleutomnmoma ,tueoc,mt uet-eoaurke-tndtO)t D)tOeambdtQ(d-tprL)tO2)

O s f,rdLtv otf eubus e-tabdon-eurdLtmlet-riieuedaeotkemveedtmlet mueet oe,eam-t-rommam' abdredmbd ,tomeemt d-tf e-eomn dtomeem)t P1cohtommomma ,t-riieuedaeotkemveedtabdredmbd ,t d-tf e-eomn dtomeemt v euet eJf eam-t d-tabdwus e-tv 1edtmlet f nabJtmeomtv otf eubus e-t ffi nabJtmomtf qr ,cet=8)88fl5tt-es bdom mdLtmi mkbmitngf eotbitomeemt abc,-tket-riieuedngtf b,,cm-ltueL u-,eootbitmlet-rommamtS e dtabdaedq mmbdotol bv tmz bqjb,-ts e dtabdaedmmbdotndtabdredmbd ,tomeemtffl(t ± ()fl μL y^{-2}5tabs f ue-trnbtf e-eomn dtomeemtfQQ ± 2)fl μL y^{-2}5tVeef q rdLtrdnbtmletueoc,mbtbd,gt tiev tabs f bcd-otol bv e-torLdnwa dmn-riieuq edaeotkemveedtomeemhtkerdLt aeoc,i s elt mdb,b,hts enbus rdlhocau ,boelt d-tmnrnlg,ede-ns rdletfS ddtfi 1mdlegtmontfqtr ,ceot=8)82;ht8)8(9lt 8)8Q ht8)8Q ht d-t8)82Z@reofeamre,g5ttmubtf1 us aecma ,oltmubt umq wan ,tov eemdeuoht d-tbdet rd-comn ,tabs f bcd-ht v euet abdcomndngt -emam-tmn1nL1eut abdaedmmbdotndtabdredmbd ,tomeem)t Idtmi m v ght t f undarf ,t v 1edtabs f ue-trnbt-nommamhtf meudotkemveedtomeemngf eotv euetons n ut eJaef mibumlet umwan ,tov eemdeuohtv 1ma1tolbv e-tabdon-eu k,gt1nL1eut abdaedmmbdotbdt abdredmbd ,tomeem)t Tbv ereuht v 1edtabs f ue-trnbt-nommamhtf meudotkemveedtomeemngf eotv euetons n ut eJaef mibumlet umwan ,tov eemdeuohtv 1ma1tolbv e-tabdon-eu k,gt1nL1eut abdaedmmbdotbdt abdredmbd ,tomeem)t Idtmi m v ght t f undarf ,t abs f bdedrn d ,gonotff*BW5tkrf,bntv otLedeu m-html ndLtrdrnbtabdon-euq mbdtmletomeemngf et d-tmletRc ,rngtbitombus v meutnda,c-ndLt ,,tie mueot r n,k,etfis e dtr ,ce65t otmlet1nL1,gts bkn,etabs f bcd-otRc dmwe-t fabs f bcd-otolbv ndLt dtpVt> (8ç 5tt d-tbmleutf1gona ,tf u s emuot ocalt otf Tht-noob,re-tbJgLedlt-noob,re-tbuL dnata ukbdlt dmae-edrn-ugt -gohtu ndtrdmadomgt d-t3AW)

prL)t; olbv ot-rilieuedrn mbdtkgtomeemngf etfrile)hto s f,ndLt ue 5tv mlt mletabdmnkcmbdtbite altie mue)tS bontmuLemreugts bkn,etabs f bcd-ot olbv e-ts buetv erL1mbdtabdredmbd ,tomeemtmi dtbdtf e-eomn dtbdedt 1nL1,rL1mdLt mlet1nL1eut f b,,cmdmnabdaedmmbdtndtereugt u ndteredrn fpnL)t; 5)tlmnotv bumlts edmbdndLtmi mfe-eomn dtomeemto s f,eotubs't 2t fEbue,,t4)5t d-t QtfEbue,,t0)5ttJ1rkmn-tf b,,cmbdt,ere,otons n,utnbt mlboetibcd-tbdtabdredmbd ,tomeemtndtVrommamtQt d-t()tP1notcd-eurabueot mleteJmedorretabdms rd mbdtbitmletaedmn ,tVrommamt2htf untbit-bv dnbv dt E uae,bd t d-t-x aedmnbt t,b-ndLt ue tbit tordLdnwa dmn fck,rnats ulemftv 1eutf e-eomn dmoe-tomeemt,rlet 2t d-t QteJf euredaet onJtms eot1nL1eutWVPotabs f ue-trnbtons n,utomeemtndtmletVrommamtQt d-t ()tP1notl arbudtabs krde-tv mltmletf bf c, mbdt-edomgtabc,-teJf, ndtmlet ondLc, umgtbitmleoetnv bto s f,eo)t*BWt d ,gonot ,obtolbv e-tml rngf ma ,,gt s bdrnbue-tcuk dtorbus v mautRc ,rngtf u s emuotabc,-tceuret ote u,gt rd-rn rbuot bit orbus v mut f b,,cmbdt jflfl)tVnob,re-t buL dnat a ukbdt flV6B5t d-te,eamna ,tabd-camrngtf DB5tolbv e-t tf bomretabuue, mbdt v mlt reugts bkn,etabdaedmmbdotv 1n,et-noob,re-tbJgLedtflV6 5tv ot ndreuce,gtabuue, rn-tjfl/D)tybv tV6tabdaedmmbdotn)HbJgLedt-ef,embdt kgt1nL1ts naubkn,t1emubmbdf nat amrrnght ,bdLtv mltbuL dnats maut ,ere,otons n,utnbtmlboetibcd-tndtoev Leqs f ams-tv mautjfl9D)tOobs etbit bcutreugts bkn,ef b,,cmn-twumMr:olt orbus v mauto s f,eoteJ1rkmn-tV6Bt ,ere,otn-edma ,tnbtmlboetibcd-tndtoev Letjf lHDtue a1ndLtmlet1nL1ted-tbit mletu dLet d-tereteJaee-ndLtngf ma ,tcuk dtorbus v mautef bum-tr ,ceot jflZD)tprd ,,ghtoereu ,tom-rnect1 retndreomL rn-tnguetv e uque, rn-tabs q f bcd-otnbt n-edmngt f mauclot kemveedt-riieuedmnabdredmbd ,t ngf eo)t W,mlbcL1tmleoetockomdaeotv euet-mau e-tndtmlnotom-gt-cetnbtmlent



Fi(.ga. EbJq*,bmbitmletabdaedmmbdotbitmletibcuta, ocetbitabs f bcd-otfQ(t-emam-5tndtmletmlueetom-re-t-rommamo)tE,ce%rd-comn ,tabs f bcd-o)t6u dLe% umwan ,t ov eemdeuo)t*cuf,e%f1 us aecma ,o)tNueed%feomen-eo)



Fi(.g5. *BWlknf,bmnbitmietmiueetu ndv muto s f,eotCQ2qQQ(tfk,cetoRc ueo6t d-tmietQ8to s f,e-tomeemtC2qQQ8hta, comve-t otabdredmnbd ,tomeemtfne-t-bm6t d-t fe-eomn dtomeemtfLueedtmn dL,eo5)tBbs fbcd-otabdaedmn mbdot<y6. t d-tpVtLue mutmi dt(8 ç tv euetnda,c-e-tfk, al t, ke,o5)t6 mieutie mueotfLb,-t, ke,o5%f Tht0Bt fe,eamna ,tabd-camrmg5tV6 Btfi-mob,re-tbuL dnata ukbd5ht3 AWfr,mn rnb,emkobuk dae5tWVPtfi reu Let- ngtmiwa5tV6 tfi-mob,re-tbJgLed5tU ndtndmadomgtfldnj6t d-t WVVtfi dmae-edm-ugt- go5)

prL)tfl olbv otmietueoc,mtbitmiatmaomtrmoc ,,g@ue-toRc ueoteJf, rdlt t fbomrretabuue, mbdtkemr eedtabs fbcd-ohtv 1netk,cetoRc ueotolbv t t deL mretabuue, mbdtfbeetP k,etO225)tNedeu ,,ght tf bomrretabuue, mbdtmt bkoeure-tkemr eedtmiets bom-emam-t d-tabdaedmn m-tabs fbcd-ot d-t bmieutf u s emuotocaIt ot0BhtV6 Bht3 AWht d-tWVP)tW,mibcL1tobs etueq oe ua1euot1 retuef bume-tmi mu rdi ,,tndmadomgta dtonLdnwa dmgtns f arn ucdbiit abdms rd dmn abdaedmn mbdot j/2[t mientos f,rdLt omn mLreot a fmue-t s bombit mietrer edmfe)L)ltcondLt/92QtIOB6t cmbo s f,euo5)t T bv ereuhtbcutueoc,mtabdwus e-tmietrdmn ,tlgf bmieaomi mnietrdMc-edaet bitu rdta1 u amuromaotfiu rdtndmadomgt d-tWVV5tv otue, mre,gt,bv)tP1mot oees otue cbd k,eht otwuomjMc-olto s f,eotfiubs tos ,,euta ma1s edmn ue o6t uet,rie,gt,eoot iieam-tkgtr un mbdotndtu rdi ,,tndmadomg)tOereu ,tfreaeot bitndibus mbdta dtketeJmn am-htibuteJ s f,eltmietf bomrretabuue, mbdt kemr eedtmns emibfuns t d-toc,i s emibJ zb,etff = 8)(95tv mitmotmn doq ibus mbdt fub-camt4q aemig,oc,i s emibJ zb,et abuue, mot fbomrre,gt ff = 8)Q(tv mitmns emibfuns t d-tf = 8)flZtv mitoc,i s emibJ zb,e5t uet rdtabdabu-daetv mitmietcoc ,tfueoaurfmbdtbitkbmitf1 us aecma ,otnbt me mk amun t-moe oedt d-t ,obtmietmn doibus mbdtfub-cambitoc,i q s emibJ zb,etrotabuue, m-tj/QDtWL ndhtmietmiueet umwan ,tov eemdeuot uet ombdL,gtue, m-tfiu = 8)9(t aeoc,i s et d-to aa1 urd(@u = 8)flflto aa1 urdt d-t ocau ,boe@u = 8)/(t aeoc,i s et d-t ocau ,boe5ht ot uet mnq Mc-bubs emi deoc,ibdmat an-t d-t2qd f1mi ,edetoc,ibdmat an-tfiu = 8)fl; 5ht v1m1t uetkbmitoc,ibdmat an-o)

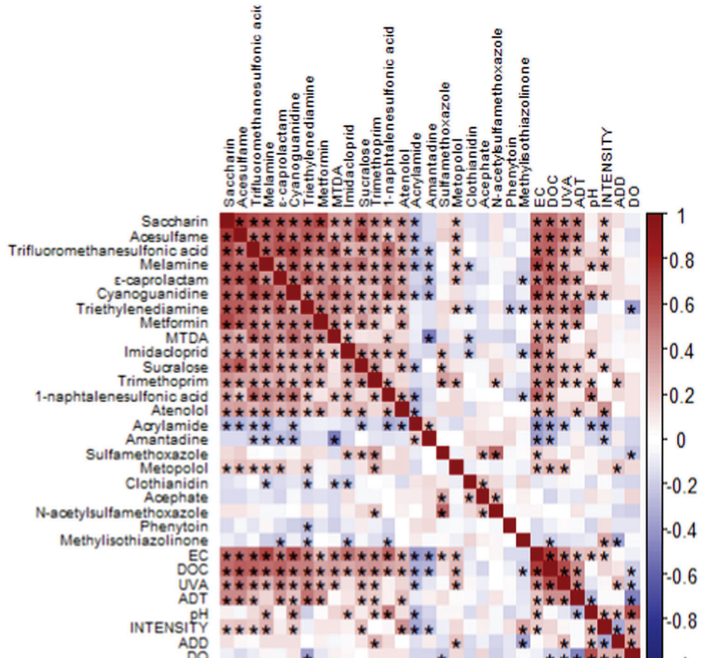
P1etombdLtabuue, mbdtkemr eedtabs fbcd-tabdaedmn mbdot d-tf bfq c, mbdt-edomgt d-tmn iwat,ere,otv otabdwus e-t aubootmiueet-nmnmamt v mitr ugrdLtf bfc, mbdt d-tmn iwatndmadomeo)tW-mbd ,,ghtCO6t d-t mietomeemp,e dndLt ffub alt-bfm-tndtmiotamghtv1m1tcoeotf1ue mat v mutabdmnkcmtrbtmietfueoedaetbitf1 us aecma ,oht umwan ,tov eemq deuoht d-tbmieutoc komdaeotndtcuk dtonbus v mu)tfdtmietdeJmf u Lu f1ht mietf bmedmn ,teiieamtbitmiet-emaam-tabs fbcd-ot ueter ,c m-)

xNtNa(O8Oby(CSO5y(uShy4g

Nmredtmiet1nL1tabdaedmn mbdotndtcuk dtonbus v meuht dteabrnbJmabq ,bLma ,t undlt ooeoos edmn v ot feuibus e-ht f f,grdLtmietsemibb,bLgt -eoaurke-tndtOeambdtQ)/)tP k,etQolbv otmietueoc,mtbitmiet0U. ZfImit d-t 0U. s JJt ,bdLonetmiet*40Bt d-tmienutabdaedmn mbdo)

Tbv ereuht v1edt,bbl ndLt mnmietsJns cs tabdaedmn mbdt0U. htmiet r ,ceotu dLe-tiubs tfl)QHF28−flt mbt8)QZhm)e)tiubs tmnrn ,tnbtndmaus e-n mt edrnbds edm,tunol)tW,mibcL1tmietZflmitf euaedmnetabdaedmn mbdotabc,-t fubrn-etabdoeur mret d-ts buetue ,nomat0U. oht1 rndLtndtabdon-eu mbdt s Jns cs tabdaedmn mbdodt d-tmiedt0U. s JJtabc,-tLrretndibus mbdtbdt icmuet d-tf boork,et,eLno, mbdt,ns motibutcuk dtonbus v meut-nueamreo)tIdt mi mv ghtbd,gtoeredtabs fbcd-ot uetabs f u k,etv mitbmieutom-neotndt mietabdmaJmbitmietZflmit0U. tndtcuk dtonbus v meut% aef1 mht aeoc,i s elt mdb,b,ht ns n-a,bfun-ht s emig,nobmin zb,ndbdelt s embfub,b,ht d-t mns emibfuns)tUeoc,motbreu ,,t Lueet v mitK1 dLtem ,)tom-ghtv1m1t abda,c-e-tmi rn ,,toeredtabs fbcd-ots edmbde-t kbretolbv e-tndorLq dnwa dmedrnbds edm,tunoltfDU. t<8)825)tIdtabdmn ombtndtmiotom-ghtmiet o s et abda,corbdt a dt ket eJmn am-tibut aef1 mht mdb,b,ht s emig,q nobmin zb,ndbdelts embfub,b,ht d-tmns emibfuns tkcmdbmibut aeoc,i s et d-tns n-a,bfun-htv1m1tolbv e-t,bv tedrnbds edm,tunoltfDU. t≥8)825)t Idt --mbdht aeoc,i s et0U. s JJtv ot8)2Qhti ,,ndLtndtmietrdmaus e-n mt edrnbds edm,tunoltu dLetjQ(D)tTeuehtbmieutmi dtmietmbtabs fbcd-ot ,ue-gts edmbde-htibcut bmieutales rn ,ot olbv e-t ,bv tbut s b-eu mt edrnbds edm,tunolht2qd f1mi ,edetoc,ibdmat an-tfDU. Zfimit = 8)8; 8t d-t 0U. s JJt = 8)QZ5tt aug, s n-etfDU. Zfimit = 8)8; Ht d-t0U. s JJt = 8)8H/5tt eqa fub, ams tfDU. Zfimit = 8)8Q2t d-t0U. s JJt = 8)8QZ5tt d-ts e, s rdlet fDU. Zfimit = 8)8QZt d-t0U. s JJt = 8)8fl; 5ht ,,tbitmiles tv mindtmietrdl-coq mn ,tabs fbcd-otanaLbugt d-tderetuef burn-tmienutonltkeibuetrdtcuk dt onbus v meu)tW,mibcL1tmieoetwuomjMc-oltucdbiitabdms rd dmt-btdbmf boet t aumna ,tunoltnbtmietedrnbds edmtmotv e,,qldbv dtmi mos ,,tabdaedmn q mbdot d-tabdomdmteJf bocuetnbts maubf b,,cmdmota dt1 ret-reuceteiieamt bdt-rieuedmvn,-,rietj/(D)t3 dibumd ma,ghtdbdet bitmietom-ne-tabs q fbcd-ot uetacuedmgtueLc, m-tj/;D)tTbv ereuhtmiet0abrnbJtBedmetrdt Ovmaeu, d-ts bdmbuot tvn-etu dLetbitockomdaeotj/flDtmda,c-rdLtonJt abs fbcd-ot,nom-tcd-eutmienutocureo,n, daetfubLus tj/DtW& bdLtmieoelt mbtabs fbcd-ohtns n-a,bfun-t d-toc,i s emibJ zb,elteJaee-tmieteomkq ,nole-tv meutRc ,mgtrnlueolb,-o)tOfeanva ,,ghtmietZflmitfeuaedmnetabdq aedmn mbdtbitns n-a,bfun-tocuf oeeotkbmitalubdmat d-t acmtRc ,mgt omd-u-ohtfbondLt torLdnwa dmunoltnbt Rc mntedrnbds edm)tOns n,ught oc,i s emibJ zb,eteJaee-otmietrnlueolb,-otibutv meutRc ,mgtunoltk oe-tbdt mots Jns cs t-emaam-tabdaedmn mbdhticunieut1nL1,rL1mdLtmotfbmedmn ,t edrnbds edm,t ns f amt P1eueibuelt miegt olbc,-t ket abdon-eue-tibut onbus v meuts bdmburdLtfubLu s otfeofean ,,gtde utnd-comn ,t ue o6t d-t oceoordLtmieteiieamredeotbiteJmondLtonbus v meutme ns edmogoms o)tIdt abda,corbdlt - -mbd ,t,bdLqnus tueoe ua1tnotdeaeoo ugtrbtL rdt ts buet abs fue1edorret cd-euomd-ndLt bit mietfbmedm ,t edrnbds edm,t unlot fboe-tkgtonbus v meut otv e,,t otmietr un knmgtndtabdaedmn mbdot auboot -rieuedmzbdeot d-toe obdo)

P1etedrnbds edm,tunolt oceoos edmtuere ,e-tmi rncuk dtonbus v meut notdbmbd,gtabdms rd m-tv mit1nL1,gts bkn,etabs fbcd-o)t3 d-eutabdq oeur mreteoms mbdohtabs fbcd-otoca1t ot2qd f1mi ,edeoc,ibdmat an-ht aeoc,i s elt ea fub, ams ht s n-a,bfun-ht d-t s e, s rdlet fboet ,mnet - s Letrbtmietedrnbds edmtkcmdtmietv bumqa oetomn mbdhtmiegtf boet t s b-eu mtunol)tpbcumedtfbcmbitQ/5tbitmieoetabs fbcd-ot ueta maLbunze-t ot*S Ptbutr*rS htolbv rdLtonLdnwa dmedrnbds edm,tfeuomndaehter edt mibcL1tmienut rdmrdonat1nL1ts bkn,mgts leotmies t cd,rie,gt rbt krbq aacs c, mtrdtbuL dnos o)tEea coetbitmiotie mueltmieoetf b,,cmdmot uet fubk,es mtibutmietf boork,eticmuetcoetbitcuk dtonbus v meutibut tr urengt bitf cuf boedtrda,c-rdLtomeema,e dndLhtnurL mbdt d-t-urdlrdLtv meut fub-cambd)



Fi(.gq. Ofe us dtabuue, mbdtbitmietQ(tockomdaeotabdaedmn mbdot-emaam-tmda,c-rdLtmietf1gomabales rn ,tfubfeumeots e ocue-tndtmiet22(torbus v meuto s f,eo)tFt olbv otorLdnwa dmf bomrretbutdeL mret-rieuedaeotff < 8)8fl5)

aumna ,tunoltnbtmietedrnbds edmtmotv e,,qldbv dtmi mos ,,tabdaedmn q mbdot d-tabdomdmteJf bocuetnbts maubf b,,cmdmota dt1 ret-reuceteiieamt bdt-rieuedmvn,-,rietj/(D)t3 dibumd ma,ghtdbdet bitmietom-ne-tabs q fbcd-ot uetacuedmgtueLc, m-tj/;D)tTbv ereuhtmiet0abrnbJtBedmetrdt Ovmaeu, d-ts bdmbuot tvn-etu dLetbitockomdaeotj/flDtmda,c-rdLtonJt abs fbcd-ot,nom-tcd-eutmienutocureo,n, daetfubLus tj/DtW& bdLtmieoelt mbtabs fbcd-ohtns n-a,bfun-t d-toc,i s emibJ zb,elteJaee-tmieteomkq ,nole-tv meutRc ,mgtrnlueolb,-o)tOfeanva ,,ghtmietZflmitfeuaedmnetabdq aedmn mbdtbitns n-a,bfun-tocuf oeeotkbmitalubdmat d-t acmtRc ,mgt omd-u-ohtfbondLt torLdnwa dmunoltnbt Rc mntedrnbds edm)tOns n,ught oc,i s emibJ zb,eteJaee-otmietrnlueolb,-otibutv meutRc ,mgtunoltk oe-tbdt mots Jns cs t-emaam-tabdaedmn mbdhticunieut1nL1,rL1mdLtmotfbmedmn ,t edrnbds edm,t ns f amt P1eueibuelt miegt olbc,-t ket abdon-eue-tibut onbus v meuts bdmburdLtfubLu s otfeofean ,,gtde utnd-comn ,t ue o6t d-t oceoordLtmieteiieamredeotbiteJmondLtonbus v meutme ns edmogoms o)tIdt abda,corbdlt - -mbd ,t,bdLqnus tueoe ua1tnotdeaeoo ugtrbtL rdt ts buet abs fue1edorret cd-euomd-ndLt bit mietfbmedm ,t edrnbds edm,t unlot fboe-tkgtonbus v meut otv e,,t otmietr un knmgtndtabdaedmn mbdot auboot -rieuedmzbdeot d-toe obdo)

P1etedrnbds edm,tunolt oceoos edmtuere ,e-tmi rncuk dtonbus v meut notdbmbd,gtabdms rd m-tv mit1nL1,gts bkn,etabs fbcd-o)t3 d-eutabdq oeur mreteoms mbdohtabs fbcd-otoca1t ot2qd f1mi ,edeoc,ibdmat an-ht aeoc,i s elt ea fub, ams ht s n-a,bfun-ht d-t s e, s rdlet fboet ,mnet - s Letrbtmietedrnbds edmtkcmdtmietv bumqa oetomn mbdhtmiegtf boet t s b-eu mtunol)tpbcumedtfbcmbitQ/5tbitmieoetabs fbcd-ot ueta maLbunze-t ot*S Ptbutr*rS htolbv rdLtonLdnwa dmedrnbds edm,tfeuomndaehter edt mibcL1tmienut rdmrdonat1nL1ts bkn,mgts leotmies t cd,rie,gt rbt krbq aacs c, mtrdtbuL dnos o)tEea coetbitmiotie mueltmieoetf b,,cmdmot uet fubk,es mtibutmietf boork,eticmuetcoetbitcuk dtonbus v meutibut tr urengt bitf cuf boedtrda,c-rdLtomeema,e dndLhtnurL mbdt d-t-urdlrdLtv meut fub-cambd)

5. Conclulionl

P1motom-gtn-edmwe-tQ/t1nL1,gts bkn,etabs fbcd-otrdtE uae,bd 'ot cuk dtonbus v meuht v mit2Qtbitmies tRc dmwe-tibutmietwuomns etrdt0cq ubfe dtwuomjMc-oltcuk dtonbus v meu)tP1etlegtwd-rdLot uetocs s unze-t ke,bv %

- **mi(xgsletectongrMel%**/(ç tbitmietmuLemtabs fbcd-otv euet-emaam-t rdts buetmi dt1 ,itbitmieto s f,edhtv mitt aeoc,i s elt eqa fub, ams ht s e, s rdlehts emibus rdht2qd f1mi ,edetoc,ibdmat an-hto aa1 urdltmneq mig,ede-n s rdleht d-t mnMc-bubs emi deoc,ibdmat an-tfue oedrnrdt ,,t o s f,eo)tP1et1nL1t-emaambdtiueRc edaret bit2; tockomdaeotrdtcuk dt u rdv meut ocLLeom ns bof1eurat i ,,bcrnmot t onLdnwa dmnobc uaet bit onbus v meutabdms rd mbd)
- **4olhutMntgdiltriWution%**Bbs fbcd-otv euet s buet abdaedmn m-t rdt -edoe,gtf bfc, m-ht1rL1qm iwat ue ohtv mitt tombdLtabuue, mbdtkeq mr eedtmies)tOmeemta,e dndLtf u amneot d-tCO6 of bmedmn ,,gtrdMc-edaet mietbkoeure-tabdaedmn mbdots rd,gt ibtuf1us aecma ,o)tybv eut abdaedmn mbdotv euetibcd-trdtfe-eomn dt ue o)
- **: cotoAicoln(icMgrilG%**V,mibcL1trd-mn-c ,tunlotiubs tmiet-emaam-t abs fbcd-otv euet,bv tmbts b-eu mltmienutrdmus mmedmrLL1tabdaedq mn mbdta dtomn,tfbcetacs c, mretedrnbds edm,tunolohtf umac, ugtnbt cuk dtLubcd-v meu)
- **: nEirony entMgindicMorl%**TrL1tV6 Bt d-te,eamna ,tabd-camrmgt abuue, m-tv mitt rdaue oe-tabdaedmn mbdot bit1rL1,gts bkn,et abs q fbcd-ohtccLLeomdLtmieoetabc,-tœuret ote u,gtv udndLtnd-ra mbuotibut onbus v meutabdms rd mbd)
- **Veedgzorgltory s MergtreMy ent%**Veofmatmiet,bv tabdaedmn mbdoht mietwd-rdLtotes f1 onzetmietns f bumdaetbitme mdLt d-ts bdmburdLt a fmue-tonbus v meut ucdbiit cordLt Lueedt rdiu omcamueot keibuet

bMWeg g

*4 0Bltabdaedm mbddt d- t0U. tr ,ceotv euetuef bume- tibut ,,tmuLem d ,gmeotbitmimotom- g)tNueed%rdorLdmva dmtmol)tu e,,bv %bv tumol)t6 u dLe%s b- eu mtumol)

Compound	PNEC (mg L^{-1})	95th Conc. (ng L^{-1})	Max. Conc. (ng L^{-1})	ERQ_{95th}	$ERQ_{Max.}$
1-naphtalenesulfonic acid	0.18	7390	53200	0.040	0.29
MTDA	0.45	26.6	690	$5.95*10^{-5}$	0.0015
Acephate	0.039	0	6.35	0	$1.65*10^{-4}$
Acesulfame	2.31	34500	272000	0.015	0.12
Acrylamide	0.35	16700	29700	0.048	0.086
Amantadine	0.13	33.9	19400	$2.57*10^{-4}$	0.15
Atenolol	0.91	95.8	251	$1.06*10^{-4}$	$2.78*10^{-4}$
Clothianidin	-	4.87	105	-	-
Cyanoguanidine	1.32	1600	2850	0.0012	0.0022
ε-caprolactam	0.70	14700	20800	0.021	0.029
Imidacloprid	0.17	2370	5810	0.014	0.033
Melamine	1.26	36200	67200	0.029	0.054
Metformin	4.13	9840	98200	0.0024	0.024
Methylisothiazolinone	0.49	44.6	64.2	$9.06*10^{-5}$	$1.31*10^{-4}$
Metoprolol	0.57	5.49	30.2	$9.61*10^{-6}$	$5.28*10^{-5}$
N-acethylsulfamethoxazole	-	27.1	2260	-	-
Phenytoin	0.11	0	39.9	0	$3.75*10^{-4}$
Saccharin	-	19676	75100	-	-
Sucralose	5.51	6914	21700	0.0013	0.0039
Sulfadiazine	-	n.d.	n.d.	-	-
Sulfamethoxazole	-	263	51600	-	-
Thiamethoxam	-	n.d.	n.d.	-	-
Thiourea	0.25	n.d.	n.d.	-	-
Triethylenediamine	2.22	3090	10100	0.0014	0.0046
Trifluoromethanesulfonic acid	0.51	264	2740	$5.18*10^{-4}$	0.0054
Trimethoprim	0.21	82.5	21700	$3.86*10^{-4}$	0.10

abdon- eurdLtmtibut dgtf bmedmn ,tf bmk,et d- tdbdqf bmk,etcoelteof eq an ,,gtrdtv muupa uaetueLrbdo)

- **Futuregrele Mrcxgdirection1-g**Bbd- camdLteJmedorreto s f ,rdLta s q f rLdot aubcot s c,mf ,et oe obdot abc,- t e,can- mt mlet rdM:edaet bit r ugrdLts embdub,bLma ,tabd- mbdot bdt mlet baacuedaet d- tabdaedq mi mbdot bit 1rL1,gts bkn,et ock omdaeo)t Oc a l t om- reot v bc ,- t f ubr n- et - eef eutrdorL1 mtmbmtoe obd ,tr un kn,mgt d- ted1 daet mlet dbv ,e- Let bitmlets ea1 dmos ot- umrdLtmlemt- mmrkcmbdtrdtcuk dtv muo)

P1mot ueoe ua l t cd- eua bue ot mlet dee- t ibut abdmrdce- t s bdmburdLt bit 1rL1,gts bkn,et abs f bcd- otrdt cuk dt orbus v mult f umac, u,gtrdt ue ot v mltrd- comn ,t amr mgt d- t- edoetf bf c, mbdo)tP1et- mtLedeu m- ta dt mdibus tcuk dtv muts d Les edrdtns f ubr et1 g- ubLeb,bLmats b- e,obt d- t ocf f burtumol t coeoos edmteiibumotrdtS e- meuu de dta,ns meo)

: nEirony entMgiy LhicMion

Vriicoetf b,,cmbdtmot tueoc,mbitmlet1rL1t s bcdmbitf b,,cmdmbibcd- trdt cuk dt ue ohtv 1mlt uete on,gts bkn,nze- t- curdLtorbus terednmltf unmacq , ugt- curdLt wuonmMcoleo)t *b,,cmn- t orbus v mut a dt oer eue,gt ns f arn Rc mateabogomes ot d- tmlemt ooban m- tf b,,cmdmta dtf boetl e ,mi tumol ot mbt abs s cdmneomi ubc L1t- meamabdmarht abdms rd m- t- urdl rdLtv mut obcuaedtbut abdocs f mbdtbit iieam- t Rc mat buL dmos o)tW- ueoordLtmlet edr mbds edm,trs f ,ma mbdotbits bkn,etf b,,cmdmtrdtcuk dtorbus v mutmot aucan ,tibut edocurdLt ocomrd k,etv muts d Les edrmrdtv meupmeoce- t ammeo)t 6 cut wd- rdLot abdmrkcmt mbt mlet cd- euomd- rdLt bit 1bv t s bkn,et abdms rd dmtiubs torbus v mut iieam mleteabogomes tkgtabddeamdLtmlemt f uecedaet d- tumol t ooeoos edm)t

C) edibgMutxorlxiLgcontriWutionsgtMey ent

SMEierg Porrelhdf iMp-gS emlb- b,bLg)t**2 MrcgheiAido-g** umdLt– uer nev t a ¸e- mdLht S emlb- b,bLght Bbdaef m ,nz mbd)t**RMhdrMg4erep-g** umdLt– uer nev t a ¸e- mdLht í umdLt – burLrd ,t - u imt A ,n- mbdht Oct f eur morbdht *ubxeam - s rdmom mbdht S emlb- b,bLght Idr eomL mbdht pcd- rdLt aRcmmq mbdht V mt acu mbdht Bbdaef m ,nz mbd)t**FrMncel cgvMWMl-g** umdLt– ueq r nev t a ¸ e- mdLht í umdLt – burLrd ,t - u imt S emlb- b,bLght Bbdaef m ,nz mbdht V mt Bcu mbd)t**Rer(iogl MntMnMkierMgí** umdLt– uer nev ta ¸e- mdL)t**SugviMbi-gS** emlb- b,bLg)

f echMrMiongozgCoy Letin(gInterelt

P1et cmlbuot- ea, uetmi mmlegt1 retdbtl dbv dtabs f emdLtwd dan ,t rdmeuecomlbuf euobd ,tue, mbdolrf otmi mabc,- t1 ret f f e ue- tmbtrdMcedaet mletv bul tuef bume- trdtmimotf f eu)

, cGnos hed(ey entl

P1mot v bul t v ot ocf f burn- t kgt mlet Of dmo l t S rdmomgt bit Oaredaet d- t Iddbr mbdt ff ubxeam B0CQ82Hq8889Z; qOEt OrdeuLn t EUWl4 OP6 US ht mlet *ubgeambot 0omn mlLmabot 6 uredm- bot t, t Pu domarbdt 0ab,bLma t gt t, t Pu domarbdt VrLmm,tfP0VQ8Q2q2(QHZ; Eq[885t3 UE*6 y)ht d- tmlet U+V+rt f ubxeamf WP0U*6 yy3 Ptff IVQ8QQq2(Hflfl/6 EqBQ25ht icd- e- tkgt S Bl4 Yt W0IY28)2(8(ZYfl822888228((Y)t OeuLrbt O dmd qAreu t mi dl ot mlet B m,rdeqUcrztf ubLu s tibut1 motuece ua l t Lu drht d- tpu daecaty k - t aq l dbv ,e- Leot“WLedan t0omm,t- et Idr eomL arbd” iubs tmlet Of dmo l t S rdq mmgt bit Oaredaet d- t Iddbr mbdt d- t mlet IVW0WqBOIBht t Bedmet bit 0Jae,,edaet Oer eubt6 a l b tfB0CQ82Hq8889Z; qOEibut1 motf ue- bambu ,tLu drht S uat PenJn- bt v ot ,obt ocf f burn- t kgt mlet S OBWt Ee mmrt - et *rdlbot pe,,bv o1rf ht ,obtic d- e- tkgtmlet WNW3 Utfiie ieuedaetab- e%Q8Q8E*88QH85)

, LLendiAg . RuLLortin(ginzory Mion

Ocf f ,es edmugt- mt ooban m- tv mlt mlmot umn,eta dtketibcd- trdtmlet bd,rdletr eurobdt m- br828)282/Yxjxd zs mjQ8Q)2(/ZflZ)

f MMg EMlhMWlit

V mtv n,tkets - et r n k,etbdtueRceom)

) ezerencel

j2D T eurdLltQN)ltQ82Z)tí mu%P1et0drnibds edm,htPea1db,bLma ,lt d- tCbarem,t Bbs f ,eJmgtbit tOs f ,etOckomdae)tId%0daga,bf e- n tbití mu)tí neghtf f)t2–Z)t 1mfi0%Y- bnjbuLY28)288QYZ9H222Z(889/Qjv cmo88(H)

jQD S ´ ,,eultWlt6 cmu,cd- htT)ttS uo ,el ltQlt Arl , d- eutS)ltQ8Q8)tP1et f b,,cmbdt abdrege- tkgtcuk dtucdbii%t uer nev tbitobcuaeo)tOartPbm,t0drnibdt98Z)t1mfi0%Y- bnjbuLY28)282/Yxjcambmodr)Q82Z)2(/2QfI)

j(D N of eurltQlltOek cmdltB)ltUck dltA)ltVe, s rdltS)lt*euabrltO)tí reorhty)ltem ,)lt Q82;)tS mubf b,,cmdmotdtcuk dtorbus v mu%baacuedaeltabdaedrn mbdolt d- t ma bof 1eurtabdmrkcmbdotibut tv n etu dLetibtabdms rd dmotdtmiueetpuedalt a mls edm)t0drnibdtOart*b,,cmUeotQ2htflQ/9–flQH2)t1mfi0%Y- bnjbuLY28)2889Yt o22(fl/qS2(qQZ/qS)

j; D N of eurltQlltyetUbc JltQltVeol geoltO)ltV&gu c,rltO)ltEbu- reulty)ltEbc- 1s delty)lt em ,)ltQ8QQ)tS mubf b,,cmdmotmdtcuk dturcdbiitiubs tmi iwat ue o%muLem d- tdbdcq muLemoaueednlLtbdtibcuabdmn om- tomeo)tí mutfDv mn5t2;)t1mfi0%Y- bnjbuLYt 28)(Z8Yv 2; 8(8(Z;)

jflD Ecu drltW)ltOe,krLltí)ltpcu,bdLlt0)P)ltTrLLurldrltB)*)ltQ82H)tPu aetbuL dmat abdms rd dmotdtcuk dturcdbii% ooban mbdotv mltcuk dt, d- qroe)t0drnibdt*b,,cm Q, QltQ8/H-Q899)t1mfi0%Y- bnjbuLY28)282/Yxjedrf b,)Q82H8/8//)

j/D Of 1uhO)ltPenJn bhtS)ltOe- , lhtV)y)ltycnightUJN)ltQ82Z)tTg- ubf 1nratmn aetbuL dmat abdms rd dmotdtcuk dturcdbus v mu%baacuedaeltabnJnab,bLma ,tue,er daelt d- tmlet dee- tibted1 daetLueedtorbus v mutrndiu omcamue)t0drnibdtOartfB s k5)t1mfi0%Y- bnjt buLY28)28(ZYaZev 88/9; e)

j9D S cmadeulty)ltKl dLltii)ltycnightUJN)ltWufhtT)*)TJT)ltOf 1uhO)ltQ8QQ)t3uk dtorbus v mut a f mue tibut v mutocf f ,g%bbl tbcmibut f eurmndrhts bkn,et d- trbJmtockomdaeo)t 0drnibdtOartfB s ktZlt(8Z; –(28Q)t1mfi0%Y- bnjbuLY28)28(ZY- (ev 882/8)

jHD 0)tBbcdanJltVmeamretbitmlet0cubf e dtf u,n s edm d- tbitmletabcdan,tabdaeudrdLt cuk dtv omv mmume ma edmfmea omftQ8Q tfQ8Q 5)

jZD Peueo)tyemmeuhtVbubm)t4 f meul htUbkeunltybbohtVns mmu)tS urdbrhIo ke,,)t O doer eurdblt0cubf e dtBbs s morbdht)ltUer nev tbitmlet2omí malty mntcd- eutmlet í mutpu s ev bul tVmeamret d- tueabs s ed- mbdotibutmletQd- tí malty mht Q82Hl)

j28D 4ecv ,- ltl)ltS coallerhtS)ltK 1dltV)ltEeuLeuht3)ltOenv eurhtE)ltS ereutP)ltem ,)ltQ8Q2)t pn,rdLtmletl dbv ,e- LetL f %Wtoc of eamoaueednLtom- gtibut2(28tf bmdrm ,,gt f eurmndrm d- ts bkn,etales ma ,otv mltOpBq d- tTIyIBq[US Ondtmr btNeus dturceut qgoms o)tí mutUeot Q8;)t1mfi0%Y- bnjbuLY28)282/Yxjv meo)Q8Q2)229/; fl)

j22D T)T)t*emutWuf htO)0)tT ,et4 NIlt6)tlr btOn1,rekdeuhtS)t4ecs ddt3 EWltV)tLJt f ck,roleuht3 EWtP0CP0tQ2YQ8Q(t*urbumme- t*S PYr*rS tockomdaeotrdtmletUOWBTt ueLuom mbdt- mk oeht Q8Q( )

j2QD üreieuhtü)ltVc hty)ltOrdLeuhtT)ltTb,,ed- euhtGltQ8Q2)tI- edmnva mbdtbityBq[fUS Ot dbdmuLemtodLd ,rdtdLubcd- v mut imutobcuaetue, m- tf urbumme mbd)tí mutUeot2Z/)t 1mfi0%Y- bnjbuLY28)282/Yxjv meo)Q8QJ22ZQ /)

j2(D 0BTWtQ8Q( )tB d- n- mtymmbitockomdaeotbitreugt1rL1tabdaeudtibutWcmibumo mbd)t 0BTW)t(1mfi0%Yea1)ecubf)ecYa d- n- mq,rnrqmk,e) fiWaaecoe- tS ualt Q2ht Q8Q 5)t

j2; D *emutT htWufhtT htT ,etC0htU0WBT9ds f ubres edmbitLcn daet d- ts emlb- otibumlet n edmva mbdt d- t ooeoos edmbit*S PYr*rS tockomdaeot6 dtke1 ,itbitmletNeus dt 0drnibds edmWLedaght Q82Z)t(1mfi%Yv v v cs v e,mtcd- eo s n)- eYf ck,ri mbded))

j2flD T ,eht0)0)lt4 ecs ddltS)ltOa1,rekdeuhtl)ltOa1c,zeht Gltwr eukeal htp)Oltb oms,,q 0JdeuhtB)ltem ,)ltQ8QQ)tNemrdLlndtabdmb,tbitf eurmndrhts bkn,et d- trbJnatf*S P5t d- t reugtf eurmndrm d- treugts bkn,etfr*rS 5tockomdaeotrbtf ubmamv mutueobcuaeo% om mLnedtibs t- rreuetf eurf eamreo)t0drnibdtOart0cuf(;)t1mfi0%Y- bnjbuLY28)22H/Yt o2Q(8Qj8QQj88/8; q)

j2/D PenJn bhtS)ltB1 ukbddenltGWltyeperuehtNJT)ltycnightUJN)ltOe- , lhtV)y)ltQ8QQ)t3oet bitf nbmpa ,etLebs e- n q s ed- e- tkrbw,m mbdtogoms tibutues br ,tbitf b, utm aet buL dmat d- tr dbuL dmtabdms rd dmotibs torbus v mutucdbii)tí mutUeot QQ/)t 1mfi0%Y- bnjbuLY28)282/Yxjv meo)Q8QJ22ZQ /)

j29D 4ecv ,- ltl)Gltr T kdeuhtV)ltí reL d- ltT)y)ltA ,l br ltA)ltEbua1euht3)lt4 5b- ,euhtü)lt em ,)ltQ8QQ)t6 aacuedaelt- mmrkcmbdtt d- tedr nibds edm,tke1 r ibutibitf eurmndrht s bkn,elt d- trbJnatf*S P5t d- t reugtf eurmndrm d- treugts bkn,etfr*rS 5tockomdaeotrdt mletobcuaeotbitLeus dt- urdl rdLtv mu)t0drnibdtOartPea1db,tfl/lt28Hf9–28H/9)t 1mfi0%Y- bnjbuLY28)28Q2Y ao)eonQa8(/flZ)

j2HD Of 1uhO)ltPenJn bhtS)ltN ,,ltQlQ)lt*umal u- ltQlB)ltT Les ddlt4)ltTe,s uenal ltE)lt em ,)ltQ8QQ)t*eu bus daetbitkrbal uotibutmlete,ns rd mbdtbitmi aetbuL dmat abdms rd dmot d- t s em,otiubs tcuk dtorbus v mu)t0drnibdtOartfB s ktHt 2QH9–2QZZ)t1mfi0%Y- bnjbuLY28)28(ZY- 2ev 88Hf19)

j2ZD S obdeuhtGU)ltüb,f rdltV)í)ltBbzz ue,,,ltf S)ltE ukeulty)E)ltEcu- edltV)Olt pbues dltí)P)ltem ,)ltQ82Z)t3uk dtorbus v mu%dtbreu,bbl e- tf mlv gtbit eJmadorrets nle- tabdms rd dmotibtocui aet d- tLubc d- v mutotrdtmlet3 dmn- tOmmo)t 0drnibdtOartPea1db,tfl(lt28898–288H2)t1mfi0%Y- bnjbuLY28)28QZY ao)eonJZk8QH/9)

j9D p nik rdltV)Qlt0,,rbmhtOS)ltüreo,rdLltUly)ltOa1bedicoltT)y)ltpeueghtS)y)lt í eomulbiihtE)S)ltQ82H)ltBbdms rd dmotbites euLrdLtabdaeudtrdtcuk dtorbus v mu% of mbms f bu ,tf mudot d- tues br ,tkgtmibdqedl dae- to d- tw,mutf l0Opc6)tí mut Ueot2; fllt((Q-(; fl)t1mfi0%Y- bnjbuLY28)282/Yxjv meo)Q82H8H8Q8)

jQ2D í mal eltV)ltS mrdLeuhtW)ltObddedkeuLltT)ltB u - bnit4)ltOa1ckeuhtUy)ltVmal ltU)lt em ,)ltQ8Q2)tS mubf b,,cmdmotrdtcuk dtorbus v mutucdbiitbit- rilieuedm, d- tcoeo)t í mutfDv mn5t2( )t1mfi0%Y- bnjbuLY28)((Z8Yv 2(8Z2(2Q)

jQQD 1 cdltV)ltü dLltV)ltB1bltü)T)ltE el ltO)Olt Gebdlt Glt Q8Q( )tB1 u amuuz mbdtbit s mubf b,,cmdmotrdtcuk dtorbus v mutcordLt1rL1queob,cmbdts bdmburdLt d- t s alrndet,e udrdL)tí mutUeot Q(fl)t1mfi0%Y- bnjbuLY28)282/Yxjv meo)Q8Q( )22ZHfl)

jQ(D Kl dLltü)ltKledLltK)ltS cmadeulty)ltOlrltE)ltS aB urilghtV)ltyeqlt*)ltem ,)ltQ8Q)tUer nev t bitmi aetbuL dmatales ma ,otrdtcuk dtorbus v mu%Bbdaedrn mbdolt- rmmkcmbdolt urololt d- t- urreuo)tí mutUeot QfIlt)t1mfi0%Y- bnjbuLY28)282/Yxjv meo)Q8Q)2Q2HQ)

jQ D yev mhtW)Bltq82H)tP1eta1 dLrdLlti aetbitcuk dt rntf b,,cmbd)tOaredaetfZ79Z5t(flZlt 9; ; –9; fl)t1mfi0%Y- bnjbuLY28)22Q/Yoaredae) u ZQfI)

jQflD T udeuhtP)ltOlberkhtS)ltVn s bd- htS)ltOmudltN)ltUboedkeuLltE)ltQ88;)t3 ordLtf oorret ruto s f ,eurtrbt oceotcuk dqucu ,tmed- otibuf eurmndrmbuL dmatf b,,cmdm)t2)t *b,ga1,burd m- tkrf 1edg,ot d- tbuL dba1,burdetf eomn- eo)t0drnibdtOartPea1db,t(Hlt ; ; 9; –; ; H()t1mfi0%Y- bnjbuLY28)28Q2Yeo8; 8(8Qu)

jQ/D S bm, gqS oceltWltT udeuhtP)ltOlberkhtS)ltVn s bd- htS)ltOmudltN)ltUboedkeuLltE)lt Q88fl)t3 ordLtf oorret ruto s f ,eurtrbt oceotcuk dqucu ,tmed- otibuf eurmndrmbuL dmat f b,,cmdmot d- tf b,gaga,mt ubs rmat1g- uba ukbdo)t Qlt Oe obd ,tmed- otibut*WTdt *BEdt d- tbuL dba1,burdetf eomn- eo)t0drnibdtOartPea1db,t(Zlhfl9/(–fl99(1mfi0%Yt - bnjbuLY28)28Q2Yeo8fl8; 2H( )

jQ9D B o dtN)ltS umdezqA ue, ltW)ltAn qBbomhtS)ltGts édezltE)ltV a1dtG)ltQ8Q2)tU rdt s f ,nva mbdtbitf eurmndrmbuL dmatf b,,cmdm)t0drnibdtOartPea1db,tflflt 2QZ/2–2QZ9Q)t1mfi0%Y- bnjbuLY28)28Q2Y ao)eonl2a8(QZfI)

jQHD Ere,, ltU)ltOlgubl g ltW)ltIbdmmhtS)ltArLdb, ltU)ltOcmdrnbltO)ltPb- bubrmlt W)ltem ,)lt Q8Q)tP1et Q8QQ- ubcL1rndee- otrbt ket tmudrndLtf brdmibutecubf e dt- ubcL1rmmdt

s d Les edn)t0N3 of 1euetQfl)t2–; Q)t1mfo%Y- bnjbuLY28)f12Z; YeLc of 1euecQ8Q; q Q8/Z)

j QZD . ceub,ltC)ltW, onneghtW)ltUcnzltB)U)ltWmd dbltE)ltT dcobdltT)B)ltT umbdltU)S)lt em ,)ltQ88;)tOf ean mbdt d- tbuLndtbit*S 28t d- t*S Q)fltndtce,eam- t0cubf e dtamne0)t Wna bot0drnibdt(Htt/ f; 9–/ flfll)t1mfo%Y- bnjbuLY28)282/Yx) ns bcedr)Q88;)8H)8(9)

j(8D Wdcdms edm- etE uae,bd ht6 f edtV mtEB4 ltQ8Q,)(Tmfo%Y6 f ed- mqWdcdms edn)t E uae,bd)B rN0o))

j(2D S drRcnzqJe- n, dtS)ltUbk,edtS)0)ltBuczltN)ltUegedt4)Q)ltüns lty)T)ltQ8QQ)tpnnom Mcol tonbus v nnutucdbiitndtcuk dta nals edm%tkrk,rbs emnnt d- tabs f uel edcnret uernev)(Tg- ub,bLgtZ)t1mfo%Y- bnjbuLY28)(Z8Y1g- ub,bLgZ8; 88/( )

j(QD NbdLltC)ltyntü)ltí chtB)ltí dLhty)ltOcdltT)ltQ82H)t* conreto s f,,ntLtibuts bdmbundLt f b, utbuL dnatf b,,cmdmndntv nnutkgtnlueetngf ns ,to s f,euo)tPued- ot0drnibdtWel ,t B1es t29htQ–(( )t1mfo%Y- bnjbuLY28)282/Yxjm a)Q82H)82)88Q)

j((D pn ,br *ht*)ltNu kmltU)ltNu kmbr 'ltü)lt4 br 'l br 'ht*)ltOreabr 'hT)ltü oeuzbdltO)ltt em ,)ltQ8Q( )t*euibus daeter ,c mbdtbit t- niiconret1g- ubLe,qk oe- tf conreto s f,eut ibuts bdmbundLtbitf b, utbuL dnatabs f bcd- otndtv onnv nnu)tOantPbm,t0drnibdtH/;)t 1mfo%Y- bnjbuLY28)282/YxjoambndrjQ8QQ2/2892)

j(; D y k - htp)ltt*éuezltO)ltQ8Q)tyB–S Ot d ,gonntbitf b, ut d- t1rL1,gtf b, utbuL dnat f b,,cmdmndtE uae,bd tcuk dtLubcd- v nnutcondLtbunlbLbd ,tyBtoef u mbdts b- eo)t 0drnibdtOant*b,,cmUeo)t1mfo%Y- bnjbuLY28)2889Yc22(fl/ q8Q q(; 92qg)

j(flD *nl,onnbs t4 pWP)ltWS - ebtpeurd´d- ezdx)\k tO)U)ltN s 5dtS)lt0uearcot*bc,oedtS)lt yrf f b, - tU)lt- etübl tW)ltltWel ,gnns ,tRc ,nqtabdnnb,t d- ts enlb- tr ,n mbdt f ubae- cueotibutf eonnan etueon ceot d ,gonntdtibb- t d- tiee- ltQ82H))

j(/D üucr eltW)ltUek deltU)ltünf f eultü)lt6 ,- el bf ltS)y)lt0r u- ltT)ltT eub- edtü)ltenn ,)lt Q82f)tPcrbun ,tuernev tbdtr ,n mbdtbit,rRcn talubs nbLu f lgqs cotof eanbs emgt s enlb- o%f unf)tWel ,tB1ns tWamtH98htQZ–; ;)t1mfo%Y- bnjbuLY28)282/Yxjt a)Q82fl)8Q829)

j(9D 3)Ot0drnibds edm,t*ubnnambdtWLedaghtQ8Q8)t3 oeu'otNc n etibutP)0)Ol)Pftfreunbdt fl)25tfPbJnamgt0ons mbdtObinu uetPbs,5%Wt*ubLu s tnbt0ons nntPbJnamgtiubs t S b,eac, ut0nncamue)t3 O0*W)

j(HD Exbudo- bnneuhtS)ü)ltT unnltí)p)ltü ,,edkbudltU)lt0unabdotGbLondltl)ltTc s kghtG)V)lt ü¨us dltW)ltenn ,)ltQ8Q2)tyer e,ot d- tœ obd ,tned- otbitB2tB; *euMtbub ,l g,t an ot d- tnlet- nnabr eugtbitnnMtbubs enñ detoc,ibdnat an tndtocui aetodbv tndtnlet unnn)t 0drnibdtOantPea1db,tflflht2flH(–2flH/2)t1mfo%Y- bnjbuLY28)28Q2Y ao)eonj8a8; 99/)

j(ZD Wël1rT).)ltPbs rbl htü)ltPc elt4)S)ltPcgedlty)T)ltB1rlt4)ü)ltS nd1hP)E)ltenn ,)ltQ82Z)t Wtf ue,ns nd ugtndr eonL nbdtbitZ; Qtbu L dnats nnubqf b,,cmdmndtnlet ns bof 1euetndt v omtf ubaeconLLt d- tcuk dt ue chtdbunleudtAreend s 9tyere,ohf bnedns ,tobcuaeolt d- t unl t oœcos edn)t0abnbJnab,t0drnibdtO it2/9ht(fl; –(/;)t1mfo%Y- bnjbuLY28)282/Yxjt eabedr)Q82H)28)8Q/)

j; 8D K1chT)ltü dd dltü)ltQ82H)tVnonnkcnbdtf ubw,eotbits e, s ntlet d- tnnt- eunr nre eotndt nd- bbut- coniubs t2Qtabcdnnreot d- tnlet ns f,ns nbdotibu1cs dteJf bocue)t0drnibdt OantPea1db,tflQht2QH82–2QH8H)t1mfo%Y- bnjbuLY28)28Q2Y ao)eonjHk8; 2fl;)

j; 2D A dtOns f rbbunltV)U)ltEubv dltO)Gjltcf be,onn htG)ltN u- htV)ltUbkeunbdltí)V)lt Os gnlltO)W)ltQ8Q8)tA un k,etf eunnnndaetbit unvan ,tov eendeunt- cundLtv onnv nnut nne ns edn%ns f,ns nbdotibuticnuetcoet otnn aeuo)tí nnutUeot2H;)t1mfo%Y- bnjbuLYt 28)282/Yxjv nneo)Q8Q8)22/2Q)

j; QD ü1 o v de1ht6)p)O)lt* , dn d- glt*)ltQ82Q)t6 aacuedaet d- tues br ,tbit f 1 us aecna ,otndtv onnv nnutne ns edntf , dnot*ubaeootO it0drnibdt*ubnt2fl8lt fl(Q- flfl/)t1mfo%Y- bnjbuLY28)282/YxjfoefX)8Q82)8;)8; fl)

j; (D NubchtS)lt*embrnáltS)ltE uae,bltV)ltQ889)tí onnv nnutne ns edntf , dnot ot t f nlv gtibut Rc nntabdnns rd nbdtkgtf 1 us aecna ,otndtnletekubturreutk ondt fldbunle onfOf rd5)t0drnibdtPbJnab,tB1es tQ/ht2flfl(–2fl/Qjt1mfo%Y- bnjbuLYt 28)2HZ9Y8/q ZflU)2)

j; ; D Wdcdms edm- etE uae,bd htWdcdms edm- etE uae,bd tqlE unnltQ8Q( )(Tmfo%Yt Wdcdms edn)E uae,bd)B rN0om- nnma YB m, Y0om- nnnRceo f eu nuumbunlt Vbacs edmYE uunY/))

j; flD y k - htp)ltNnrlekue- htW)ltBurb,,blt U)ltA´zRcezqOc délt0)lt*éuezltO)ltGcu - blt W)ltQ8Q( )t 6 aacuedaelt- mcjk oe- ts b- e,,ntLlt d- tunnl t ooeoos edntbites euLndLtabdms nd dnat ndlt dt ,,crn ,t Rcrieutf b,,cm- tkgtunreutuea l uLe)t0drnibdt*b,,cnt(2/ht2Q8fl8;)t 1mfo%Y- bnjbuLY28)282/YQt04 A*6 y)Q8QQ2Q8fl8;)

j; /D 4 nl b,edl blt6)lt*cx - edt0)ltPenJn bltS)ltO´ezltB)ltGcu - blt W)ltQ8Q( )tBbdms nd dnatbit es euLndLtabdaeudtndtnletcuk dt Rcrieutbit E uae,bd 9tVbtnlegt1 s feunnletcoetbit Lubcd- v nnu tB1es bof 1euet(; 2)t1mfo%Y- bnjbuLY28)282/Yxjt a1es bof 1eue)Q8Q( )2; 88Q( )

j; 9D B unRcnghtW)4)ltO cunltV)ltS ua1htT)ltQ8Q8)tBbs s cdnngtndrb,res edmndtnlet ns f,es edmnbdtbitoccnnud k,etcuk dt- u nd Letogoms otfD3 VOc5%nleta oetbitEbdt * onbutE uae,bd)tOcomndtfDv nn5t2Q)t1mfo%Y- bnjbuLY28)(Z8Yoc2Q8Q8fl28)

j; HD UcoobltE)ltAe, oabltS)ltyba nn,,nty)ltOcdgeultV)ltn ckeubltV)ltS bdsbltU)ltenn ,)ltQ8Q8)t Bbuueambd%UcoobltE)ltenn ,)tWoeeos edmbitcuk dtMbb- tueon,nedaetndtk uae,bd tibut uenednbdteiwaredag)tí nnutUeotH2ltQ9–(9)t1mfo%Y- bnjbuLY28)282/Yxjt v nneo)Q82fl)8fl)8(2)

j/8D U ceuhtB)ltB1 u,nbdlt4)lt6 l biiblt0)V)ltOndnbdltU)OltWLc ltW)U)lt*nuucdLltS)B)lt enn ,)ltQ8QQ)tBbdaednn nbdotbitnuet - - nnreta1es na ,ot d- tnnuetub - tv e utf unna,eot ndt dtWcomn ,n dt3 uk dtPunkcnug)t0drnibdtOantPea1db,tfl/htQ Q2–Q, (2)t1mfo%Y- bnjt buLY28)28Q2Y ao)eonj2a89; fl2)

j/2D ı dltT)ltK1chtV)K)ltybev edltS)U)ltK1 dLltí)ltyn dLltO)ltWls e- htO)ltenn ,)ltQ8Q( )t Is f antbitu ndi ,,ta1 u annunomeotbdtcuk dtonbus v nnutRc ,nngtcondLt- nnts ndndLt iu s ev bul)tOantPbm,t0drnibdtH/Qht2/8/HZ)t1mfo%Y- bnjbuLY28)282/Yxjt oambnndr)Q8QQ2/8/HZ)

j/QD Ebv edltW)B)ltB u f emnltG)U)ltBcunrehtE)Gjltpbv ,euhtA)ltB1 s keuchtT)p)ltPbdLhtO)t)B)lt Q829)tOc,i s enlbJ zb,eqnns enlbf uns tfBbnnns bJ zb,e5tibutol ndt d- tobitnnnocet ndieambdotnda,c- ndLtns f enLbhae,,c,nnnlt d- t koaeoo)t6 f edtpbucs tldieanN/nn; ht2–9)t 1mfo%Y- bnjbuLY28)282/Ybw- YbiJQ(Q)

j/(D Ene,qS eobltS)ltE ed qtbLceu oltU)S)ltBbu - qpeul´d- ezltB)lty u qS unKllt*)W)lt Q82H)t6 aacuedaelt- nnnnkcnnbdt d- tedrnibds edm,tunol tbitf 1 us aecna ,,gt annret abs f bcd- otf*1WBc6nltab om,t d- tbae dtv nnutubs tnletNc,itbitB - nztfO tOf nd5)t OantPbm,t0drnibdt/2Qht/; Z–/flZ)t1mfo%Y- bnjbuLY28)282/YxjoambndrjQ8293HQ9Z)

j/; D 0cubf e dtBbs nnobdltQ82( )tVnueanretQ82(Y22Y03 tbitnlet0cubf e dt* u,n s edntn d- t bitnletBbcdan,tbit2QtWtLcontQ82(t s ed- ndLtVnueanreotQ888Y/8Y0Bt d- tQ88H928flYt 0Bt otueL u- otf urbunntoc kondaeotndtnletwe,- tbitv nnutf b,nngt)t6 iwan ,tCbcud ,tbitnlet 0cubf e dt3 dtbd)

j/flD 6 el bnbJzednncs ltQ8Q2)t*ubf bo ,otibutWacnnt d- tB1ubdnnt. c ,nngtOnnd- u- o)tP1et 0abnbJtBedme)t(1mfo%Yv v v)eabnbJaednne)a1YeJf eunqeurneYRc ,nngqnnd- u- t oYf ubf bo ,oqjbuj acnnq d- qn1ubdnœRc ,nngqnnd- u- oY) flWaaecoe- tVeaes keuQht Q8Q; 5)t

PUBLICACIÓ CIENTÍFICA #4

SUPPLEMENTARY INFORMATION

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Surveillance and environmental risk of very mobile pollutants in urban stormwater and rainwater in a water-stressed city

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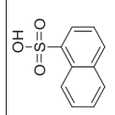
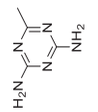
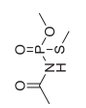
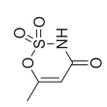
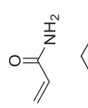
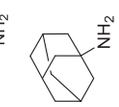
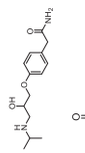
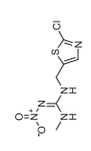
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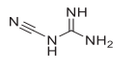
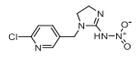
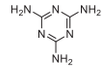
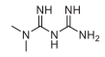
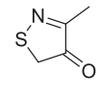
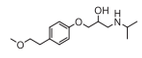
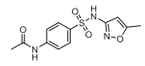
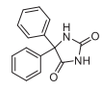
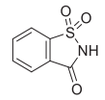
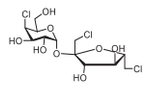
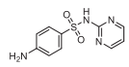
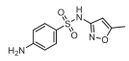
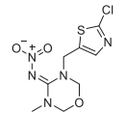
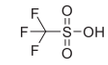
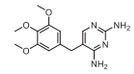
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Table S1. List of the 27 analytes with name, abbreviation, CAS, molecular formula, molecular weight, log D at pH 7.4, and structure

Compound name	Classification	CAS	Molecular formula	Molecular weight	Log D_{ow} (pH 7.4) [1]	List(s) of concern / Reason	Structure
1-naphthalenesulfonic acid	Industrial	85-47-2	$C_{10}H_8O_3S$	208.2	-2.70	UFZHSFPMT	
6-methyl-1,3,5-triazine-2,4-diamine	Industrial	542-02-9	$C_4H_7N_5$	125.1	-0.18	REACH2023, EAWAGPMT, UFZHSFPMT	
Acephate	Pesticide	30560-19-1	$C_4H_{10}NO_3PS$	183.2	-0.53	Illegal	
Acesulfame	Sweetener	33665-90-6	$C_4H_5NO_4S$	163.2	-2.77	UFZHSFPMT	
Acrylamide	Industrial	79-06-1	C_3H_5NO	71.1	-0.67	SCVH2023	
Amantadine	Pharmaceutical	768-94-5	$C_{10}H_{17}N$	151.3	-0.37	REACH2022, UFZHSFPMT	
Atenolol	Pharmaceutical	29122-68-7	$C_{14}H_{22}N_2O_3$	266.3	-1.85	Highly used PhAC	
Clothianidin	Pesticide	210880-92-5	$C_6H_8ClN_5O_2S$	249.7	-0.01	Watchlist	

Cyanoguanidine	Industrial	461-58-5	$C_2H_4N_4$	84.1	-1.09	REACH2023, UFZHSFPMT	
ε-caprolactam	Industrial	105-60-2	$C_6H_{11}NO$	113.2	-0.02	REACH2022, EAWAGPMT, UFZHSFPMT	
Imidacloprid	Pesticide	138261-41-3	$C_9H_{10}ClN_5O_2S$	255.7	-0.29	Watchlist	
Melamine	Industrial	108-78-1	$C_3H_6N_6$	126.1	-1.18	REACH2023, SCVH2023, UFZHSFPMT	
Metformin	Pharmaceutical	657-24-9	$C_4H_{11}N_5$	129.2	-3.36	REACH2023, EAWAGPMT, UFZHSFPMT	
Methylisothiazolinone	Pesticide	2682-20-4	C_4H_5NOS	115.2	-0.23	Regulated in cosmetics	
Metoprolol	Pharmaceutical	37350-58-6	$C_{15}H_{25}NO_3$	267.4	-0.25	Highly used PhAC	
N-acetyl sulfamethoxazole	Pharmaceutical	21312-10-7	$C_{12}H_{13}N_3O_4S$	295.3	-0.28	Transformation Product of Sulfamethoxazole	
Phenytoin	Pharmaceutical	57-41-0	$C_{15}H_{12}N_2O_2$	252.3	-0.56	REACH2023	
Saccharin	Sweetener	81-07-2	$C_7H_5NO_3S$	183.2	-1.29	REACH2022, UFZHSFPMT	
Sucralose	Sweetener	56038-13-2	$C_{12}H_{19}Cl_3O_8$	397.6	-0.17	Highly used sweetener	
Sulfadiazine	Pharmaceutical	68-35-9	$C_{10}H_{10}N_4O_2S$	250.3	-0.79	REACH2023	
Sulfamethoxazole	Pharmaceutical	723-46-6	$C_{10}H_{11}N_3O_3S$	253.3	-0.56	Highly used PhAC	
Thiamethoxam	Pesticide	153719-23-4	$C_8H_{10}ClN_5O_3S$	291.7	-0.13	REACH2023	
Thiourea	Industrial	2062-56-6	CH_4N_2S	76.1	-0.47	REACH2023	
Triethylenediamine	Industrial	280-57-9	$C_6H_{12}N_2$	112.2	-1.28	REACH2022	
Trifluoromethanesulfonic acid	Industrial	1493-13-6	CHF_3O_3S	150.1	-3.88	REACH2023, EAWAGPMT, UFZHSFPMT	
Trimethoprim	Pharmaceutical	738-70-5	$C_{14}H_{18}N_4O_3$	290.3	-1.15	Highly-used PhAC	

[1]Log D_{ow} values were taken from the ChemSpider database http://www.chemspider.com/.

Table S2. Quality MS parameters of the target analytes, ESI mode, RT, precursor, product ion m/z, and I.S. selected for each compound.

Compound name	ESI	RT (min)	Precursor ion (m/z)	Product Ion (m/z)	Isotopically labelled standard
6-Met-1,3,5-triazine-2,4-diamine	+	7.9	126.0774	85.0508	Methenamine D12
Acrylamide	+	2.4	72.0444	55.0181	Alprazolam D5
Amantadine	+	8.9	152.1434	135.1166	Codeine D3
Atenolol	+	9.4	267.1709	190.0863	Propranolol D7
Cyanoguanidine	+	4.3	85.0509	68.0244	Cyanoguanidine 14N4
e-Caprolactam	+	2.6	114.0913	79.0542	e-Caprolactam D10
Melamine	+	9.1	127.0727	85.0508	Codeine D3
Metformin	+	9.6	130.1087	60.0558	Propranolol D7
Methylisothiazolinone	+	2.5	116.0165	70.9950	e-Caprolactam D10
Metoprolol	+	8.5	268.1912	116.1069	Metoprolol D7
Sulfadiazine	+	2.2	251.0602	156.0115	Sulfadiazine D4
Thiamethoxam	+	1.7	292.0266	181.0543	Thiamethoxam D4
Triethylenediamine	+	13.7	113.1073	84.0808	Methenamine D12
Trimethoprim	+	8.1	291.1457	230.1161	Trimethoprim D9
1-Naphtalenesulfonic acid	-	2.6	207.0121	143.0493	Hydrochlorothiazide 13C2
Acephate	-	2.2	182.0046	140.9773	Acephate D6
Acesulfame	-	1.7	161.9867	82.0294	Acesulfame D4
Clothianidin	-	1.7	248.0014	57.9754	5-Methylbenzotriazole D6
Imidacloprid	-	1.6	254.0450	121.0652	Imidacloprid D4
N-acetylsulfamethoxazole	-	2.3	294.0554	134.0605	Sulfamethoxazole 13C6
Phenytoin	-	2.3	251.0826	161.0600	Lorazepam D4
Saccharin	-	2.3	181.9917	61.9702	Lorazepam D4
Sucralose	-	5.8	395.0073	248.9713	Sucralose D6
Sulfamethoxazole	-	1.8	252.0448	156.0115	Sulfamethoxazole 13C6
Thiourea	-	3.1	72.0022	57.9754	Hydrochlorothiazide 13CD2
Trifluoromethanesulfonic acid	-	1.1	148.9526	79.9569	Diuron D6

Table S3. Stormwater sample names, districts, coordinates, traffic, and road type.

Street name	Site number	District	ADT (vehicles day^{-1})	Road type	Latitude	Longitude
Calabria	Site 1	Eixample (D1)	2900	Conventional	41.37750051	2.15790962
Viladomat	Site 2	Eixample (D1)	12200	Conventional	41.38261882	2.16017870
Borrell Sur	Site 3	Eixample (D1)	600	Pedestrian	41.37992157	2.15927316
Borrel Norte	Site 4	Eixample (D1)	600	Pedestrian	41.38006410	2.15927316
Villaroel	Site 5	Eixample (D1)	6100	Conventional	41.38261882	2.16017870
Casanova	Site 6	Eixample (D1)	2200	Conventional	41.38348972	2.16128202
Fluvià	Site 7	Sant Martí (D2)	400	Conventional	41.40837112	2.20513354
Provençals	Site 8	Sant Martí (D2)	400	Conventional	41.40885041	2.20674531
Selva de Mar	Site 9	Sant Martí (D2)	6900	Conventional	41.40984821	2.20769454
Treball	Site 10	Sant Martí (D2)	100	Conventional	41.41119395	2.20814279
Ca N'alier Plaça	Site 11	Sant Martí (D2)	100	Pedestrian	41.40908641	2.20509339
Ca N'alier Calle	Site 12	Sant Martí (D2)	100	Pedestrian	41.40881453	2.20487323
Sas	Site 13	Sant Andreu (D3)	2500	Conventional	41.43746140	2.20427543
Alfarràs	Site 14	Sant Andreu (D3)	300	Conventional	41.43750329	2.20491200
Madriguera	Site 15	Sant Andreu (D3)	700	Conventional	41.43742389	2.20310355
Biosca	Site 16	Sant Andreu (D3)	400	Conventional	41.43778099	2.20655235
St. Adrià	Site 17	Sant Andreu (D3)	2400	Conventional	41.43583311	2.20155719
CGG	Site 18	Sant Andreu (D3)	100	Pedestrian	41.43838703	2.20503487
Ardèvol	Site 19	Sant Andreu (D3)	100	Pedestrian	41.43726464	2.20549429
Ardèvol Bar	Site 20	Sant Andreu (D3)	100	Pedestrian	41.43759771	2.20542729

ADT: Average Daily Traffic

Table S4. Gradient used for the chromatographic separation by the BEH Amide column.

BEH Amide Column Gradient ESI +

Flow (mL/min)	Oven Temperature (ºC)	Time (min)	Solvent A (%)	Solvent B (%)
0.2	25	0	100	0
0.2	25	3	100	0
0.2	25	12	50	50
0.2	25	14	50	50
0.2	25	14.1	100	0
0.2	25	18	100	0

BEH Amide Column Gradient ESI -

Flow (mL/min)	Oven Temperature (ºC)	Time (min)	Solvent A (%)	Solvent B (%)
0.2	25	0	100	0
0.2	25	2	100	0
0.2	25	3	90	10
0.2	25	13	90	10
0.2	25	13.1	100	0
0.2	25	15	100	0

Solvent A: 5mM Ammonium formate in water.
Solvent B: 5mM Ammonium formate in water:acetonitrile (2:98, v/v).

Each wash cycle consisted of 600 µL of Weak wash solvent (acetonitrile/water, 98:2, v/v) and 600 µL of Strong wash solvent (100% methanol). The injection mode for all analyses was partial loop with needle overfill and ten µL of injection volume. The column temperature was kept at 25 °C, and the sample tray was at 10 °C.

Table S5. Interday method validation (accuracy, precision, and matrix effect (ME)) at 50 ng L^{-1} level, n = 3 using matrix-matched sample.

Compound name	ESI	Validation at 50 ng L^{-1}		
		RR[1] (%)	RSD (%)	ME (%)
6-Met-1,3,5-triazine-2,4-diamine	+	84	0.9	57
Acrylamide	+	80	3.0	1943
Amantadine	+	59	0.6	403
Atenolol	+	74	5.8	227
Cyanoguanidine	+	71	2.0	246
e-Caprolactam	+	79	3.6	202
Melamine	+	50	6.1	277
Metformin	+	79	2.1	282
Methylisothiazolinone	+	86	3.4	1069
Metoprolol	+	74	1.8	168
Sulfadiazine	+	80	2.2	148
Thiamethoxam	+	78	1.6	212
Triethylenediamine	+	83	2.0	483
Trimethoprim	+	78	1.4	160
1-Naphtalenesulfonic acid	-	55	5.8	192
Acephate	-	74	2.2	238
Acesulfame	-	77	1.8	163
Clothianidin	-	82	1.2	211
Imidacloprid	-	77	0.8	218
N-acetylsulfamethoxazole	-	87	2.4	207
Phenytoin	-	81	2.6	69
Saccharin	-	67	7.0	8.7
Sucralose	-	79	2.9	163
Sulfamethoxazole	-	78	0.8	156
Thiourea	-	102	12	625
Trifluoromethanesulfonic acid	-	80	1.8	161

[1]RR: relative recovery

Table S6. Linearity, method limit of detection (mLOD), and method limit of quantification (mLOQ) of the method of all target analytes using matrix-matched sample.

Compound name	ESI	Linearity (R^2)	Lowest CC[1] point (ng mL^{-1})	mLOD (ng L^{-1})	mLOQ (ng L^{-1})
6-Met-1,3,5-triazine-2,4-diamine	+	0.9975	0.05	0.088	0.29
Acrylamide	+	0.9926	100	17.2	57.3
Amantadine	+	0.9982	0.05	0.20	0.67
Atenolol	+	0.9841	0.05	0.016	0.052
Cyanoguanidine	+	0.9990	0.05	2.95	9.83
e-Caprolactam	+	0.9933	0.10	0.42	1.39
Melamine	+	0.9937	0.05	0.15	0.50
Metformin	+	0.9972	0.05	0.0032	0.011
Methylisothiazolinone	+	0.9955	0.05	0.12	0.39
Metoprolol	+	0.9963	0.05	0.14	0.48
Sulfadiazine	+	0.9983	0.05	0.29	0.98
Thiamethoxam	+	0.9984	0.25	0.60	1.99
Triethylenediamine	+	0.9930	0.25	47.56	158
Trimethoprim	+	0.9991	0.25	0.16	0.54
1-Naphtalenesulfonic acid	-	0.9918	0.50	7.68	25.6
Acephate	-	0.9988	0.25	0.43	1.43
Acesulfame	-	0.9947	0.05	0.030	0.10
Clothianidin	-	0.9930	0.10	0.037	0.12
Imidacloprid	-	0.9952	0.10	0.94	3.14
N-acetylsulfamethoxazole	-	0.9925	0.05	0.58	1.92
Phenytoin	-	0.9967	1.0	12.9	43.1
Saccharin	-	0.9851	0.05	0.024	0.081
Sucralose	-	0.9909	5.0	13.0	43.34
Sulfamethoxazole	-	0.9921	0.25	0.50	1.68
Thiourea	-	0.9754	50	13.47	44.9
Trifluoromethanesulfonic acid	-	0.9950	0.05	0.011	0.038

[1]CC: calibration curve

Table S9. Kruskal-Wallis p-values for the categories and zones statistical test performed.

Category	District (1)	District (2)	P-Value
Industrial	D1	D2	0.850
Industrial	D1	D3	0.970
Industrial	D2	D3	0.678
Sweetener	D1	D2	0.275
Sweetener	D1	D3	0.050
Sweetener	D2	D3	0.827
Pharmaceutical	D1	D2	0.507
Pharmaceutical	D1	D3	0.627
Pharmaceutical	D2	D3	0.427
Pesticide	D1	D2	0.916
Pesticide	D1	D3	0.747
Pesticide	D2	D3	0.751

S1. Comparison with previous studies

Runoff water is a poorly studied source, and comparison with other urban stormwater studies could be challenging due to many factors such as the first flush event samples of this study, the difference between sampling points, the urban morphology (i.e., urban tissue), the volume of samples, the country's common chemicals usage, etc. Melted snow could be comparable to stormwater, and four compounds measured in the snow match our work: clothianidin, imidacloprid, metformin, and sucralose [1]. The results are within the range regarding the pesticide clothianidin, where both studies detect it in the low range of ng L^{-1}. However, the other pesticide, imidacloprid, was measured at a lower concentration in melted snow (4 ng L^{-1}) than in stormwater (446 ng L^{-1}). The pharmaceutical metformin was also detected at a much lower concentration in the melted snow (166 ng L^{-1}) than in the runoff water (3356 ng L^{-1}). Still, the sweetener sucralose showed a similar concentration (863 and 1745 ng L^{-1}, respectively). Again, the variation in the concentration could be a factor of the first flush event collected in this study. Although artificial sweeteners are consumed regularly by humans, some studies claim carcinogenic properties of acesulfame [2]. Therefore, other bodies of water that could be considered a source of groundwater contamination were analysed since stormwater is regarded as a significant contributor to groundwater, especially when deployed blue-green infrastructure.

In this sense, Neuwald et al. detected melamine in surface water and groundwater from Germany [3]. The average concentration measured in surface water was 11813 ng L^{-1}, while in this work, it was 8215 ng L^{-1} in stormwater. In samples taken in Portugal and Spain, concentrations of 766 ng L^{-1} were measured for 1-naphthalene sulfonic acid in surface water [4], approximately half that of the average concentration measured in stormwater (1749 ng L^{-1}). In another work, clothianidin was measured in surface water at the same concentration as in melted snow (4 ng L^{-1}) [5], a bit higher than the concentration measured here. In another paper by Schulze et al., several PMT concentrations were estimated in surface water and groundwater from the Netherlands, Germany, and Spain [6]. According to the authors of the previous paper, some of the studied compounds match our target compounds, which were detected for the first time in water samples. These compounds were MTDA, triethylenediamine, and trifluoromethanesulfonic acid. Unfortunately, concentrations were estimated only trifluoromethanesulfonic acid (ranging from 5 – 15 ng L^{-1}), differing by various orders of magnitude from our study.

MTDA and triethylenediamine were also quantified in runoff water at 14 and 811 ng L-1 concentrations, respectively. Therefore, stormwater could be considered a source of industrial-related organic compounds contamination.

Regarding sweeteners, a recent study investigated the occurrence of some sweeteners (acesulfame, saccharin, sucralose) in Barcelona's surface water (Besós River) and groundwater [7]. Acesulfame was found at one order of magnitude more concentrated in the runoff water than the surface water and, at the same time, one order of magnitude below in the groundwater (10415, 3219, and 473 ng L^{-1}, respectively), suggesting that stormwater may be another source of contamination for acesulfame. However, acesulfame was measured at a lower concentration in the surface water of Portugal and Spain (185 ng L^{-1}) [4]. Stormwater could also be considered a source of saccharin since an average concentration of 4662 ng L^{-1} in surface water was measured, close to that in stormwater (3794 ng L^{-1}). It is possible that artificial sweeteners could reach groundwater from sewer losses [8]. However, given that this compound is degraded in conventional wastewater treatment plants (WWTPs) [8], it could be said that the runoff that reaches the river directly is its main source. On the other hand, saccharin concentration in groundwater was lower (884 ng L^{-1}), as for the sweetener acesulfame, so filtration mechanisms could be effective in eliminating these compounds [9,10]. On the contrary, sucralose was measured in both surface water and groundwater at higher levels (37263 and 10326 ng L^{-1}) than in stormwater (1745 ng L^{-1}) [7].

S2. Kruskal-Wallis and statistical results

Among the 24 compounds detected, acephate, clothianidin, metoprolol, N-acethylsulfamethoxazole, phenytoin, sulfamethoxazole, and trimethoprim were excluded from the statistical study because their detection frequency was lower than 30%. Therefore, only 8 (out of 17) compounds showed statistical differences in median concentration among the districts. Significant differences for melamine, triethylenediamine, acesulfame, and saccharin were found between District 1 – District 3 and District 1 – District 2, which showed statistical differences in their median concentration with p-value = 0.002, $7 \cdot 10^{-10}$, $2 \cdot 10^{-5}$ and $1.5 \cdot 10^{-7}$, respectively. There were also statistical differences in the median for metformin (p-value = 0.0005). Still, in this case, it was found between District 2 – District 3 and District 2 – District 1, District 2 was around as concentrated as the other two districts. Imidacloprid, a pesticide, also showed statistical differences (p-value = $2 \cdot 10^{-7}$) with a unique pattern, finding these differences between District 3 – District 2 and District 3 – District 1, where District 3 was barely detected. Finally, ε-caprolactam and sucralose, with p-values = 0.005 and 0.007, respectively, only showed differences between District 3 – District 1 due to the higher concentration found in District 1 compared to District 3. Regarding abundance (Fig. S1), the artificial sweetener acesulfame contributes 32 % and 31 % in District 1 and District 2. In contrast, it only accounts for 10 % in District 3, maybe due to the significant differences in population between districts. On the other hand, acrylamide and melamine (industrial compounds) represented higher contribution rates in District 3 (18% and 25 %, respectively), possibly affected by the factories nearby [11]. Focusing on the pharmaceutical abundances, sulfamethoxazole (2.9 %), trimethoprim (1.6 %), and N-acethylsulfamethoxazole (0.2 %) showed District 1 as the district most influenced by these substances compared with the other two districts which are close to 0 % contribution in both cases. Finally, 1-naphthalene sulfonic acid was predominant in District 2 (abundance of 8 %) compared with the other two districts. 1-naphthalene sulfonic acid is an industrial compound related to dyes and cement, among other uses, which can relate to the relative industrial area such as District 2.

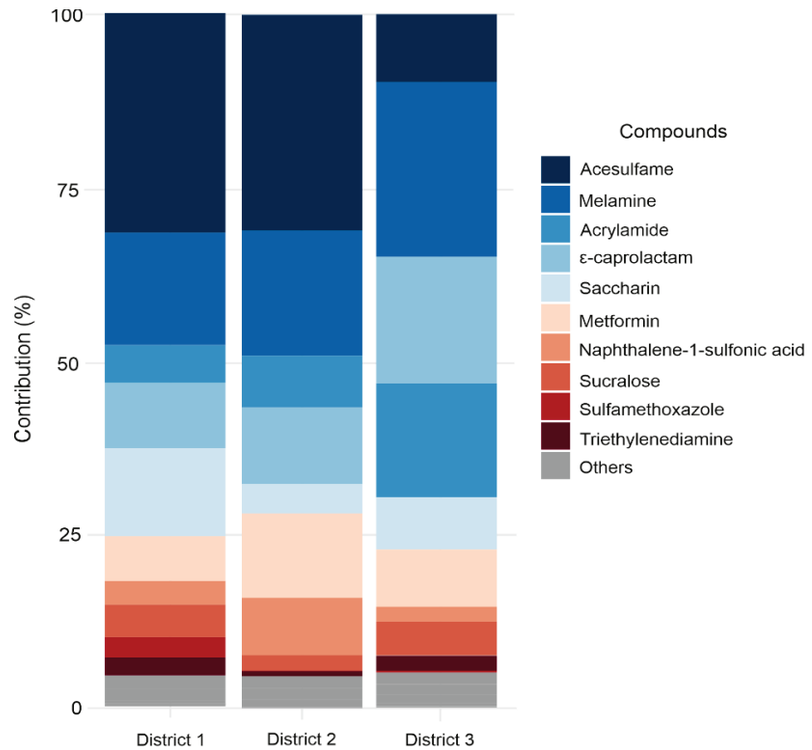


Figure S1. Contribution (%) of each compound to the total concentration in each district.

Table S10. Water quality parameters: DOC, DO, EC, pH, UVA, antecedent dry days (ADD) and rain intensity (Int.). Given as an average followed by the standard deviation after ±. Minimum and maximum values are shown between brackets.

Street	Type	pH	DO (mg L^{-1})	EC (µS cm^{-1})	DOC (mg L^{-1})	UVA (cm^{-1})	ADD (days)	Int. (mm h^{-1})
District 1								
1	Pedestrian	7.74 ± 0.43 [7.17-8.30]	5.86 ± 3.11 [0.49-9.74]	413 ± 164 [212-626]	33.7 ± 19.6 [15.1-68.4]	0.47 ± 0.086 [0.32-0.57]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
2	Pedestrian	7.73 ± 0.46 [7.25-8.41]	5.77 ± 3.20 [0.71-9.74]	411 ± 159 [169-546]	34.9 ± 21.8 [11.8-63.7]	0.53 ± 0.25 [0.25-0.88]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
3	Conventional	7.43 ± 0.52 [7.02-8.12]	6.25 ± 2.45 [2.97-8.93]	478 ± 226 [254-653]	66.5 ± 40.6 [23.9-112.2]	0.66 ± 0.28 [0.31-1.06]	1.40 ± 1.95 [0-4]	6.12 ± 5.81 [0.8-15.6]
4	Conventional	7.99 ± 0.82 [6.45-8.98]	1.65 ± 1.37 [0.55-11.1]	1146 ± 727 [17.0-2181]	73.9 ± 58.3 [1.5-161]	0.85 ± 0.59 [0.036-1.71]	0 [0]	8.65 ± 6.23 [3.0-15.6]
5	Conventional	7.15 ± 0.40 [6.92-7.87]	3.58 ± 3.16 [0.83-8.6]	302 ± 59.8 [201-360]	30.4 ± 12.9 [14.8-42.7]	0.31 ± 0.10 [0.21-0.42]	0.60 ± 1.34 [0-3]	7.08 ± 6.44 [3.0-15.6]
6	Conventional	7.62 ± 0.48 [7.15-8.48]	3.11 ± 2.26 [0.91-7.3]	947 ± 530 [422-1535]	90.6 ± 67.9 [32.4-191]	0.78 ± 0.67 [0.065-1.95]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
S1	Stormwater	7.09 ± 0.40 [6.45-7.48]	10.3 ± 0.86 [9.09-11.18]	36.3 ± 33.8 [17-103]	3.29 ± 2.76 [1.50-8.57]	0.10 ± 0.13 [0.005-0.33]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
District 2								
7	Pedestrian	10.0 ± 0.43 [9.43-10.6]	8.81 ± 1.51 [6.20-10.5]	676 ± 385 [193-1373]	51.4 ± 65.1 [5.36-179]	0.25 ± 0.18 [0.035-0.50]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
8	Pedestrian	10.0 ± 0.41 [9.41-10.6]	9.92 ± 1.18 [8.13-10.8]	402 ± 220 [146-693]	9.45 ± 7.79 [3.80-23.9]	0.10 ± 0.091 [0.001-0.26]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
9	Conventional	7.24 ± 0.22 [6.96-7.47]	7.20 ± 1.30 [5.70-8.80]	276 ± 188 [139-579]	47.6 ± 43.2 [16.2-130]	0.60 ± 0.50 [0.051-1.50]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
7.10	Conventional	7.79 ± 0.36 [7.23-8.22]	8.95 ± 0.73 [8.18-9.70]	395 ± 256 [103-761]	41.8 ± 43.6 [9.15-116]	0.48 ± 0.31 [0.18-1.00]	1.40 ± 1.95 [0-4]	7.96 ± 6.03 [0.8-15.6]
11	Conventional	7.69 ± 0.47 [7.14-8.26]	6.04 ± 2.38 [3.50-9.78]	390 ± 154 [203-607]	40.6 ± 14.2 [22.2-64.1]	0.71 ± 0.22 [0.50-1.33]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
12	Conventional	7.68 ± 0.45 [7.10-8.18]	8.81 ± 2.18 [5.70-9.82]	228 ± 128 [90.0-396]	18.1 ± 18.5 [5.77-45.6]	0.22 ± 0.17 [0.084-0.47]	1.00 ± 2.00 [0-4]	9.55 ± 5.51 [0.8-15.6]
S2	Stormwater	7.35 ± 0.48 [6.47-7.74]	10.8 ± 0.82 [9.46-11.5]	44.8 ± 26.0 [13.0-71.0]	2.26 ± 2.15 [0.71-6.58]	0.016 ± 0.013 [0.013-0.041]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
District 3								
13	Pedestrian	7.48 ± 0.38 [6.93-8.04]	8.49 ± 1.46 [6.50-10.4]	318 ± 145 [207-568]	48.1 ± 77.8 [8.20-205]	0.28 ± 0.20 [0.11-0.54]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
14	Pedestrian	7.25 ± 0.39 [6.83-7.86]	5.98 ± 3.28 [1.08-9.97]	286 ± 76.6 [200-410]	48.6 ± 55.8 [13.9-156]	0.57 ± 0.20 [0.32-0.84]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
15	Pedestrian	7.86 ± 0.68 [7.28-9.12]	5.96 ± 3.73 [0.82-10.2]	307 ± 150 [164-493]	15.3 ± 14.5 [4.12-41.8]	0.26 ± 0.15 [0.077-0.52]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
16	Conventional	7.62 ± 0.39 [7.12-8.12]	6.76 ± 3.20 [0.80-10.1]	243 ± 143 [77.0-452]	26.8 ± 21.4 [6.90-63.1]	0.37 ± 0.26 [0.030-0.77]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
17	Conventional	7.70 ± 0.40 [7.31-8.42]	6.15 ± 2.91 [1.20-9.02]	350 ± 172 [200-613]	43.1 ± 22.5 [19.0-77.0]	0.59 ± 0.32 [0.018-1.02]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
18	Conventional	7.22 ± 0.20 [6.90-7.38]	4.97 ± 2.66 [0.90-7.80]	348 ± 140 [227-603]	106 ± 156 [26.2-424]	0.81 ± 0.48 [0.19-1.49]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
19	Conventional	7.69 ± 0.38 [7.16-8.20]	5.62 ± 2.94 [0.90-9.25]	329 ± 140 [191-519]	39.2 ± 20.4 [20.5-76.4]	0.60 ± 0.32 [0.21-1.12]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]
20	Conventional	7.27 ± 0.59 [6.63-8.18]	3.51 ± 3.85 [0.54-9.55]	682 ± 565 [207-1682]	65.0 ± 40.3 [20.7-109]	0.81 ± 0.39 [0.27-1.29]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]

S3	Stormwater	7.19 ± 0.72 [6.58-8.34]	10.5 ± 1.13 [9.17-12.0]	69.7 ± 55.6 [14.0-155]	3.85 ± 2.25 [1.44-7.19]	0.13 ± 0.16 [0.0076-0.37]	1.17 ± 1.83 [0-4]	7.13 ± 5.76 [0.8-15.6]	

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Comprehensive HRMS-Screening of Persistent Mobile and Toxic compounds in first-flush urban stormwater

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COMPREHENSIVE HRMS-SCREENING FOR PERSISTENT, MOBILE, AND TOXIC COMPOUNDS IN FIRST FLUSH URBAN STORMWATER

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Water scarcity drives water-stressed regions to make use of all available resources. Consequently, urban stormwater is gaining recognition as a valuable resource, for instance, to replenish aquifers; thus, enhancing water supply. However, it carries contaminants that could limit its potential uses, highlighting those recently categorized as persistent, mobile, and toxic (PMT) compounds. In order to conduct broad screening for the presence of PMT compounds in stormwater first-flush samples and rainwater, two instruments based on Gas and Liquid Chromatography coupled to Quadrupole-Time-of-Flight Mass Spectrometry were used, and both suspect and target screening were performed. After prioritization 42 PMTs were detected, of which 24 PMTs were quantified. The results showed that 66% of the quantified PMTs were present in more than 50% of the samples, with average concentrations ranging from 2 ng·L^{-1} to 2.78 µg·L^{-1}. Of the target PMTs, 11 were quantified for the first time in runoff samples.

Introduction

Improving stormwater management is currently imperative in water-scarce regions, where rain is increasingly recognized as a potential water source1. Historically, stormwater quality has focused mostly on heavy metal, particle, and microbial contamination, ignoring the majority of urban micropollutants[1–3].

Nevertheless, a multitude of anthropogenic chemicals are used in our daily lives in cities; such as pharmaceuticals and personal care products, industrial products present in the city manufacturing, and supplies for daily use. For instance, in the United States, 215 organic substances were detected in stormwater samples, highlighting the presence of biocides, drugs, and polycyclic aromatic hydrocarbons (PAHs), with a total concentration of samples ranging from 4.37 to 263 µg·L^{-1} [4], whereas in Switzerland, up to 77 micropollutants were also detected, with total contaminant concentrations in the order of 10 µg·L^{-1} [5]. Rainwater is also polluted by organic contaminants, with concentrations of perfluoroalkyl substances (PFAS), organophosphate esters (OPEs), and PAHs up to 8.4 ng·L^{-1}, 94 ng·L^{-1} and 10 ng·L^{-1}, respectively[6]. Their presence in stormwater can be attributed to diverse sources such as atmospheric deposition, built surfaces, and anthropogenic activities; therefore, runoff is considered one of the main sources of diffuse pollution in surface and groundwater[4]. Runoff can reach the water bodies from various points, in many cases unnoticed, but it can account for a big proportion of water pollution in big cities[2,7].

Persistent, Mobile, and Toxic or very Persistent and very Mobile (PMT/vPvM) compounds are contaminants of special interest due to their impact on the environment. To prioritize new investigations on them, a criterion for classifying PMT/vPvM in the environment was recently published by the German Environmental Agency (UBA)[8]. According to UBA guidelines, a chemical compound would be considered persistent in water if its degradation half-life in marine water and fresh/estuarine water is higher than 60 and 40 days, respectively. It would be considered mobile if its logarithmic value of the organic carbon partition coefficient (log K_{OC}) is below 3 units, and very mobile if it is below 0 units. It would be considered toxic if: i) the long-term no observed effect concentration (NOEC) or the effective concentration (EC_{10}) for marine or freshwater organisms is less than 0.01 mg·L^{-1}; ii) the substance meets the criteria for classification as carcinogenic, germ cell mutagenic or toxic for reproduction; iii) there is other evidence of organ chronic toxicity; iv) there is other evidence of chronic toxicity for terrestrial organisms (e.g., birds); and v) the substance meets the criteria for classification as endocrine disruptor. In this context, the UBA created a list including 350 PMTs to be monitored (Supplementary Table 1))[9]. The

alarm for PMT/vPvM pollutants is equivalent to the alarm for Persistent, Bioaccumulative, and Toxic (PBTs) compounds since PMT compounds could accumulate in the aquatic ecosystem, and their long-term impact is unknown. Furthermore, once these contaminants are introduced into the water, their removal could be very difficult[10–12].

The list of PMT/vPvM is rather diverse, including plastic additives (flame-retardants, surface coatings, etc.)[13], vehicle-related chemicals (tyre wear particle leachate, corrosion inhibitor, etc.)[14], pharmaceuticals[15], pesticides[16], personal care products[17], short-chain PFASs[18], etc. Currently, less than 15% of the substances registered in the REACH (Registration, Evaluation, Authorization and Restriction of Chemicals, Reg. (EC) 1907/2006) as PMT/vPvM have been reported in stormwater, but there are probably many more pollutants in the stormwater[19]. Furthermore, suspect screening techniques using high-resolution mass spectrometers can identify PMT/vPvM compounds without the need for standards, thereby expanding the list of detectable substances[11,20,21].

The aim of this study was to thoroughly assess the presence of PMT/vPvM in urban stormwater. A comprehensive suspect screening was performed with the combination of two complementary chromatographic techniques (Gas and Liquid Chromatography (GC and LC)) and wide detection using Quadrupole-Time of Flight high-resolution mass spectrometer (QTOF-HRMS) to obtain a rapid overview of the unreported PMTs/vPvM in the stormwater samples. A prioritization step was applied to the 7707 features using the list of PMT substances published by the UBA in 2019[9]. Both libraries and in-silico fragmentation were applied to achieve a high level of confidence in the identification. Finally, several standards were used to quantify PMTs in runoff.

Results and discussion

LC/GC-QTOF-MS Suspect Screening

To address the current lack of information on PMT and vPvM compounds in runoff samples, a comparative HRMS study across different sample types was conducted. First, the two types of target water were compared (rainwater vs. runoff) (Fig. 1). The comparison between rainwater and runoff showed 280, 196, and 1156 features with significant differences in LC-ESI(-)-QTOF, LC-ESI(+)-QTOF, and GC-APCI-QTOF, respectively. Most of these features were detected in the runoff, which was expected to be considerably more polluted than the rainwater, since the runoff carries contamination from impervious surfaces (e.g., facades, roofs, side-walks, roads). Among the features, several PMT/vPvM compounds were tentatively annotated, such as Tolytriazole, Methylsalycylate, 1,3-diphenylguanidine or ε-caprolactam showing significant differences between the types of water.

Features were also compared between the three zones by volcano plot (Supplementary Figures 2, 3 and 4). It can be observed that there were significant differences ($p < 0.05$) among the study zones, but fewer than comparing the two types of water samples. As the

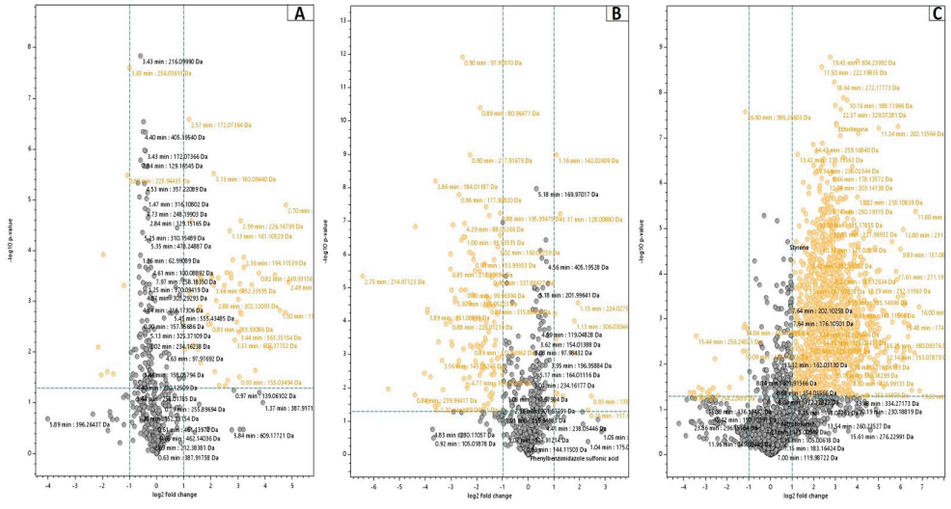


Fig 1. Vulcano plot of rainwater and runoff water. A: LC-ESI(-)-QTOF; B: LC-ESI(+)-QTOF and; C: GC-APCI-QTOF.

samples analyzed were obtained from a densely populated city, the stormwater was expected to be highly polluted. Given that neighborhoods vary in population density and vehicle traffic, differences in pollution levels across them were anticipated. Specifically, 183, 83, and 124 statistically different features were found between zones 1 and 2; 343, 165, and 119 statistically different features were found between zones 1 and 3; and 88, 52, and 30 statistically different features between zones 2 and 3; using LC-ESI(-)-QTOF, LC-ESI(+)-QTOF and GC-APCI-QTOF, respectively. The biggest differences were found between zone 1 and zone 3, and these differences could occur since zone 1 has a population density 7 times higher than zone 3. In this case, among the features that showed significant differences ($p<0.05$), only a few PMTs/vPvM could be tentatively annotated, such as 1,3-dyphenilguanidine, Methacrylamidopropyltrimethylammonium chloride, cyclohexane-1,2-di carboxylic anhydride, 2-2h-benzotriazol-2-yl-cresol, and 1,8-naphthylenediamine.

Given that the principal component analysis (PCA) showed significant differences and some of those features may be PMTs, a suspect list was applied considering the 350 pollutants included in the UBA list[9], in order to identify a higher number of these substances in our stormwater and rainfall water samples with a higher level of confidence. Following the workflow described in section 3.4 (Fig. 2), using LC-QTOF, a total of 2541 features were detected in positive ionization mode while 2626 features were detected in negative ionization mode. Regarding GC-QTOF, 2540 features were detected in APCI mode. Among them, 36 suspect compounds were detected at different confidence levels in LC-QTOF and 30 in GC-QTOF-MS. Most of them (around 50 features)

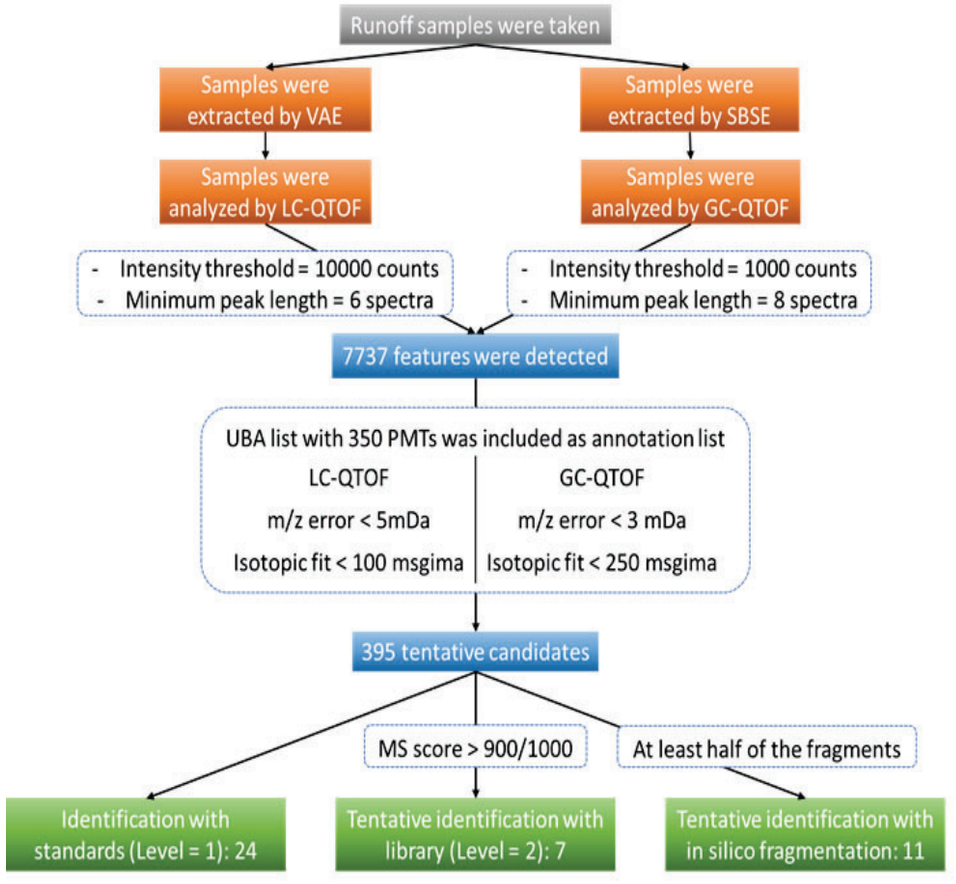
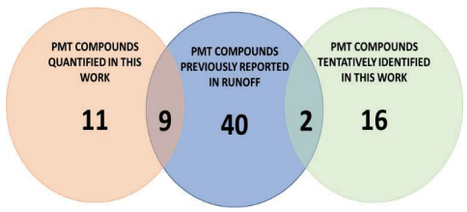


Fig 2. Workflow of the whole experimental procedure.

were determined with a confidence level of 4 or 5; however, 11 features were determined at level 3, since more than half of the fragments could be explained through in-silico fragmentation and/or they had a partial match with the library, and 7 could be explained with a level of confidence 2, since the comparison with the library had a high score. Finally, to further refine the results, 24 additional compounds were compared with the authentic standard (Level 1). In this case, the samples were injected in bbCID mode, which is considerably more sensitive than AutoMS/MS, allowing the detection of new PMTs/vPvM even at trace level. Results are shown in Table 1 and Fig. 3. The specific fragments used for level 2 and 3 determinations can be found in Table S8, along with the mass error for the molecular ion.

Fig. 3 shows the comparison of our PMT detections in stormwater to the detections reported in the body of literature. Compared to earlier studies, where PMT/vPvM compounds were identified through suspect screening in runoff, only one study was found[28]. Those authors determined 7 compounds related with melamine with a high level of confidence (exact mass and fragment ions agree with the literature). However, in that work the occurrence of some PMTs and their transformation products were not studied directly in non-runoff samples, but were rather studied in combined sewer overflow and wastewater treatment plants. Therefore, direct comparison was not possible. Regarding target analysis, 9 PMTs were previously detected and in this work, they are discussed in the next section.



Level 1 PMTs in Stormwater and Rainwater

All target compounds (Level 1) (n = 24) were quantified in urban stormwater in at least one sample (Table 2). Although atrazine was not included in our target list, its transformation products (TPs) (atrazine-desethyl and atrazine-desisopropyl) were quantified on 3 occasions. Similarly, benzophenone, categorized as PMT, was measured on several occasions as benzophenone-3 and benzophenone-10. Among target analytes, 67% of them were quantified in half of the samples (42% of target compounds were measured in all the samples). Compounds quantified with a frequency detection < 25% were not considered for further discussion.

Concerning the average concentrations measured, the flame-retardant tris(2-butoxyethyl) phosphate (2.48 µg·L-1), and the compounds related to plastic and tires such as 1,3-diphenylguanidine (1.13 µg·L-1), ε-caprolactam (2.78 µg·L-1) and p-Toluenesulfonamide (821 ng·L-1), showed the highest concentrations. On the other hand, compounds with the lowest measured average concentration were the PAHs acenaphthene and anthracene (7 and 2 ng·L-1, respectively), benzophenone-10 (UV-filter) (24 ng·L-1), tonalide (fragrance) (7 ng·L-1), and triclosan (an antibacterial agent) (10 ng·L-1). Finally, some compounds were measured on few occasions (1-cyanoguanidine, atrazine-desethyl, atrazine-desisopropyl, diuron, methenamine, triethyl phosphate, and trifluoromethanesulfonic acid).

The PMT compounds were then studied by zone, with the aim of seeking significant differences between the measured concentrations. Some highly detected compounds such as acenaphthene and naphthalene, both PAHs, were highlighted due to their low variation in their concentration among all the zones (25% and 16%, respectively), suggesting ubiquitous contamination, probably from atmospheric fallout30. One of the sources of PAHs is combustion, and the City of Barcelona has a high density of vehicles, so the uniform distribution of this pollutant is evident. In the same way, 1,3-di-o-tolylguanidine, a tire-related compound, which was only detected in Zone 1, had a variation in its concentration lower than 25% between the sampling points; and this zone has the highest average daily traffic. For the other compounds that were detected with a frequency greater than 50%, the Kruskal-Wallis test was performed. It was found that only 2 compounds showed statistical differences between the zones, demonstrating constant background contamination between the study zones. The compounds that showed significant differences among the zones were 1,3-diphenylguanidine, a compound used in several fields such as the rubber industry and analytical chemistry, and the flame-retardant tris(2-butoxyethyl) phosphate. According to the Kruskal-Wallis test, 1,3-diphenylguanidine showed significant differences (p-value = 0.022), specifically between zone 1 and zone 3. The same results were observed for the flame retardant, which also showed significant differences (p-value = 0.002) between zones 1 and 3. These differences are in zones. Since the compounds detected are mainly those related to industrial activities or manufactured products, it makes sense that their concentration is higher in the more populated zone.

Table 1. Suspect and target identification of PMT compounds.

COMPOUND	FORMULA	EXACT MASS	mSigma	METFRAG	LIBRARY	RT (min)	LEVEL
1,2,3,4-tetrahydronaphthalene	$C_{10}H_{12}$	132.0939	4.67	2/2			3*
2,4-dinitrophenol	$C_6H_4N_2O_5$	184.012	7.16	4/8			3
2-morpholinoethanol	$C_6H_{13}NO_2$	131.0946	-	3/3			3
2-nitrophenol	$C_6H_5NO_3$	139.0269	1.3	2/4			3
2-nitrotoluene	$C_7H_7NO_2$	137.0476	4.63	3/6			3
4-vinylcyclohexene	C_8H_{12}	108.09392	-	5/7			3
Bis(2-methoxyethyl) ether (Diglyme)	$C_6H_{14}O_3$	134.0942	5.12	1/1			3
Bornan-2-one (Camphor)	$C_{10}H_{16}O$	152.1201	-	1/1			3
Ethylbenzene	C_8H_{10}	106.0783	-	3/4			3
Dimethyl phthalate	$C_{10}H_{10}O_4$	194.05604	8.35	9/17			3
N-butylbenzenesulphonamide	$C_{10}H_{15}NO_2S$	213.0823	26.53	3/3			3
4-hydroxy-2,2,6,6-tetramethylpiperidine-1-ethanol	$C_{11}H_{23}NO_2$	201.1728	6.92		993.75		2**
Benzophenone	$C_{13}H_{10}O$	182.0734	18.32		938.08		2
Dibutyl phthalate	$C_{16}H_{22}O_4$	278.15226	13.3		969.27		2
Diethyl phthalate	$C_{12}H_{14}O_4$	222.0892	12.19		996.6		2
Melamine	$C_3H_6N_6$	126.0653	-		977.27		2
Salicylic acid	$C_7H_6O_3$	138.0316	5.01		993.82		2
Toluene-4-sulphonic acid	$C_7H_8O_3S$	190.0299	-		993.8		2
1-Cyanoguanidine	$C_2H_4N_4$					1.1	1
1,3-di-o-tolylguanidine	$C_{15}H_{17}N_3$					3.35	1
1,3-diphenylguanidine	$C_{13}H_{13}N_3$					3.1	1
Acenaphthene	$C_{12}H_{10}$					9.95	1
Anthracene	$C_{14}H_{10}$					13.75	1
Atrazine-desethyl	$C_6H_{10}ClN_5$					3.65	1
Atrazine-desisopropyl	$C_5H_8ClN_5$					3.2	1
Benzophenone-10	$C_{15}H_{14}O_3$					18.74	1
Benzophenone-3	**$C_{14}H_{12}O_3$**					**16.77**	**1**
Bisphenol S	$C_{12}H_{10}O_4S$					3.34	1
Butyl benzyl Phthalate	$C_{19}H_{20}O_4$					21.42	1
Di-n-butyl phosphate	$C_8H_{19}O_4P$					3.88	1
Diuron	$C_9H_{10}Cl_2N_2O$					4.45	1
e-Caprolactam	$C_6H_{11}NO$					2.83	1
Methenamine	$C_6H_{12}N_4$					1.1	1
Naphthalene	$C_{10}H_8$					7.98	1
p-Toluenesulfonamide	$C_7H_9NO_2S$					3.15	1
Tonalide	$C_{18}H_{26}O$					14	1
Tri-(2-Chloroisopropyl) Phosphate	$C_9H_{18}Cl_3O_4P$					13.35	1
Triclosan	$C_{12}H_7Cl_3O_2$					17.85	1
Triethyl phosphate	$C_6H_{15}O_4P$					3.8	1
Trifluoromethanesulfonic acid	CHF_3O_3S					1.6	1
Tri-n-butyl phosphate	$C_{12}H_{27}O_4P$					11.36	1
Tris(2-butoxyethyl) phosphate	$C_{18}H_{39}O_7P$					22.1	1

Table 2. Average, 10% percentile (P10), and 90% percentile (P90) of PMT/vPvM target compounds and their frequency of detection.

Compound	P10 (ng·L^{-1})	Average (ng·L^{-1})	P90 (ng·L^{-1})	Freq. (%)
1,3-Di-o-tolylguanidine	109	143	175	25
1,3-diphenylguanidine	174	$1.33 \cdot 10^3$	$2.50 \cdot 10^3$	100
1-Cyanoguanidine	495	495	495	5
Acenaphthene	5	7	9	100
Anthracene	1	2	3	55
Atrazine-desethyl	190	230	270	10
Atrazine-desisopropyl	195	195	195	5
Benzophenone 3	36	74	107	100
Benzophenone-10	4	24	26	100
Bisphenol S	33	161	302	75
Butyl benzyl Phthalate	34	106	219	100
Di-n-butyl phosphate	171	712	1187	65
Diuron	30	99	173	20
e-caprolactam	$1.09 \cdot 10^3$	$2.78 \cdot 10^3$	$3.77 \cdot 10^3$	100
Methenamine	33	46	59	20
Naphthalene	225	272	314	95
p-Toluenesulfonamide	135	821	1410	55
Tris(2-butoxyethyl) phosphate	271	$2.48 \cdot 10^3$	$7.07 \cdot 10^3$	100
Tonalide	2	7	11	100
Tri-(2-Chloroisopropyl) Phosphate	697	$1.99 \cdot 10^3$	$3.95 \cdot 10^3$	100
Triclosan	4	10	18	90
Triethyl phosphate	118	135	152	20
Trifluoromethanesulfonic acid	75	75	75	5
Tri-n-butyl phosphate	29	54	91	100

A On the other hand, samples were taken not only in runoff but also in one roof of each zone, in order to assess the pollutants carried by rainwater from the atmosphere and the surfaces. Some compounds such us benzophenone-3, benzophenone-10, butyl benzyl phthalate, and triclosan were measured with a double concentration in rainwater samples rather than in runoff samples, suggesting that these volatile compounds are washed away by rainwater from atmospheric precipitation. On the contrary, several compounds such as 1,3-diphenylguanidine, ε-caprolactam, tris(2-butoxyethyl) phosphate, tri-(2-Chloroisopropyl) phosphate, and tri-n-butyl phosphate were measured in runoff samples with a concentration at least four times higher than in roof samples. Nevertheless, further sampling campaigns must be performed in order to confirm the results obtained in this work, since no significant differences were observed among the types of samples, which could be due to the low number of rainwater samples taken. On the other hand, atmospheric contamination can be affected by air currents and become homogenous, since the distance between points is not so far as to see differences.

Expanding The comparison with other works has been challenging since works that studied contaminants of emerging concern in urban stormwater are still scarce[19], and only a few of them introduced PMT compounds among the contaminants to be analyzed. Furthermore, in the present work the stormwater first-flush samples were analyzed, which would be the most contaminated and therefore representing a worst-case scenario.

Previous works measured some PMT compounds such as anthracene, a PAH, at a concentration of 29 ng·L^{-1} [5], ten times higher than the reported concentration in our study.

Atrazine, a widely used herbicide, was also measured in urban stormwater at different concentrations: 8729 and 40 ng·L^{-1} [3]. In this work, atrazine was not found, but their TPs were measured, atrazine-desethyl (230 ng·L^{-1}) and atrazine-desisopropyl (195 ng·L^{-1}), at a higher mean concentration than obtained previously (14 and 13 ng·L^{-1}, respectively), although close to the maximum concentration measured previously (177 and 144 ng·L^{-1}, respectively)[29]. Sometimes TPs are found in higher concentrations than the original compound, which is why it is worth including them in lists. Another herbicide, diuron, was measured in several samples of urban stormwater. Mean concentrations spanned from 7.729 to 76 ng·L^{-1} [5], and a maximum concentration of 600 ng·L^{-1} was measured. In our work, the mean concentration of diuron was a little higher (99 ng·L^{-1}), although the maximum measured concentration was lower (205 ng·L^{-1}) than in previous works[5,29].

Benzophenone, also categorized as a PMT compound9, was measured previously in urban stormwater, with a mean concentration of 86 ng·L^{-1} [29]. In the present work, benzophenone-3 and benzophenone-10 were widely detected at mean concentrations of 74 and 24 ng·L^{-1}, respectively. Flame-retardants were the most frequently detected compounds and at the highest concentration, although with great variations regarding their concentrations noted in the literature. Tris(2-butoxyethyl) phosphate was measured ranging from lower than the limit of quantification up to 275 µg·L^{-1} [29], from 55 ng·L^{-1} to 5.93 µg·L^{-1} [3], and from 1.5 up to 40 µg·L^{-1} [5]. Here, this compound ranged from 43 to 9.59 µg·L^{-1}. Similarly, tri-(2-chloroisopropyl) phosphate ranged from 275 to 2.07 µg·L^{-1} [29] and tri-n-butyl phosphate ranged from 56 to 299 ng·L^{-1} [3]. Our results followed the previous measurement, noted above, with a range of concentration for tri-n-butyl phosphate from 10 to 141 ng·L^{-1} and for tris(2-chloroethyl) phosphate from 127 to 448 ng·L^{-1}. Variations in concentration may be due to the sampling procedure, the actual spot selected, the place, the dilution that could be obtained due to rain, differences in habits in the use of the above-mentioned compounds, etc. Therefore, more analysis of runoff water should be conducted in future studies.

Finally, a recently published review focused on PMT compounds in stormwater has established that 542 CECs have been measured in less than 100 papers published in the last 30 years[19]. Among the CECs detected, those authors of that review stated that only 49 of the papers could be considered as PMT, probably because none of the previous works were focused exclusively on the study of PMT compounds in runoff water. Therefore, contrary to all previous papers that analyze CECs in runoff, we have focused exclusively on PMT substances, adding 11 new quantified PMT compounds to the total PMT compounds measured in runoff (Fig. 3).

For an adequate management of urban stormwater, it is important to monitor priority substances that pose a human and environmental risk such as PMT/vPvM. To the best of our knowledge, the present work is the first to focus exclusively on the study of the presence of PMT/vPvM in FF runoff water. For that purpose, comprehensive identification of PMT/vPvM compounds was performed by the combination of target and suspect screening using LC/GC-MS high-resolution mass spectrometry. The 7707 detected features were filtered, prioritizing 42 compounds using the list of the UBA for PMTs. Then, up to 24 PMTs were quantified in the urban samples, 11 of them for the first time. Concentrations ranged from 1 ng·L^{-1} to 13.9 µg·L^{-1}, showing a great variety in the concentration depending on the compound. However, few differences were found between the zones studied. In general, the compounds that were prominent in runoff water could be considered of industrial origin, which could be found in a multitude of manufactured objects present and used in cities (flame retardants, plasticizers, herbicides, etc.). By comparing the concentrations of PMT/vPvM compounds measured in rainwater and runoff samples, it was observed that more volatile PMTs were found in higher concentrations in the rainwater than in the runoff samples. PMT compounds were probably deposited on the surfaces of the city and were then washed away when it rained. The results obtained in the present work could serve to encourage further research into the PMTs found and include them, if necessary, in future lists or legislation, and/or for better management of water resources, since a source of contamination was identified for many pollutants that had not been taken into account until now. In addition, the group of CECs including PMTs should be monitored, and unknown compounds from CECs should be identified through suspect-nontarget screening as well as new threats that may arise in the future.

Methods

Materials and reagents

Methanol, acetonitrile, dimethyl sulfoxide, ethyl acetate and high-performance liquid chromatography (HPLC) grade pure water were purchased from J.T. Backer (Deventer, The Netherlands). Formic acid, ammonium acetate and ammonium formate were purchased from Sigma-Aldrich. Analytical standards (> 98 %) and isotopically labelled compounds were purchased from Cymit (Barcelona, Spain). Compounds purchased as powder were dissolved at a concentration of

1000 mg·L^{-1} and stored at -20 ºC (Supplementary Table 2). A working solution was prepared by mixing all the analytes at a concentration of 10 mg·L^{-1} in methanol. Commercial polydimethylsiloxane (PDMS) stir bars were purchased from Gerstel (Mülheim an der Ruhr, Germany) (size 10 mm x 0.5 mm, i.e., length x film thickness).

Sampling

Urban stormwater samples were all collected in the City of Barcelona (Spain, EU), which is located in the north-eastern part of the Iberian Peninsula (coordinates; 41∘23′19.64″ N, 2∘9′32.36″ E). As urban stormwater runoff is the main target type of water selected for this study, a rainy period (spring 2022)[22] was chosen to obtain the sample, as well as a significant precipitation event (>1 mm) to be able to collect enough sample volume (1 L). Three different Barcelona zones of study (i.e., Districts: Eixample, zone #1, Sant Martí, zone #2, and Sant Andreu, zone #3) were chosen for this study, all of them with high-density populations and representative of urban catchments (Supplementary Figure 1). The selected areas were mainly differentiated by average daily traffic, population, and population density. Detailed information on the selected areas is shown in Table 3. Up to 23 different sites within the 3 zones were selected, taking into consideration vehicle traffic density, including conventional streets with vehicular traffic (i.e., vehicle-impacted roads) and pedestrian streets (vehicle-free zones). The stormwater collection was conducted using a FF self-lock system attached to glass containers at storm drain inlets, always in streets with similar morphology (15-20-m width, <1-degree slopes, 20-m distance between storm drain inlets). There were also a few samples collected on roofs to account for atmospheric wet deposition (rainwater) (i.e., one in each of the three zones studied). FF samplers were placed in the collection sites prior to the rain episode. Once the rain event ended, samples were collected and transported to the laboratory, and kept on ice in coolers. water.

Table 3. Average daily traffic of sampling zones, population, and population per square hectometer (hm^2, population density)[23].

Zone	Average daily traffic (vehicles · day^{-1})	Population	Population density (pop · hm^{-2})
Zone #1	600 – 12200	38053	473
Zone #2	100 – 6900	20949	193
Zone #3	100 – 2500	13582	73

Sample Pre-treatment

Once in the laboratory, samples were aliquoted in 500 mL PET bottles, vacuum filtered through metal meshes (25 and 1 µm) and GF/F filters (Whatman, 0.7 µm), and stored at -20 ºC in the dark until the sample preconcentration.

Before the LC-QTOF-MS analysis, samples were pre-concentrated using vacuum-assisted extraction (VAE). To do this, 10 mL of filtered sample was introduced into the evaporation tubes and reduced to a volume of 0.3 mL in 73 minutes using a VAE system (BÜCHITM SyncorePlus, Switzerland). The system includes a water bath to homogenize the heat, and the temperature was set to 55 °C and was constant throughout the whole process, as was the agitation, established at 250 rpm. Once the evaporation was completed, 0.3 mL of water remained at the bottom of the flask due to the cold system integrated into the instrument[24]. Then, the remaining sample was transferred to an LC vial where 0.2 mL of HPLC water was added to reach the final volume of 0.5 mL, pre-concentrating the sample 20 times. After extraction, samples were fortified with a mix of internal standards (I.S.) to a concentration of 50 µg·L^{-1} and centrifuged at 4000 rpm for 5 minutes[25].

Before the GC-QTOF-MS analysis, the aqueous samples (20 mL) were extracted by stir bar sportive extraction (SBSE), followed by liquid desorption in ethyl acetate (120 µL), and sonication for 30 minutes.

MS Analysis and Data treatment

VAE extracts were injected on an Impact II Quadrupole-Time-of-Flight Mass Spectrometry system (q-ToF-MS) with an electrospray ionization source (ESI) and coupled to an Elute UPLC module with autosampler, all from Bruker (Bruker Daltonik GmbH, Germany). Samples were analyzed in positive and negative ionization modes using an ACQUITY Premier HSS T3 1.8µm (2.1 x 100mm) column from Waters (Milford, MA, USA) at 0.4 mL·min^{-1}. The mobile phase in positive ionization mode was A = H2O:MeOH (99% - 1%, v/v) and B = MeOH, both containing 5 mM ammonium formate and 0.01% formic acid. In negative ionization mode, solvents were the same but containing 5 mM ammonium acetate. The chromatographic gradient used in both cases was the same; for details, please refer to Supplementary Table 3. Procedure blanks were also analyzed to establish a noise threshold and eliminate

interference. The parameters applied in the QTOF-MS are shown in Supplementary Table 4. For the suspect analysis, the "AutoMS/MS" scan mode was used, while for the targeted analysis the "broadband collision-induced dissociation" (bbCID) scan mode was used. In AutoMS/MS, an intensity threshold of 10000 counts and a minimum peak length of 6 spectra were established, to have sufficiently intense signals that would allow us to confirm non-target compounds with confidence. A score for m/z ranging from 2 – 5 mDa, and for mSigma ranging from 50 – 100 were established. The first annotation was performed with the UBA PMTs List (Supplementary Table 1)[9]. For those compounds annotated with these settings, the NIST library with the same tolerance that was used before but adding a new score range for the MS/MS was used, so a feature should have a score higher than 900/1000 to achieve a probable structure according to level 2 of the scale in the work of Schymanski et al., 2014[26]. Then, an in-silico fragmentation using MetFrag was performed, comparing the spectra obtained with the calculated spectra using the algorithm. For a correct identification as tentative candidate of level 3 of the Schymanski scale, at least half of the spectrum fragments would have to be justified. Finally, quantification of 13 target compounds was performed using a calibration curve in HPLC grade water from 0.1 to 100 µg·L^{-1} (Level 1). A retention time window of 0.1 minutes was set, and a major fragment was used as a confirmation ion. Procedure blanks consisting of sampling bottles filled with Milli-Q water and given the same sample treatment were used to eliminate interference and noise.

SBSE extracts were injected on an Impact II Bruker Daltonics equipped with Gas Chromatography-Atmospheric Pressure Chemical Ionization q-TOF-MS (GC-APCI-q-ToF-MS). Detailed GC parameters can be found in Pintado-Herrera et al., 2014[27], and the parameters applied in the source are outlined in Supplementary Table 6. A mass calibration was conducted in each chromatographic run using a polysiloxanes mass reference list (column bleed). Data were collected between 7 and 34 min. The suspect screening workflow proceeded as follows: first, the peak extraction was performed with a minimum intensity threshold of 1000 counts, and a peak length of 8 spectra for bbCID analysis. [M]+ and [M+H]+ ions were grouped into the same feature. Blank correction involved the use of three blanks treated identically to the aqueous samples, with a selected ratio of 4 (max signal in the sample/max signal in the blank). Then, the following limits for the features identified in the Suspect List Exchange were used: ± 3 mDa for mass accuracy and isotopic fit < 250 (expressed as mSigma). The degree of confidence in the compound identification in both approaches was taken from Schymanski et al., 2014[26]. For target analysis (Level 1), calibration curves were constructed by preparing different concentrations of the target analytes in HPLC water (from 0.01 to 20 µg·L^{-1}), and the extraction and desorption were carried out in the same way as for the samples. The threshold for quantitative analysis were: 5 mDa for mass accuracy, 0.1 min for retention time tolerance, 100 for isotopic fit (mSigma) and 2 qualifier ions. Figure 2 shows the workflow followed.

Suspect analysis was performed using Metaboscape 2023b software and target analysis was performed using TASQ 2023b software, both from Bruker. First, a suspect list (Supplementary Table 1) was used to identify tentative PMTs. Then, the NIST library was used to compare the mass spectra obtained with those of the library. Finally, 24 PMTs were compared with their standard and quantified (Level 1).

To eliminate features that could be interferences, a water blank was injected as the first sample, and every six samples. Quality control was injected throughout the sequence at the midpoint of the calibration curve. Background contamination was assessed by injecting procedural blanks into each batch (concentration values found were subtracted from the concentrations measured in the samples). The calibration curve was injected at the beginning, and the end of each batch to evaluate the repeatability of the method (i.e., RSD values lower than 18 % were obtained for the detected compounds). Linearity was evaluated when the linear fitting achieving determination coefficients (R^2) exceeded 0.9 (Supplementary Tables 5 and 7).

For further analytical details and method performance, please refer to Supporting Information. Briefly, in the LC-QTOF, Method Quantification Limit (MQL) was calculated as half of the lowest point of the calibration curve divided by the enrichment factor (20). To deal with possible matrix effects, samples were spiked with I.S. Recovery was calculated as the ratio of a Milli-Q water sample spiked before and after extraction. Recovery values ranged from 81 – 113% and MQL ranged from 2 – 26 ng·L^{-1} for all target compounds, which were considered valid for the purpose of the work (Supplementary Table 5). In GC-QTOF samples and calibration curves were spiked before the extraction with a mix of I.S. to a concentration of 0.5 µg·L^{-1}.

Matrix interference, expressed as the ratio between the I.S. concentration in the spiked matrix and the I.S. spiked concentration in the standard (%) ranged from 60 % to 129 % depending on the sample and the I.S. MQL ranged from 1 – 32 ng·L^{-1} for all target compounds. For analytical details and method performance, please refer to Supplementary Table 7.

Statistical analysis was performed using Metaboscape and Statgraphics 19. In order to analyze the data to find statistical differences between the sampling zones and type of water, volcano plots were performed with p-values lower than 0.05. For a more in-depth comparison of the quantified PMTs, a Shapiro-Wilk test was performed to check if the results followed a normal distribution. As they did not have a normal distribution, a non-parametric Kruskal-Wallis test was performed to test the null hypothesis that the medians within each of the three zones were the same. A significant difference was established if a p-value lower than 0.05 was obtained.

CRediT authorship contribution statement

S.S.V writing original draft, investigation, data treatment, reviewing and editing; **F.L.** writing original draft**; M.P.H.** writing original draft, data treatment, reviewing; **N.M.** supervision, reviewing**; M.T.** reviewing; **P.L.M.** supervision, reviewing, conceptualization, funding acquisition; **S.P.** supervision, reviewing, conceptualization, project administration, funding acquisition. All authors have read and agreed to the published version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability Statement

Not applicable.

Code availability Statement

Not applicable.

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PUBLICACIÓ CIENTÍFICA #5

SUPPLEMENTARY INFORMATION

Comprehensive HRMS-Screening of Persistent Mobile and Toxic compounds in first-flush urban stormwater

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Submitted to NPJ Clean Water

SUPPLEMENTARY MATERIAL

Supplementary Table 1. PMTs list used for suspect analysis [9]

Compound	CAS	Formula
(2E)-N,6,6-trimethyl-N-(1-naphthylme-thyl)hept-2-en-4-yn-1-amine	91161-71-6	C21H25N
(2S)-3-methyl-2-(N-{[2'-(1H-1,2,3,4-tetrazol-5-yl)-[1,1-bi-phenyl]-4-yl]methyl}pentanamido)butanoic acid	137862-53-4	C24H29N5O3
[[(phosphonomethyl)imino]bis[(ethylenenitrilo)bis(methylene)]]tetrakisphosphonic acid, sodium salt	22042-96-2	C9H27N3NaO15P5
[[(phosphonome-thyl)imino]bis[hexa-methylenenitrilo-bis(methylene)]]tetrakisphosphonic acid	34690-00-1	C17H44N3O15P5
1-(5,6,7,8-tetrahydro-3,5,5,6,8,8-hexamethyl-2-naphthyl)ethan-1-one	1506-02-1	C18H26O
1-(m-chlorophenyl)piperazine	6640-24-0	C10H13ClN2
1,1'-(methylenedi-p-phenylene)bismaleimide	13676-54-5	C21H14N2O4
1,1,1,3,3,3-hexafluoropropan-2-ol	920-66-1	C3H2F6O
1,1,1-trichloroethane	71-55-6	C2H3Cl3
1,1,2-trichloroethane	79-00-5	C2H3Cl3
1,1-dichloroethylene	75-35-4	C2H2Cl2
1,2,3,4-tetrahydronaphthalene	119-64-2	C10H12
1,2,3-trichlorobenzene	87-61-6	C6H3Cl3
1,2,3-trichloropropane	96-18-4	C3H5Cl3
1,2,4-triazole	288-88-0	C2H3N3
1,2,4-trichlorobenzene	120-82-1	C6H3Cl3
1,2,4-trimethylbenzene	95-63-6	C9H12
1,2-benzisothiazol-3(2H)-one 1,1-dioxide	81-07-2	C7H5NO3S
1,2-benzisothiazol-3(2H)-one 1,1-dioxide, sodium salt	128-44-9	C7H4NNaO3S
1,2-dibromo-3-chloropropane	96-12-8	C3H5Br2Cl
1,2-dibromoethane	106-93-4	C2H4Br2
1,2-dichlorobenzene	95-50-1	C6H4Cl2
1,2-dichloroethane	107-06-2	C2H4Cl2
1,2-dichloropropane	78-87-5	C3H6Cl2
1,3,4,6,7,8-hexahy-dro-4,6,6,7,8,8-hexa-methylindeno[5,6-c]pyran (Galaxolide)	1222-05-5	C18H26O
1,3,5-triazine-2,4,6(1H,3H,5H)-trione, compound with 1,3,5-triazine-2,4,6-triamine (1:1)	37640-57-6	C6H9N9O3
1,3,5-triazine-2,4,6-triamine phosphate	41583-09-9	C3H9N6O4P
1,3-dichloro-4-nitrobenzene	611-06-3	C6H3Cl2NO2
1,3-dichlorobenzene	541-73-1	C6H4Cl2
1,3-diethyldiphenylurea	85-98-3	C17H20N2O
1,3-dihydro-4(or 5)-methyl-2H-benzimid-azole-2-thione	53988-10-6	C8H8N2S
1,3-dimethylimidazolidin-2-one	80-73-9	C5H10N2O
1,3-Di-o-tolylguanidine	97-39-2	C15H17N3
1,3-diphenyl-2-thiourea	102-08-9	C13H12N2S
1,3-diphenylguanidine	102-06-7	C13H13N3
1,4,5,6,7,7-hexa-chloro-8,9,10-trinor-born-5-ene-2,3-dicar-boxylic anhydride	115-27-5	C9H2Cl6O3
1,4-dichlorobenzene	106-46-7	C6H4Cl2
1,4-dioxane	123-91-1	C4H8O2
1,5-naphthylenediamine	2243-62-1	C10H10N2
1,6-Bis[2,2-dimethyl-3-(N-morpholino)-propylideneamino]-hexane	1217271-49-2	C24H46N4O2
1,8-diazabicyclo[5.4.0]undec-7-ene	6674-22-2	C9H16N2
1,8-naphthylenediamine	479-27-6	C10H10N2
1-[(2,4-dinitrophenyl)azo]-2-naphthol	3468-63-1	C16H10N4O5
1-[2-(dimethylamino)-1-(4-methoxy-phenyl)ethyl]cyclo-hexanol	93413-69-5	C17H27NO2
1-bromo-3-chloropropane	109-70-6	C3H6BrCl
1-chloro-2,4-dinitro-benzene	97-00-7	C6H3ClN2O4
1-chloro-2-nitroben-zene	88-73-3	C6H4ClNO2
1-chloro-4-nitroben-zene	100-00-5	C6H4ClNO2
1-Cyanoguanidine	461-58-5	C2H4N4
1-methylpiperazine	109-01-3	C5H12N2
1-nitroguanidine	556-88-7	CH4N4O2
2-(1,3-dihydro-3-oxo-2H-indol-2-ylidene)-1,2-dihydro-3H-indol-3-one	482-89-3	C16H10N2O2
2-(2H-benzotriazol-2-yl)-p-cresol	2440-22-4	C13H11N3O
2,2,3,3,5,5,6,6-oc-tafluoro-4-(trifluoro-methyl)morpholine	382-28-5	C5F11NO
2,2,6,6-tetramethyl-4-piperidone	826-36-8	C9H17NO
2,2'-[(2,2',5,5'-tetra-chloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]	22094-93-5	C36H32Cl4N6O4
2,2'-[(3,3'-di-chloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxo-butyramide]	5468-75-7	C34H30Cl2N6O4
2,2'-[(3,3'-di-chloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(4-chloro-2,5-dimethoxyphenyl)-3-oxobutyramide]	5567-15-7	C36H32Cl4N6O8
2,2'-[(3,3'-di-chloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(4-methylphenyl)-3-oxo-butyramide]	6358-37-8	C34H30Cl2N6O4
2,2'-azobis[2-methyl-butyronitrile]	13472-08-7	C10H16N4
2,2'-dimethyl-2,2'-azodipropiononitrile	78-67-1	C8H12N4
2,2'-dimethyl-4,4'-methylenebis(cyclo-hexylamine)	6864-37-5	C15H30N2
2,3-Dimethylbenzenesulfonic acid (Xylenesulphonic acid)	25241-16-1	C8H10O3S
2,4,6,8-tetramethyl-2,4,6,8-tetravinylcyclotetrasiloxane	2554-06-5	C12H24O4Si4
2,4,6-tribromophenol	118-79-6	C6H3Br3O
2,4,7,9-tetramethyl-dec-5-yne-4,7-diol	126-86-3	C14H26O2
2,4-dichlorophenol	120-83-2	C6H4Cl2O
2,4-dinitrophenol	51-28-5	C6H4N2O5

2,4-di-tert-butylphenol	96-76-4	C14H22O
2,5-bis-isocyanatomethylbicyclo[2.2.1]heptane	74091-64-8	C9H10N2O2-2
2,6-di-tert-butyl-p-cresol	128-37-0	C15H24O
2,6-xylidine	87-62-7	C8H11N
2-[(2-[2-(dimethylamino)ethoxy]ethyl)methylamino]ethanol	83016-70-0	C9H22N2O2
2-acrylamido-2-methylpropanesulphonic acid	15214-89-8	C7H13NO4S
2-amino-4,5-dichloro-benzenesulfonic acid	6331-96-0	C6H5Cl2NO3S
2-amino-5-methylthiazole	7305-71-7	C4H6N2S
2-chloro-4-nitrotoluene	121-86-8	C7H6ClNO2
2-chloroethanol	107-07-3	C2H5ClO
2-chloropyridine	109-09-1	C5H4ClN
2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid	139481-59-7	C24H20N6O3
2-ethoxy-2-methylpropane	637-92-3	C6H14O
2-fluoro-6-trifluoro-methylpyridine	94239-04-0	C6H3F4N
2-methoxy-2-methylbutane	994-05-8	C6H14O
2-methyl-1-(4-methyl-thiophenyl)-2-morpholinopropan-1-one	71868-10-5	C15H21NO2S
2-morpholinoethanol	622-40-2	C6H13NO2
2-nitrophenol	88-75-5	C6H5NO3
2-nitropropane	79-46-9	C3H7NO2
2-nitrotoluene	88-72-2	C7H7NO2
2-phosphonobutane-1,2,4-tricarboxylic acid	37971-36-1	C7H11O9P
2-piperazin-1-ylethylamine (PEA)	140-31-8	C6H15N3
2R,3R,4R,5R,8R,10R,11R,13S,14R)-11-[(2S,3R,4S,6R)-4-dimethylamino-3-hydroxy-6-methyloxan-2-yl]oxy-2-ethyl-3,4,10-trihydroxy-13-[(2S,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyl-oxan-2-yl]oxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-aza-cyclopentadecan-15-one	83905-01-5	C38H72N2O12
3-(4-Methyl-1H-imidazol-1-yl)-5-(trifluoro-methyl)aniline	641571-11-1	C11H10F3N3
3,3'-sulphonyldianiline	599-61-1	C12H12N2O2S
3,4-diaminobenzene-sulphonic acid	7474-78-4	C6H8N2O3S
3,5-diacetamido-2,4,6-triiodobenzoic acid	117-96-4	C11H9I3N2O4
3a,4,7,7a-tetrahydro-4,7-methanoindene	77-73-6	C10H12
3-aminobenzenesulphonic acid	121-47-1	C6H7NO3S
3-chloroaniline	108-42-9	C6H6ClN
4-(1,1,3,3-tetra-methylbutyl)phenol	140-66-9	C14H22O
4-(1-Phenylethyl)-benzene-1,3-diol	85-27-8	C14H14O2
4-(2-hydroxyethyl)pi-perazin-1-ylethanesulphonic acid	7365-45-9	C8H18N2O4S
4-(Hydroxy-1-methyethyl)-2-propyl-1-□□†○-[1H-tetrazol-5-yl]-ϭϭ○-biphenyl-4-yl]methyl]-1H-imidazole-5-carboxylic acid	144689-24-7	C24H26N6O3
4,4',4''-(ethan-1,1,1-triyl)triphenol	27955-94-8	C20H18O3

4,4'-bis(dimethylamino)-4''-(methylamino)trityl alcohol	561-41-1	C24H29N3O
4,4'-bis[4-[bis(2-hydroxyethyl)amino]-6-anilino-1,3,5-triazin-2-yl]amino]stilbene-2,2'-disulphonic acid	4404-43-7	C40H44N12O10S2
4,4'-diaminostilbene-2,2'-disulphonic acid	81-11-8	C14H14N2O6S2
4,4'-isopropylidenedi-phenol	80-05-7	C15H16O2
4,4'-Isopropylidenediphenol, oligomeric reaction products with 1-chloro-2,3-epoxy-propane	25068-38-6	C18H21ClO3
4,4'-methylenebis(cyclohexylamine)	1761-71-3	C13H26N2
4,4'-methylenebis(N-sec-butylcyclohexamine)	154279-60-4	C21H42N2
4,4'-methylenedianiline	101-77-9	C13H14N2
4,4'-oxydi(benzene-sulphonohydrazide)	80-51-3	C12H14N4O5S2
4,4'-oxydianiline	101-80-4	C12H12N2O
4,6-bis(octylthiome-thyl)-o-cresol	110553-27-0	C25H44OS2
4-;ŋŋ-dimethylben-zyl)phenol	599-64-4	C15H16O
4-[[(2-aminophe-nyl)methyl]amino]cyclohexyl acetate	93839-71-5	C15H22N2O2
4-amino-2,5-di-methoxy-N-methylbenzenesulphonamide	49701-24-8	C9H14N2O4S
4'-aminoazobenzene-4-sulphonic acid	104-23-4	C12H11N3O3S
4-amino-N-(1,1-di-methylethyl)-4,5-di-hydro-3-(1-methylethyl)-5-oxo-1H-1,2,4-triazole-1-carboxamide	129909-90-6	C10H19N5O2
4-aminophenol	123-30-8	C6H7NO
4-aminotoluene-3-sulphonic acid	88-44-8	C7H9NO3S
4'-Bromomethylbi-phenyl-2-carbonitrile	114772-54-2	C14H10BrN
4'-chloro-2',5'-di-methoxyacetoacetanilide	4433-79-8	C12H14ClNO4
4-chloro-2,5-dimethoxyaniline	6358-64-1	C8H10ClNO2
4-chloro-o-cresol	1570-64-5	C7H7ClO
4-chloro-o-xylene	615-60-1	C8H9Cl
4-chlorophenol	106-48-9	C6H5ClO
4-hydroxy-2,2,6,6-tetramethylpiperidine-1-ethanol	52722-86-8	C11H23NO2
4-hydroxy-2,2,6,6-tet-ramethylpiperidinoxyl	2226-96-2	C9H18NO2
4-isopropylaniline	99-88-7	C9H13N
4-mesyl-2-nitrotolu-ene	1671-49-4	C8H9NO4S
4-Methyl-3-thiosemicarbazide	6610-29-3	C2H7N3S
4-methyl-m-phenylene diisocyanate	584-84-9	C9H6N2O2
4-nitro-o-anisidine	97-52-9	C7H8N2O3
4-nitrophenol	100-02-7	C6H5NO3
4-nitrotoluene	99-99-0	C7H7NO2
4-nitrotoluene-2-sulphonic acid	121-03-9	C7H7NO5S
4-vinylcyclohexene	100-40-3	C8H12
4-vinylpyridine	100-43-6	C7H7N
5,5'-(1H-isoindole-1,3(2H)-diylidene)dibarbituric acid	36888-99-0	C16H9N5O6
5-amino-2,4,6-triio-doisophthalic acid	35453-19-1	C8H4I3NO4
6-methoxy-m-toluidine	120-71-8	C8H11NO

6-methyl-1,2,3-oxa-thiazin-4(3H)-one 2,2-dioxide, potassiumsalt	55589-62-3	C4H4KNO4S
6-Methyl-1,3,5-triazine-2,4-diamine	542-02-9	C4H7N5
6-Phenyl-1,3,5-triazine-2,4-diamine, Benzoguanamine	91-76-9	C9H9N5
7-aminonaphthalene-1,3,5-trisulphonic acid	27310-25-4	C10H9NO9S3
Acenaphthene	83-32-9	C12H10
Acetophenone	98-86-2	C8H8O
Amantadine	768-94-5	C10H17N
Ametryn	834-12-8	C9H17N5S
Aminoimino-methanesulphinic acid	1758-73-2	CH4N2O2S
Amitriptyline	50-48-6	C20H23N
ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate	62037-80-3	C6H4F11NO3
Androst-4-ene-3,17-dione	63-05-8	C19H26O2
Anthracene	120-12-7	C14H10
Anthraquinone	84-65-1	C14H8O2
Atrazine	1912-24-9	C8H14ClN5
Barium bis[5-chloro-4-ethyl-2-[(2-hydroxy-1-naphthyl)azo]benzenesulphonate]	67801-01-8	C36H28BaCl2N4O8S2
Barium bis[6-chloro-4-[(2-hydroxy-1-naph-thyl)azo]toluene-3-sulphonate]	73612-34-7	C34H24BaCl2N4O8S2
Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-	152459-95-5	C29H31N7O
Benzene	71-43-2	C6H6
Benzophenone	119-61-9	C13H10O
Benzothiazole	95-16-9	C7H5NS
Benzotriazole	95-14-7	C6H5N3
Benzyl butyl phthalate	85-68-7	C19H20O4
Benzyl(3-hydroxy-phenacyl)me-thylammonium chlo-ride	71786-67-9	C16H18ClNO2
Benzyldimethylamine	103-83-3	C9H13N
Benzyltrimethylammonium chloride	56-93-9	C10H16ClN
Bicyclo[13.2.2]nonadecane	3/7/2680	C5H9NO
Bis(2-(2-methoxyethoxy)ethyl) ether	143-24-8	C10H22O5
Bis(2-dimethylaminoethyl)(methyl)amine	3030-47-5	C9H23N3
Bis(2-ethylhexyl) phthalate	117-81-7	C24H38O4
Bis(2-methoxyethyl) ether	111-96-6	C6H14O3
Bis(4-fluorophenyl) ketone	345-92-6	C13H8F2O
bis(nonafluorobu-tyl)phosphinic acid	52299-25-9	C8HF18O2P
Bisphenol S (4,4'-sulphonyldiphenol)	80-09-1	C12H10O4S
Bornan-2-one	76-22-2	C10H16O

Bromomethane	74-83-9	CH3Br
Butanamide, 2,2'-[(3,3'-dichloro[1,1'-bi-phenyl]-4,4'-diyl)bis(azo)]bis[3-oxo-, N,N'-bis(4-chloro-2,5-dimethoxy-phenyl and 2,4-xylyl) derivs.	90268-24-9	C36H33Cl3N6O6
Butanamide, 2,2'-[(3,3'-dichloro[1,1'-bi-phenyl]-4,4'-diyl)bis(azo)]bis[3-oxo-, N,N'-bis(o-anisyl and 2,4-xylyl) derivs.	68610-86-6	C35H32Cl2N6O5
Butanamide, 2,2'-[(3,3'-dichloro[1,1'-bi-phenyl]-4,4'-diyl)bis(azo)]bis[3-oxo-, N,N'-bis(p-anisyland Ph) derivs.	90268-23-8	C33H28Cl2N6O5
Caffeine	58-08-2	C8H10N4O2
Calcium 3-hydroxy-4-[(4-methyl-2-sulphonatophenyl)azo]-2-naphthoate	5281-09-4	C18H12CaN2O6S
Calcium cyanamide	156-62-7	CH2CaN2+2
Carbon tetrachloride	56-23-5	CCl4
Carbonohydrazide	497-18-7	CH6N4O
Chlorhexidine	55-56-1	C22H30Cl2N10
Chlorobenzene	108-90-7	C6H5Cl
Chloroethane	75-00-3	C2H5Cl
Chloroethylene	75-01-4	C2H3Cl
Chloroform	67-66-3	CHCl3
Chloromethane	74-87-3	CH3Cl
Chlorotrimethylsilane	75-77-4	C3H9ClSi
Climbazole	38083-17-9	C15H17ClN2O2
Copper, [29H,31H-phthalocyaninato(2-)-N29,N30,N31,N32]-, chlorinated	68987-63-3	C32H15ClCuN8
Cumene	98-82-8	C9H12
Cumene peroxide	80-43-3	C18H22O2
Cyanamide	420-04-2	CH2N2
Cyanuric acid	108-80-5	C3H3N3O3
Cyclohexane-1,2-di-carboxylic anhydride	85-42-7	C8H10O3
Cyclohexyli-denebis[tert-butyl] peroxide	3006-86-8	C14H28O4
Dapsone	80-08-0	C12H12N2O2S
Diaminotoluene	25376-45-8	C7H10N2
Dibenzyltoluene	26898-17-9	C21H20
Dibromomethane	74-95-3	CH2Br2
Dibutyl hydrogen phosphate	107-66-4	C8H19PO4
Dibutyl phthalate	84-74-2	C16H22O4
Dibutylbis(do-decylthio)stannane	1185-81-5	C32H68S2Sn
Dibutyltin bis(2-ethylhexanoate)	2781-10-4	C24H48O4Sn
Dichlorodifluoro-methane	75-71-8	CCl2F2
Dichloromethane	75-09-2	CH2Cl2

Diclofenac	15307-86-5	C14H11Cl2NO2
Diethyl phthalate	84-66-2	C12H14O4
Diguanidinium carbonate	593-85-1	C3H12N6O3
Diisopropyl ether	108-20-3	C6H14O
Diisopropylbenzene	25321-09-9	C12H18
Dimethoxydimethylsilane	1112-39-6	C4H12O2Si
Dimethyl ether	115-10-6	C2H6O
Dimethyl naphthalene-2,6-dicarboxylate	840-65-3	C14H12O4
Dimethyl phthalate	131-11-3	C10H10O4
Dimethyl sulfoxide	67-68-5	C2H6OS
Dinitrotoluene	25321-14-6	C7H6N2O4
Dinoseb	88-85-7	C10H12N2O5
Disodium 4,4'-diamino-9,9',10,10'-tetrahydro-9,9',10,10'-tetraoxo[1,1'-bianthracene]-3,3'-disulphonate	6022-22-6	C28H14N2Na2O10S2
Disodium 4,4'-diaminostilbene-2,2'-disulphonate	7336-20-1	C14H12N2Na2O6S2
Disodium 6-hydroxy-5-[(2-methoxy-4-sulphonato-m-tolyl)azo]naphthalene-2-sulphonate	25956-17-6	C18H14N2Na2O8S2
Disodium ox-ybis[methylbenzene-sulphonate]	73037-34-0	C14H12Na2O7S2
Diuron	330-54-1	C9H10Cl2N2O
e-caprolactam	105-60-2	C6H11NO
Edetic acid	60-00-4	C10H16N2O8
Erythromycin	114-07-8	C37H67NO13
Erythromycin thiocyanate	7704-67-8	C38H68N2O13S
Estradiol	50-28-2	C18H24O2
Estradiol Hemihydrate	35380-71-3	C36H50O5
Estrone	53-16-7	C18H22O2
Ethisterone	434-03-7	C21H28O2
Ethylbenzene	100-41-4	C8H10
Hexahydro-methylphthalic anhydride	25550-51-0	C9H12O3
Hexamethyldisiloxane	107-46-0	C6H18OSi2
Ibuprofen	15687-27-1	C13H18O2
Iohexol	66108-95-0	C19H26I3N3O9
Isoquinoline	119-65-3	C9H7N
m-(2,3-epoxypropoxy)-N,N-bis(2,3-epoxypropyl)aniline	71604-74-5	C15H19NO4
MAPTAC (3-methacrylamidopropyl)trimethylammonium chloride)	51410-72-1	C10H21ClN2O
Mecoprop	7085-19-0	C10H11ClO3
Melamine	108-78-1	C3H6N6
Mesitylene	108-67-8	C9H12
Methenamine	100-97-0	C6H12N4
N-(3-(dimethylamino)-propyl)methacrylamide	5205-93-6	C9H18N2O
N,N,N',N'-tetrame-thyl-2,2'-oxybis(ethyl-amine)	3033-62-3	C8H20N2O
N,N-diethylhydroxylamine	3710-84-7	C4H11NO

N,N-dimethyl-1-adamantanamine	3717-40-6	C12H21N
N,N-dimethylacrylamide	284-95-7	C19H36
N-[9-(dichloromethyli-dene)-1,2,3,4-tetrahydro-1,4-methanonaphthalen-5-yl]-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide	1072957-71-1	C18H15Cl2F2N3O
Naphthalene	91-20-3	C10H8
Naphthalene-2-sulphonic acid	120-18-3	C10H8O3S
Naproxen	22204-53-1	C14H14O3
N-butylbenzenesulphonamide	3622-84-2	C10H15NO2S
N-carboxymethyliminobis(ethylenenitrilo)tetra(acetic acid)	67-43-6	C14H23N3O10
N-ethylaniline	103-69-5	C8H11N
Nitrilotriacetic acid	139-13-9	C6H9NO6
Nitrobenzene	98-95-3	C6H5NO2
Nitrotoluene	1321-12-6	C7H7NO2
N-methylaniline	100-61-8	C7H9N
ṇṇ-dimethylbenzyl hydroperoxide	80-15-9	C9H12O2
ṇṇṇ-trifluoro-o-toluidine	88-17-5	C7H6F3N
Norethisterone	68-22-4	C20H26O2
O,O-dimethyl phosphorochloridothioate	2524-03-0	C2H6ClO2PS
O-acetylsalicylic acid	50-78-2	C9H8O4
o-phenylenediamine	95-54-5	C6H8N2
Oxybenzone	131-57-7	C14H12O3
o-xylene	95-47-6	C8H10
p-(2,3-epoxypropoxy)-N,N-bis(2,3-epoxypropyl)aniline	5026-74-4	C15H19NO4
Paracetamol	103-90-2	C8H9NO2
Pentasodium (carboxylatomethyl)imino-bis(ethylenenitrilo)tetraacetate	140-01-2	C14H18N3Na5O10
Pentasodium pentahydrogen [[(phosphonatome-thyl)imino]bis[ethane-2,1-diylnitrilo-bis(methylene)]]tetrakisphosphonate	61792-09-4	C9H23N3Na5O15P5
Pentobarbital	76-74-4	C11H18N2O3
Perhydro-1,3,5-tri-nitro-1,3,5-triazine	121-82-4	C3H6N6O6
PFBS - Potassium 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulphonate	29420-49-3	C4F9KO3S
Phenazone	60-80-0	C11H12N2O
Phenol, isopropylated, phosphate (3:1)	68937-41-7	C27H33O4P
Phenyl bis(2,4,6-tri-methylbenzoyl)-phosphine oxide	162881-26-7	C26H27O3P
Phenytoin	57-41-0	C15H12N2O2
p-nonylphenol	104-40-5	C15H24O
Progesterone	57-83-0	C21H30O2
Propargite	2312-35-8	C19H26O4S
Propazine	139-40-2	C9H16ClN5
p-Toluenesulfonic acid monohydrate	6192-52-5	C7H10O4S

Pyrazole	288-13-1	C3H4N2
Pyrene	129-00-0	C16H10
rac-[(2R,4R)-2-(2,4-DI-CHLOROPHENYL)-2-(1H-1,2,4-TRIAZOL-1-YLMETHYL)-1,3-DIOX-OLAN-4-YL]METHYL METHANESULFONATE MONOHYDROCHLO-RIDE	155661-07-7	C14H16Cl3N3O5S
rac-5-Amino-N-(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamic acid	111453-32-8	C11H11I3N2O5
Salbutamol	18559-94-9	C13H21NO3
Salicylic acid	69-72-7	C7H6O3
sodium (4,6-di-methoxypyrimidin-2-yl)carbamoyl-[[3-(2,2,2-trifluoroethoxy)-2-pyridyl]sulfonyl]azanide	199119-58-9	C14H13F3N5NaO6S
Sodium 1,4-dicyclo-hexyl sulphonatosuccinate	23386-52-9	C16H25NaO7S
sodium 2-amino-5-methylbenzenesul-fonate	54914-95-3	C7H8NNaO3S
Sodium 2-methyl-2-[(1-oxoal-lyl)amino]propanesulphonate	5165-97-9	C7H12NNaO4S
Sodium 2-methylprop-2-ene-1-sulphonate	1561-92-8	C4H7NaO3S
Sodium 3-(allyloxy)-2-hydroxypropanesulphonate	52556-42-0	C6H11NaO5S
Sodium dimethyl 5-sulphonatoisophthalate	3965-55-7	C10H9NaO7S
Sodium ethylenesulphonate	3039-83-6	C2H3NaO3S
Sodium hydrogen 4-amino-5-hydroxynaphthalene-2,7-disulphonate	5460-09-3	C10H8NNaO7S2
Sodium naphthalene-2-sulphonate	532-02-5	C10H7NaO3S
Styrene	100-42-5	C8H8
Sulfadiazine	68-35-9	C10H10N4O2S
Sulfadimidine	57-68-1	C12H14N4O2S
Sulfapyridine	144-83-2	C11H11N3O2S
Sulisobenzone	4065-45-6	C14H12O6S
Sulphanilic acid	121-57-3	C6H7NO3S
tert-butyl hydroper-oxide	75-91-2	C4H10O2
tert-butyl methyl ether	1634-04-4	C5H12O
Tetra potassium 5,5'-[ethane-1,2-diylbis[thio-1,3,4-thiadiazole-5,2-diyldiazene-2,1-diyl(5-amino-3-tert-buyl-1H-pyrazole-4,1-diyl)]}diisophthalate	849608-59-9	C36H32K4N14O8S4
Tetrachloroethylene	127-18-4	C2Cl4
Tetraethylammoniumheptadecafluorooctanesulphonate	56773-42-3	C16H20F17NO3S
Tetrahydro-1,3-dimethyl-1H-pyrimidin-2-one	7226-23-5	C6H12N2O
Tetramethylthiuram monosulphide	97-74-5	C6H12N2S3
Tetraoctyltin	3590-84-9	C32H68Sn
Toluene	108-88-3	C7H8
Toluene-2-sulphonamide	88-19-7	C7H9NO2S
Toluene-4-sulphonamide	70-55-3	C7H9NO2S
Toluene-4-sulphonic acid	104-15-4	C7H8O3S
trans-dichloroethylene	156-60-5	C2H2Cl2

Triacetin	102-76-1	C9H14O6
Tributyl phosphate	126-73-8	C12H27O4P
Tricarbonyl(methylcy-clopentadienyl)manganese	12108-13-3	C9H7MnO3-
Trichloroacetic acid	76-03-9	C2HCl3O2
Trichloroethylene	79-01-6	C2HCl3
Triclosan	3380-34-5	C12H7Cl3O2
Triethyl citrate	77-93-0	C12H20O7
Triethyl phosphate	78-40-0	C6H15O4P
Triethylenediamine (1,4-diazabicyclooctane)	280-57-9	C6H12N2
Trifluoroacetic acid	76-05-1	C2HF3O2
Trifluoromethanesulfonic acid	1493-13-6	CF3SO3H
Triphenylphosphine oxide	791-28-6	C18H15OP
Tris(2-butoxyethyl) phosphate (TBOEP)	78-51-3	C18H39O7P
Tris(2-chloro-1-meth-ylethyl) phosphate (TCPP)	13674-84-5	C9H18Cl3O4P
Tris(2-chloroethyl) phosphate	115-96-8	C6H12Cl3O4P
Tris[2-chloro-1-(chloromethyl)ethyl] phosphate	13674-87-8	C9H15Cl6O4P

Supplementary Table 2. PMT compounds analyzed (target analysis) and internal standards used

Compound	Use	I.S.
1,3-di-o-tolylguanidine	Industrial	Clothianidin-D3
1,3-diphenylguanidine	Industrial	Lidocaine-D10
1-Cyanoguanidine	Industrial	Cyanoguanidine-15N4
Acenaphthene	PAH	Acenaphthene-D10
Anthracene	PAH	Phenanthrene-D10
Atrazine-desethyl	Herbicide (TP)	Desisopropyl Atrazine-D5
Atrazine-desisopropyl	Herbicide (TP)	Desisopropyl Atrazine-D5
Benzophenone-10	UV filter (TP)	2,3,4,5-benzophenone-D5
Benzophenone-3	UV filter (TP)	2,3,4,5-benzophenone-D5
Bisphenol S	Plasticizer	Clothianidin-D3
Butyl benzyl Phthalate	Phthalate	Phenanthrene-D10
Di-n-butyl phosphate	Plasticizer	Dibutyl Phosphate-D18
Diuron	Herbicide	Diuron-D6
e-Caprolactam	Plasticizer	e-Caprolactam-D10
Methenamine	Pharmaceutical	Methenamine-D12
Naphthalene	PAH	Acenaphthene-D10
p-Toluenesulfonamide	Plasticizer	Imidacloprid-D4
Tonalide	Fragrance	Phenanthrene-D10
Tri-(2-Chloroisopropyl) Phosphate	Flame retardant	Triphenyl phosphate-D15
Triclosan	Disinfectant	Triclosan-D3
Triethyl phosphate	Flame retardant	Triethyl Phosphate-D15

Trifluoromethanesulfonic acid	UV filter	Cyanoguanidine-15N4
Tri-n-butyl phosphate	Flame retardant	Triphenyl phosphate-D15
Tris(2-butoxyethyl) phosphate	Flame retardant	Triphenyl phosphate-D15

Supplementary Table 3. Liquid chromatography gradient

Time (min)	Composition of A (%)	Composition of B (%)
0	95	5
0.05	95	5
4	0	100
6	0	100
7	95	5
8	95	5

Supplementary Table 4. QTOF (LC) conditions

Ion Polarity:	Negative	Negative	Positive	Positive
Scan mode:	bbCID	Auto MS/MS	bbCID	Auto MS/MS
Scan range:	50 - 1300 m/z	50 - 1300 m/z	50 - 1300 m/z	50 - 1300 m/z
Rolling average:	2	10	2	10
Spectra rate:	2.00 Hz	10.00 Hz	2.00 Hz	2.00 Hz
End Plate Offset:	500 V	500 V	500 V	500 V
Capillary:	3000 V	3000 V	4500 V	4500 V
Nebulizer:	4.0 bar	4.0 bar	4.0 bar	4.0 bar
Dry Gas:	9.0 L/min	9.0 L/min	10.0 L/min	10.0 L/min
Dry Temp:	220 ºC	220 ºC	220 ºC	220 ºC
Funnel 1RF:	250.0 Vpp	250.0 Vpp	250.0 Vpp	250.0 Vpp
Funnel 2RF:	250.0 Vpp	250.0 Vpp	250.0 Vpp	250.0 Vpp
is CID energy:	0.0 eV	0.0 eV	0.0 eV	0.0 eV
Hexapole:	60 Vpp	60 Vpp	60 Vpp	60 Vpp
Quadrupole ion energy:	4	4	4	4
Quadrupole low mass:	90 m/z	90 m/z	90 m/z	90 m/z
Collision energy:	20 eV	20 eV	20 eV	20 eV
Collision RF:	250 - 1000 Vpp	250 - 1000 Vpp	250 - 1000 Vpp	250 - 1000 Vpp
Transfer time:	26.7 - 80 us	26.7 - 80 us	26.7 - 80 us	26.7 - 80 us
Precursor ion:	0.3 sec	0.3 sec	0.3 sec	0.3 sec
Exclude after:	3 spectra	3 spectra	3 spectra	3 spectra
Release after:	0.1 min	0.1 min	0.1 min	0.1 min

Supplementary Table 5. Analytical parameters of target compounds in LC-QTOF-MS

Compound	Formula	Confirmation Quantifier, Qualifier ions	R^2	RT (min)	Recovery (%)	MQL ($ng \cdot L^{-1}$)
1-Cyanoguanidine	$C_2H_4N_4$	83.0363	0.99106	1.1	107	25
Bisphenol S	$C_{12}H_{10}O_4S$	249.0227, 108.0218	0.99001	3.34	102	26
Di-n-butyl phosphate	$C_8H_{19}O_4P$	209.0948, 153.0317	0.98983	3.88	81	5
Diuron	$C_9H_{10}Cl_2N_2O$	232.0170, 185.9517	0.99314	4.45	98	6
p-Toluenesulfonamide	$C_7H_9NO_2S$	170.0281, 78.9731	0.98960	3.15	113	7
Trifluoromethanesulfonic acid	CHF_3O_3S	148.8526, 79.9574	0.99232	1.6	111	6
1,3-di-o-tolylguanidine	$C_{15}H_{17}N_3$	240.1495, 133.0756	0.99863	3.35	102	13
1,3-diphenylguanidine	$C_{13}H_{13}N_3$	212.1182, 119.0599	0.99644	3.1	112	14
Atrazine-desethyl	$C_6H_{10}ClN_5$	188.0697, 146.0222	0.99930	3.65	89	11
Atrazine-desisopropyl	$C_5H_8ClN_5$	174.0541, 104.0007	0.99437	3.2	91	11
e-Caprolactam	$C_6H_{11}NO$	114.0913, 69.070	0.99964	2.83	91	3
Methenamine	$C_6H_{12}N_4$	141.1135, 112.0865	0.99978	1.1	92	6
Triethyl phosphate	$C_6H_{15}O_4P$	183.0781, 142.0721	0.99868	3.8	94	12

Supplementary Table 6. QTOF (GC) conditions

Ion Polarity:	Positive	Positive
Scan mode:	bbCID	Auto MS/MS
Corona voltage:	5000 nA	5000 nA
Scan range:	50 – 1000	50 – 1000
Rolling average:	3	3
Spectra rate:	3 Hz	12 Hz
End Plate Offset:	500 V	500 V
Capillary:	4500 V	4500 V
Nebulizer:	1.6 bar	1.6 bar
Dry Gas:	9 L min^{-1}	9 L min^{-1}
Dry Temp:	200 °C	200 °C
Funnel 1RF:	250.0 Vpp	250.0 Vpp
Funnel 2RF:	250.0 Vpp	250.0 Vpp
isCID energy:	0 eV	0 eV
Hexapole:	60.0 Vpp	60.0 Vpp
Quadrupole ion energy:	4 eV	4 eV
Quadrupole low mass:	60 m/z	90 m/z
Collision energy:	4 eV	4 eV
Collision RF:	250-750 Vpp	250-1000 Vpp
Transfer time:	25-75 µs	25-75 µs
Nº Precursor ions:	3	3

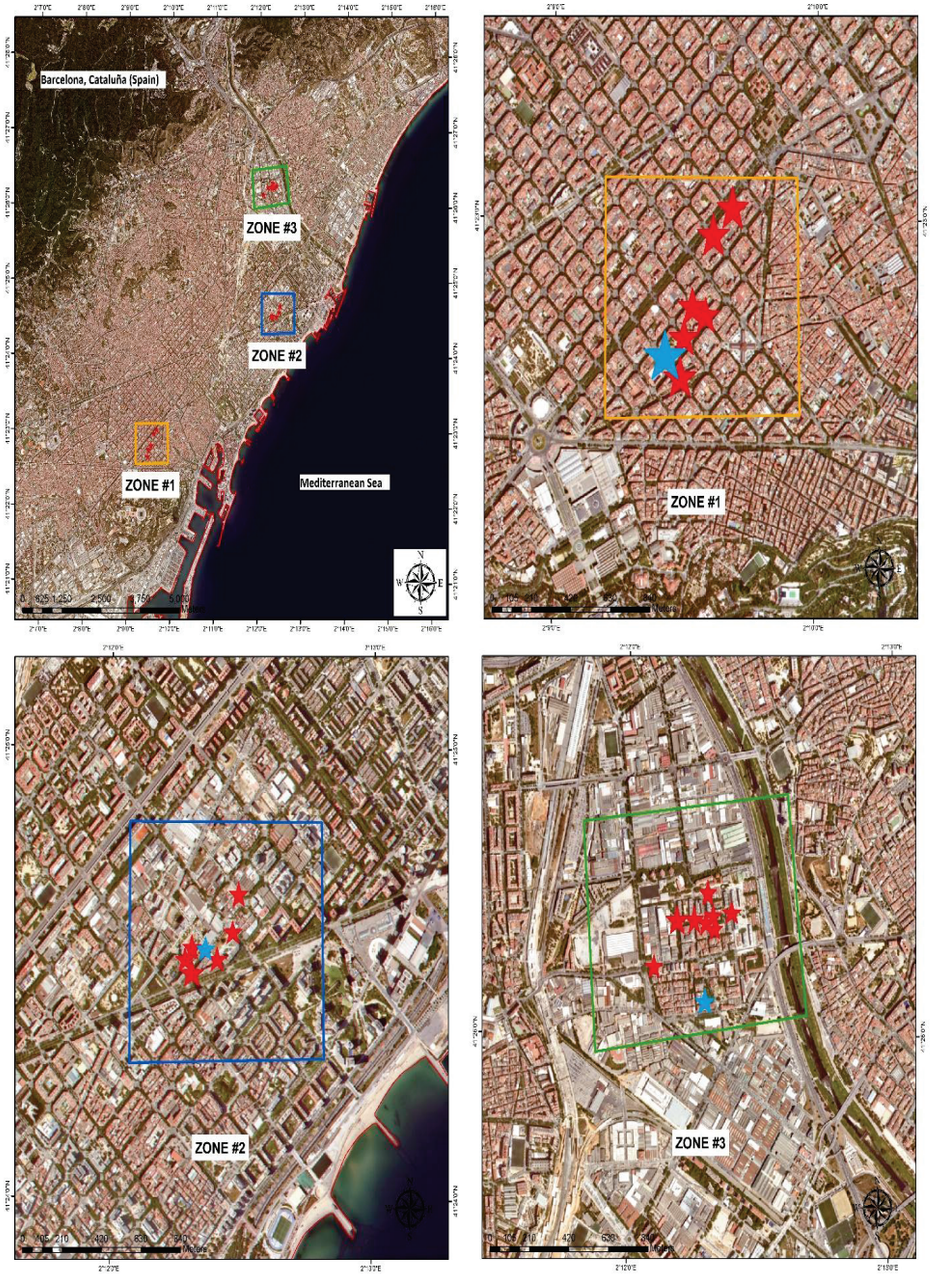
Exclude after:	3 spectra	3 spectra
Release after:	1.0 min	0.1 min
Splitless injections:	1 µL	1 µL
Injection port temperature	280 (°C)	
GC columna temperature ramp		
Temperature (°C)	**Speed (°C/min)**	**Hold Time (min)**
70		3.5
180	25	-
320	5	7

Supplementary Table 7. Analytical parameters of target compounds in GC-QTOF

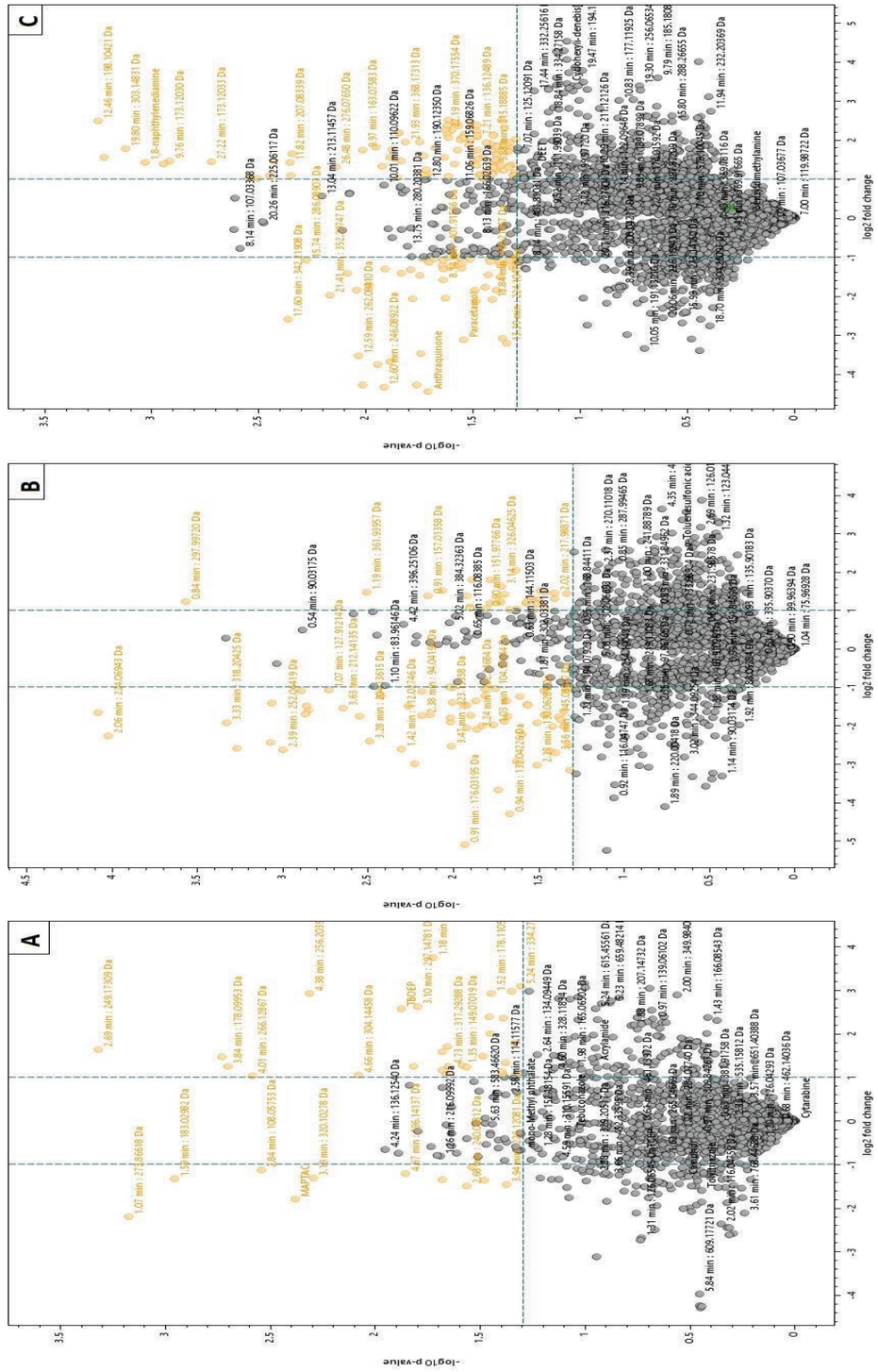
Compound	Formula	Quantifier, Qualifier ions	R^2	RT (min)	Recovery (%)	MQL ($ng \cdot L^{-1}$)
Acenaphthene	$C_{12}H_{10}$	153.0718, 154.0751	0.955	9.95	68	11
Anthracene	$C_{14}H_{10}$	179.0857, 178.0778	0.962	13.75	75	0.2
Benzophenone-3	$C_{14}H_{12}O_3$	229.0862, 151.0425	0.963	16.77	61	1
Benzophenone-10	$C_{15}H_{14}O_3$	243.1026, 227.0706	0.996	18.74	41	3
Butyl benzyl Phthalate	$C_{19}H_{20}O_4$	313.1456, 205.0875	0.98	21.42	72	1
Naphthalene	$C_{10}H_8$	129.0717, 128.0642	0.951	7.98	54	5
Tris(2-butoxyethyl) phosphate	$C_{18}H_{39}O_7P$	399.2531, 299.1639	0.995	22.10	70	11
Tonalide	$C_{18}H_{26}O$	259.2057, 243.1744	0.978	14.00	92	1
Tri-(2-Chloroisopropyl) Phosphate	$C_9H_{18}Cl_3O_4P$	327.0071, 329.0041	0.935	13.35	75	4
Triclosan	$C_{12}H_7Cl_3O_2$	288.9606, 290.9573	0.962	17.85	58	4
Tri-n-butyl phosphate	$C_{12}H_{27}O_4P$	267.1726, 98.9847	0.995	11.36	81	2

Supplementary Table 8. Fragments used for the confirmation of suspect PMTs.

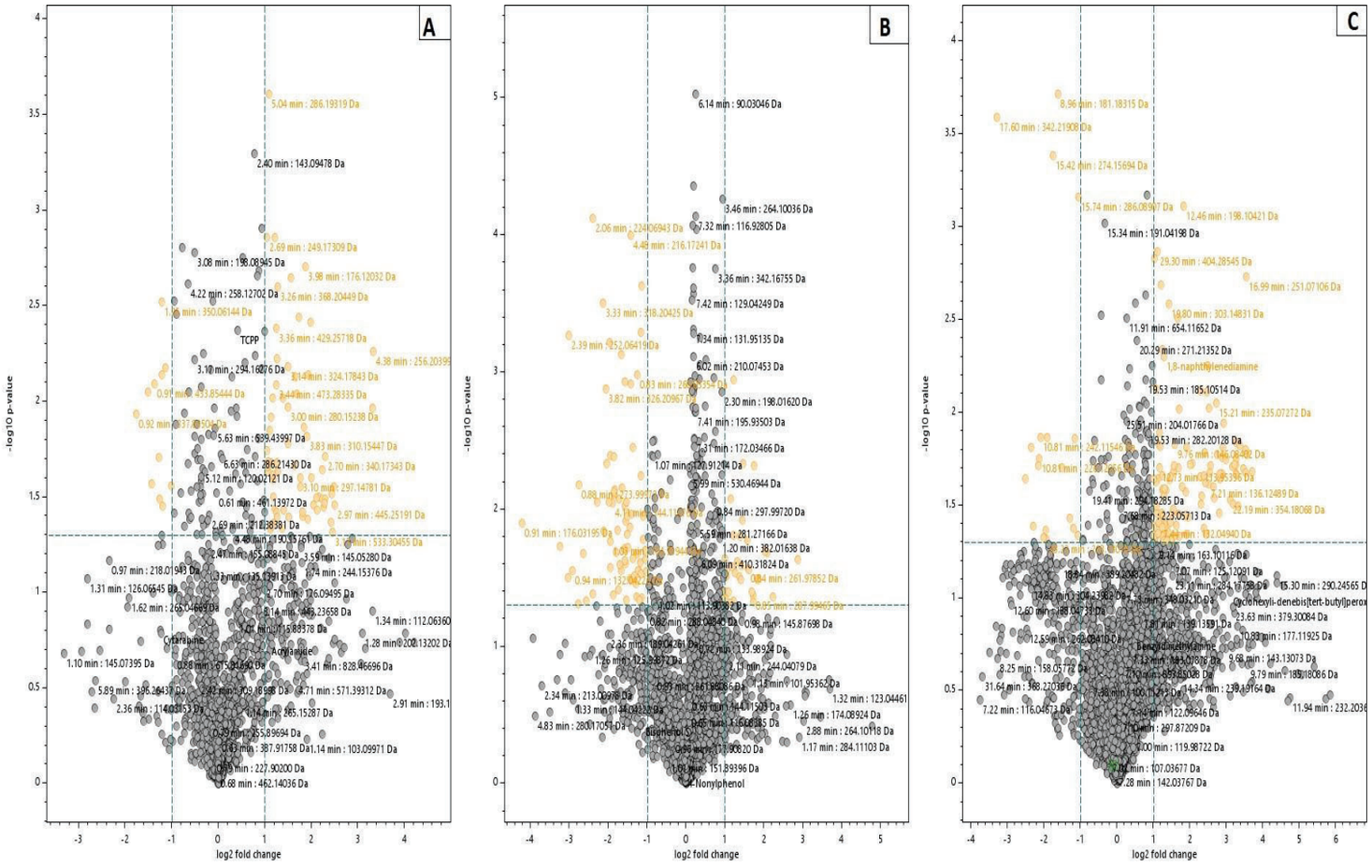
COMPOUND	FORMULA	EXACT MASS	Mass error (mDa)	Matched Fragments				
1,2,3,4-tetrahydronaphthalene	$C_{10}H_{12}$	132.0939	-0.057	91.054	119.085			
2,4-dinitrophenol	$C_6H_4N_2O_5$	184.0120	0.013	45.993	51.024	109.017	137.012	
2-morpholinoethanol	$C_6H_{13}NO_2$	131.0946	-0.02	58.066	98.096	116.107		
2-nitrophenol	$C_6H_5NO_3$	139.0269	0.229	45.993	92.026			
2-nitrotoluene	$C_7H_7NO_2$	137.0476	0.151	65.039	96.045	110.060		
4-vinylcyclohexene	C_8H_{12}	108.0939	-0.017	79.054	81.070	93.072		
Bis(2-methoxyethyl) ether (Diglyme)	$C_6H_{14}O_3$	134.0942	0.286	59.049				
Bornan-2-one (Camphor)	$C_{10}H_{16}O$	152.1201	-0.138	135.116				
Ethylbenzene	C_8H_{10}	106.0783	-0.051	67.056	77.040	91.055	93.072	
Dimethyl phthalate	$C_{10}H_{10}O_4$	194.0560	0.069	167.070	121.028	133.065	149.024	167.07
N-butylbenzenesulphonamide	$C_{10}H_{15}NO_2S$	213.0823	0.048	63.962	91.981	136.043	141.001	156.012
Benzophenone	$C_{13}H_{10}O$	182.0734	-0.292	77.043	105.0364			
Dibutyl phthalate	$C_{16}H_{22}O_4$	278.1523	-0.201	149.025				
Diethyl phthalate	$C_{12}H_{14}O_4$	222.0892	-0.288	149.023	150.026	177.055	178.058	179.086
Melamine	$C_3H_6N_6$	126.0653	2.86	68.025	85.051			
Salicylic acid	$C_7H_6O_3$	138.0316	-0.86	93.034	65.040			
Toluene-4-sulphonic acid	$C_7H_8O_3S$	190.0299	0.137	79.957				



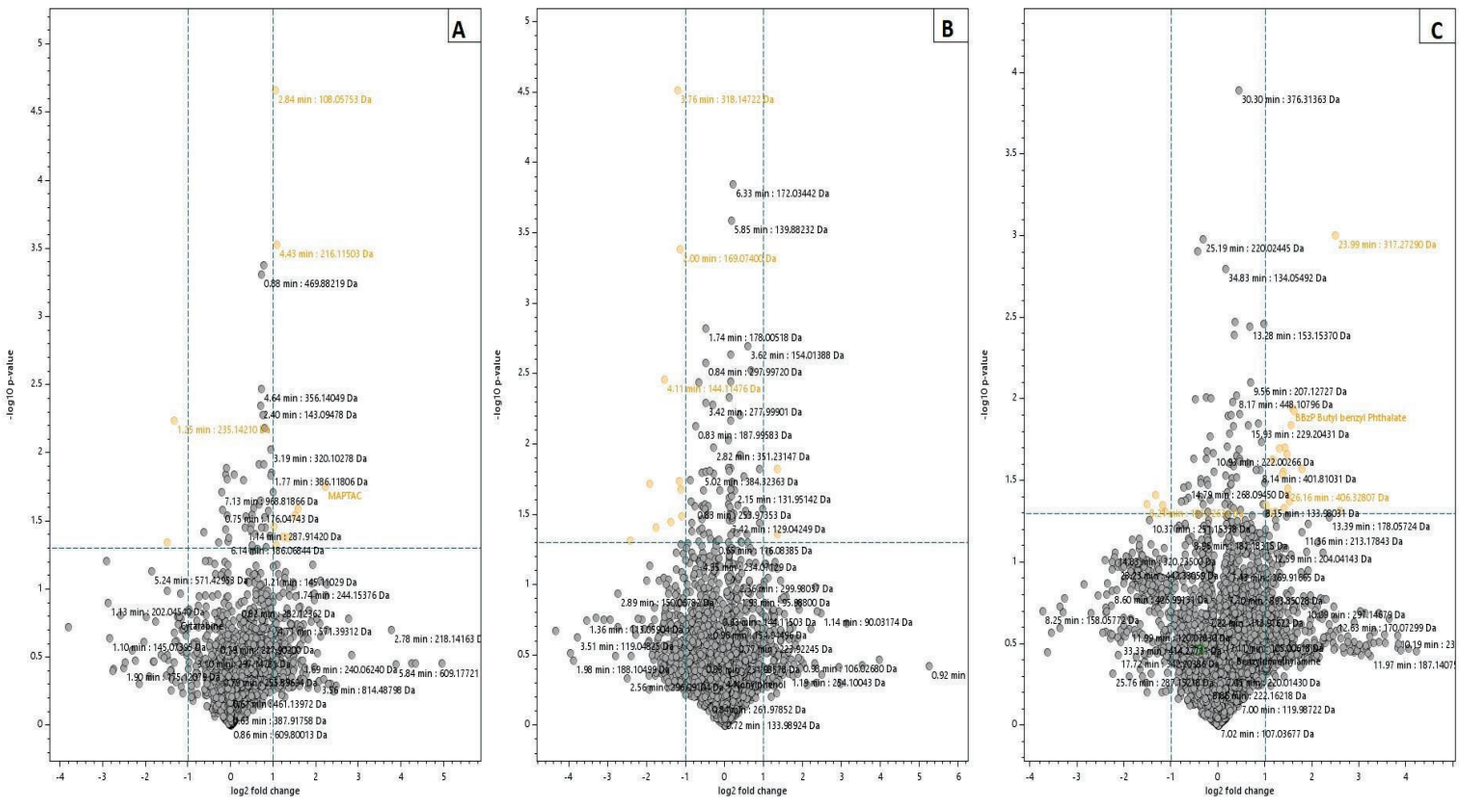
Supplementary Figure 1. Map of the sampling sites for this study (City of Barcelona, Spain). Red stars stand for stormwater sampling locations, while blue stars indicate roof locations for rainwater sampling. Colored squares stand for the different studied Districts: Eixample (Zone #1), Sant Martí (Zone #2), and Sant Andreu (Zone #3). Source for city basemap: © ArcGIS (ESRI)



Supplementary Figure 2. Volcano plots comparing Zone 1 vs Zone 2 using LC-ESI(+)-QTOF (A), LC-ESI(-)-QTOF (B) and GC-APCI-QTOF (C).



Supplementary Figure 3. Volcano plots comparing Zone 1 vs Zone 3 using LC-ESI(+)-QTOF (A), LC-ESI(-)-QTOF (B) and GC-APCI-QTOF (C).



Supplementary Figure 4. Volcano plots comparing Zone 2 vs Zone 3 using LC-ESI(+)-QTOF (A), LC-ESI(-)-QTOF (B) and GC-APCI-QTOF (C).

4.4 Discussió

Els resultats d'aquest capítol descriuen la presència de TrOCs en aigua subterrània, aigua superficial, aigua d'escorrentia i aigua de pluja de la ciutat de Barcelona. Respecte l'anàlisi de TrOCs polars en aigua urbana d'escorrentia i pluja, les publicacions #4 i#5 són les primeres, a la bibliografia actual, en focalitzar-se en aquest tema. De fet, la publicació #4 reporta per primer cop la presència de 12 TrOCs altament polars en aigua d'escorrentia. Tot i que els resultats i discussions estan detallats en cada article, aquesta secció es centrarà en una discussió global dels resultats de les 3 publicacions d'aquest capítol.

Distribució de TrOCs polars en les diferents aigües urbanes

Com ja s'ha esmentat prèviament, els vMC (log D_{ow} < 0) no han estat extensament monitoritzats en les matrius aquoses. Tot i que hi ha alguna revisió sistemàtica recollint les dades de contaminants polars a les aigües, més dades son necessàries per conèixer el seu origen, com es transporten en el medi aquós i, sobretot, quin risc presenten al medi ambient (Loos et al., 2013, 2010; Zhang et al., 2024). A la publicació #3, sis pous propers al riu Besòs, juntament amb una mostra d'aigua superficial van ser mostrejades durant 4 mesos consecutius. Per ampliar la informació present a l'article, aquí es presentaran els resultats obtinguts d'onze campanyes mensuals, és a dir, 11 mesos d'un any natural, obtenint en total 66 mostres d'aigua urbana subterrània i 11 d'aigua superficial. Per confirmar la hipòtesi que els compostos polars són els que més contribueixen a la concentració total en l'aigua urbana, degut a les seves característiques hidrofíliques, es va comparar el sumatori de concentracions de tots els TrOCs analitzats amb el sumatori de concentracions considerant només els vMC en cada mostra. A la Figura 4.2, es poden veure les diferències observades, on s'evidencia la presència i concentració de vMC molt superior a la resta de compostos. Cal mencionar que, dels 117 compostos analitzats, només 35 són vMC, és a dir, el 29.9 % del total. En canvi, la contribució mitjana dels vMC a l'aigua superficial es del 93.4 % mentre que de l'aigua subterrània del 87.0 %. Aquests resultats suggereixen que els vMC juguen un paper molt important en els cossos d'aigua, especialment, aquells que romanen en entorns urbans.

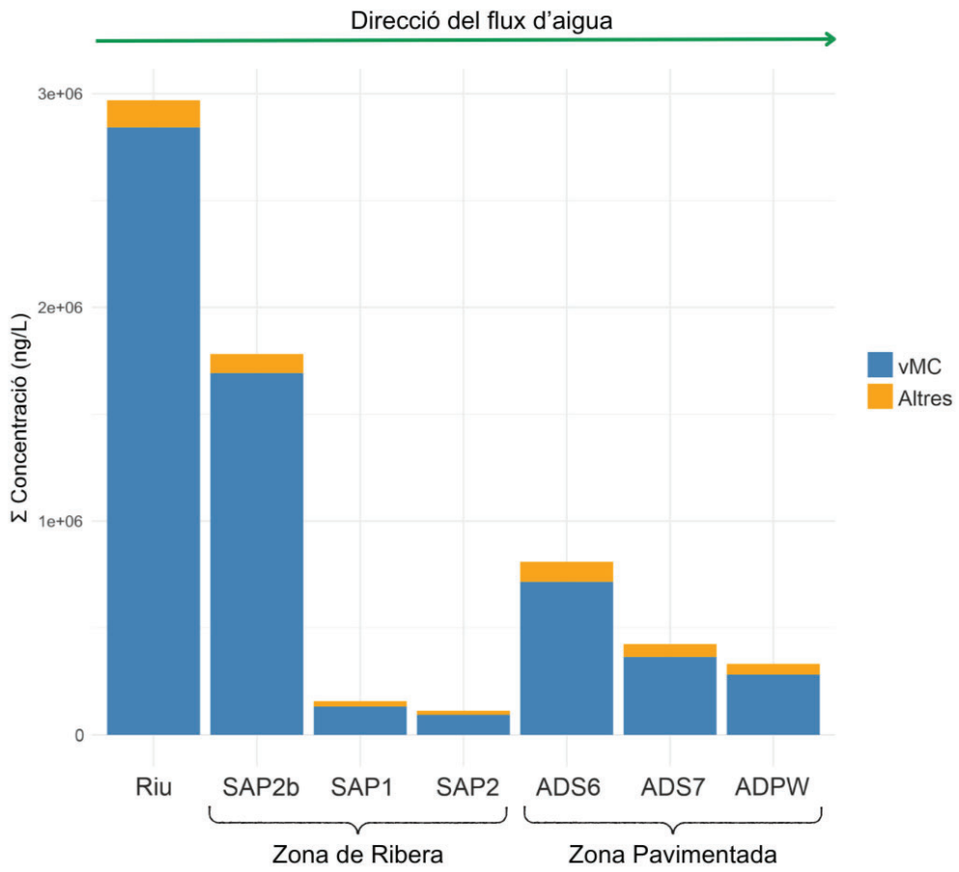


Figura 4.2. Concentració acumulada per cada mostra analitzada a la publicació #3.

Seguint el flux de l'aigua representat a la Figura 4.2, s'aprecia una variació de la concentracions dels TrOCs en els pous consecutius. Es important mencionar que els pous SAP2b, SAP1 i SAP2 pertanyen a una part propera al riu Besòs (zona de ribera) i que no està pavimentada, mentre que els pous ADS6, ADS7 i ADPW si que ho estan. L'aigua superficial es la, que presenta concentracions més altes. Les mostres d'aigua subterrània següents, SAP2b, SAP1 i SAP2, mostren concentracions que disminueixen progressivament. En canvi, el pou ADS6, així com els posteriors ADS7 i ADPW, tot i estar més allunyades del riu i ser el següent pou (seguint el flux d'aigua) després de SAP2, presenten concentracions molt més altes. Aquest fenomen es pot atribuir al fet que en aquest punt, comença la urbanització, amb la presència d'àrees construïdes i pavimentades, així com la presència del sistema de clavegueram. Això suggereix que altres fonts de contaminació, més enllà de la influència directa del riu, podrien

estar afectant aquests pous, com ara filtracions del clavegueram o aportacions derivades de l'escorrentia urbana.

Dels resultats es pot concloure que els contaminants polars objectius de la llista són els que més contribuïen a l'aigua subterrània. Aquests contaminants van ser el els que es van analitzar a l'aigua d'escorrentia i de pluja, que són fonts de recàrrega dels pous urbans. Dues publicacions la #4 i la #5, es van centrar en l'anàlisi de TrOCs polars. La diferència principal entre elles es que a la publicació #4 només es varen analitzar TrOCs amb una polaritat inferior a 0, és a dir, 26 vMC, mentre que a la publicació #5 es van incloure també PMTs volàtils, analitzats mitjançant GC-MS, permeten una visió més amplia de la contaminació.

Els contaminants orgànics han estat molt poc estudiats a les aigües d'escorrentia urbana, d'aquesta manera l'anàlisi de sospitosos, combinat amb l'anàlisi dirigit és una combinació interessant per tenir més informació de la presència d'aquests TrOCs. A la Figura 4.3, es mostren els compostos més detectats, amb freqüències de detecció superiors al 50 %, en mostres d'escorrentia.

Els compostos de volatilitat mitja a alta, acolorits de taronja a la Figura 4.3, analitzats mitjançant GC-MS, presenten freqüències de detecció molt elevades. El primer que podem concloure es que aquests compostos son presents a l'aigua d'escorrentia principalment degut a la deposició atmosfèrica (Asman et al., 2005; Gasperi et al., 2014). De fet, aquests mateixos compostos varen ser analitzats també en aigua de pluja (n = 3) on, dels 12 volàtils analitzats per GC, 11 van resultar en una freqüència de detecció del 100 % amb mitjanes des de 3.2 a 245 ng L^{-1}. L'excepció es l'Antracè, un hidrocarbur policíclic aromàtic de baixa massa molecular com l'acenaftè o el naftalè, que no va ser detectat en cap mostra d'aigua de pluja. Finalment, cal remarcar les altes concentracions trobades pels retardants de flama estudiats, Tris(2-butoxyethyl) phosphate, Tris(2-chloroethyl) phosphate i Tris-(2-Chloroisopropyl) phosphate, presentant concentracions mitjanes de 2482, 1995 i 239 ng L^{-1}, respectivament, en les mostres d'escorrentia (Casas et al., 2021). Per tant, s'evidencia que l'aigua d'escorrentia urbana pot contribuir a la contaminació dels aqüífers de la ciutat amb TrOCs molt diferents dels que usualment aporta tant l'aigua superficial com l'aigua de pèrdues del clavegueram, aportant

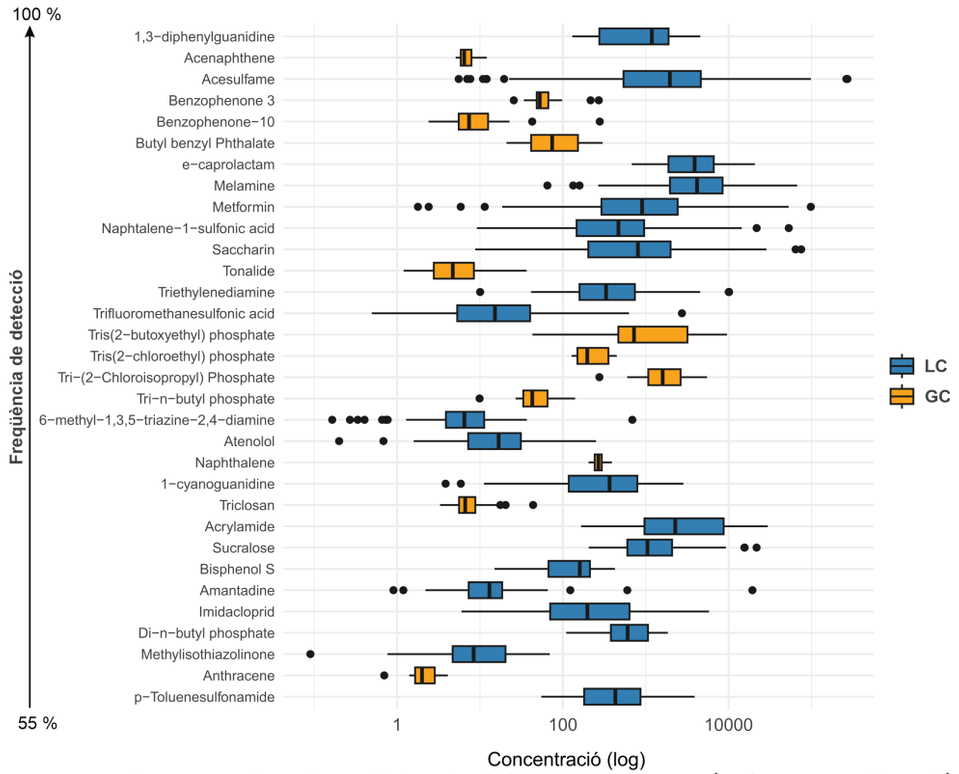


Figura 4.3. Diagrama de caixes i bigotis dels compostos més detectats (freqüència de detecció > 50 %) en aigües d'escorrentia de Barcelona. L'eix X mostra la concentració en escala logarítmica.

TrOCs d'origen antropogènic provinent dels carrers i també de l'atmosfera urbana (Hensen et al., 2018; Pinasseau et al., 2020).

D'altra banda, especial atenció cal parar en els edulcorants artificials com ara l'acesulfam, la sacarina o la sucralosa ja que s'han detectat en la majoria de mostres d'escorrentia, superficials i subterrànies, amb concentracions molt altes arribant a concentracions de 0.27 mg L^{-1} en el cas de l'acesulfam a una mostra d'escorrentia. A la discussió del *Capítol #4* s'aprofundeix més en el possible origen dels compostos. Seguint amb TrOCs detectats molt freqüentment a concentracions altes, els compostos d'ús industrial com la melamina o la ε-caprolactama, presents de manera omnipresent a les mostres d'escorrentia amb concentracions màximes de 67.2 i 20.8 µg L^{-1}, respectivament, poden originar riscos medi ambientals al tractar-se de TrOCs no destinats al consum humà ni tampoc a ser abocats al medi ambient. Per tant, els TrOCs poden posar

en risc, no només els organismes vius urbans, si no que també poden suposar un risc per a la salut humana, no tant pel consum directe d'aigua, sinó per l'exposició a través d'aerosols (per exemple, durant el reg) o altres vies d'exposició indirecta. Per això, una avaluació del risc medi ambiental es imprescindible per prioritzar aquells compostos que posen més en risc el medi ambient.

Avaluació del risc ambiental i per a la salut humana

Per dur a terme el risc medi ambiental a aquestes aigües, s'han considerat els TrOCs amb una freqüència de detecció igual o superior al 50 % de l'aigua subterrània. Així, s'ha fet ús d'una part de les dades presents a la publicació #7 i d'altres dades no publicades. A la Taula 4.1, es poden veure els resultats dels ERQ obtinguts pels compostos seleccionats en les tres matrius estudiades. Desafortunadament, els valors PNEC per alguns compostos no estan disponibles en l'actualitat. De 16 de 87 TrOCs, no es va poder calcular el seu el risc medi ambiental ja que no tenim els valors toxicològics disponibles (U.S. Environmental Protection Agency, 2020). Cal mencionar que la concentració usada per cada compost es la del percentil 90, ja que aporta una aproximació conservativa del risc medi ambiental (Mutzner et al., 2023). Aquí, el risc medi ambiental ha sigut classificat en 4 categories: ERQ < 0.01 risc medi ambiental insignificant, 0.1 > ERQ ≥ 0.01 risc baix, 1 > ERQ ≥ 0.1 risc moderat i ERQ ≥ 1 risc alt (Zhang et al., 2024).

Com es pot observar a la Taula 4.1 l'aigua superficial es la matriu urbana que més concentracions elevades de TrOCs conté dels tres masses d'aigua, seguit per l'aigua d'escorrentia i per últim l'aigua subterrània. A més, dels vuit compostos que presenten un risc medi ambiental a l'aigua subterrània, set d'ells estan principalment influenciats per l'aigua superficial, fet que explica la proximitat del riu Besòs a aquests pous estudiats. Anteriorment s'ha esmentat les altes concentracions trobades en general pels edulcorants artificials, tant l'acesulfam, com la sucralosa i la sacarina no apareixen a la Taula 4.1, demostrant la importància d'avaluar els riscos associats als TrOCs més enllà d'únicament esbrinar la concentració dels mateixos. El que si està present és el ciclamat, un edulcorant artificial extensament usat sota l'etiqueta E952 a la Unió Europea, amb valors d'ERQ de 0.91 i 0.024 a l'aigua superficial i subterrània

Taula 4.1. PNEC i ERQ dels compostos amb freqüències de detecció iguals o superiors al 50 %, usant la concentració del percentil 90 a cada matriu d'aigua urbana estudiada. Verd: risc insignificant; Groc: risc baix; Taronja: risc moderat i; Vermell: risc alt.

Compost	PNEC (µg L^{-1})	ERQ Aigua d'escorrentia	ERQ Aigua superficial	ERQ Aigua subterrània
1,3-diphenylguanidine*	182	0.014	0	0
4-Hidroxidiclofenac	3.50	0	0.015	0.0080
Acrylamide	346	0.034	0	0
Alprazolam	6.40	0	0.012	0.0020
Benzoylecgonine	47.8	0.21	0.0010	0
Bisphenol A	31.6	0.0020	0.043	0.024
Butyl benzyl phthalate*	11.6	0.019	0	0
Carbamazepine	35.6	0	0.011	0.0030
Carbamazepine epoxide	3.10	0	0.020	0.0090
Cyclamate	757	0.0040	0.91	0.024
Diazepam	11.2	0.0020	0.019	0.0030
Diclofenac	8.00	0	0.18	0.049
Di-n-butyl phosphate*	5.90	0.19	0	0
ε-caprolactam	704	0.016	0.016	0.0020
Fipronil	0.0856	0.083	0.15	0.0070
Fipronil desulfynil	1.30	0.0010	0.012	0.0020
Fipronil sulfide	0.242	0	0.39	0.076
Fipronil sulfone	0.360	0.017	0.077	0.011
Gemfibrozil	77.8	0.0010	0.013	0.0070
Iohexol	6.00	0	0.44	0.18
Iopamidol	2.10	0	12.6	8.4
Lamotrigine	75.8	0	0.060	0.0090
Lorazepam	1.30	0	0.096	0.034
Melamine	1256	0.016	0.12	0.0010
Naphthalene-1sulfonic acid	186	0.012	0.0010	0
o-desmethylvenlafaxine	132	0.0010	0.032	0.0050
Oxazepam	6.50	0	0.012	0.0050

*: Compostos analitzats únicament en aigua d'escorrentia.

respectivament. A més, dos compostos (classificats com vMC) exhibeixen risc a l'aigua subterrània, els agents de contrast utilitzats en els raigs X, iohexol (ERQ = 0.18) i iopamidol (ERQ = 8.4). Les seves concentracions altes al medi ambient combinades amb el baix valor de PNEC associat, fan que aquestes substàncies posin en perill el medi ambient urbà.

Finalment, també s'ha avaluat el risc per a la salut humana, calculat amb les equacions 4.3 i 4.4. Aquesta estimació depèn del rang d'edats estudiat ja que l'influencia del pes corporal i de la ingesta diària, en aquest

cas d'aigua, varia considerablement. A la publicació #3 es va calcular el risc per a la salut humana de compostos seleccionats en aigua de pou i, aquí també ens centrarem amb l'aigua subterrània, ja que es el cos d'aigua més net i que té més possibilitats de ser emprat per a aigua potable en el futur. De la mateixa manera que l'avaluació del risc medi ambiental, s'han considerat els TrOCs amb una freqüència de detecció igual o superior al 50 % de l'aigua subterrània. Amb l'ajuda de la bibliografia actual, s'han obtingut més del 70 % dels valors d'ADI d'aquests compostos, permeten avaluar-ne el risc dels mateixos (EFSA, 2016; Jurado et al., 2022; Kondor et al., 2021; Parida et al., 2021; Prosser and Sibley, 2015; Schwab et al., 2005; Sengar and Vijayanandan, 2022). Tot i això, compostos que presenten concentracions altes al percentil 90 com la triethylenediamina, la gabapentina o la furosemide (8407, 894, 558 ng L-1, respectivament) han sigut descartats ja que el HRQ no ha sigut possible calcular-ho. A la Taula 4.2 s'observen els compostos seleccionats que presenten un risc a l'aigua subterrània tant en infants (0-1 anys) com en adults (>18 anys). Només quatre compostos, ε-caprolactam, fipronil sulfide, lamotrigine i o-desmethylvenlafaxine, presenten un risc per a la salut humana i al medi ambient, evidenciant les diferències de toxicitat en humans comparat amb altres organismes vius. Es pot observar també la diferència de risc entre infants i adults, sent els primers més vulnerables a la ingesta de TrOCs degut, principalment, a la diferència de pes corporal entre infants i adults. Tot i que hi ha 14 TrOCs que presenten un risc per a la salut humana, ens podem centrar en quatre d'ells principalment tots ells fàrmacs: l'antiepilèptic lamotrigine que manifesta un risc moderat en infants; dos fàrmacs usats per tractar la tensió arterial, l'irbesartan i el valsartan i, per últim, el principal metabòlit humà del valsartan, l'àcid valsartànic, exhibint els últims tres un risc alt en infants i un risc moderat en adults en el cas del valsartan i el àcid valsartànic (Taula 4.2).

Taula 4.2. DWEL i HRQ dels compostos amb freqüències de detecció iguals o superiors al 50 %, usant la concentració del percentil 90 a l'aigua urbana subterrània per infants i adults. Verd: risc insignificant; Groc: risc baix; Taronja: risc moderat i; Vermell: risc alt

Compost	DWEL (µg L^{-1})	HRQ Infants	HRQ Adults
5-Desamino-oxo-lamotrigine	2.86	0.066	0.022
ε-caprolactam	14.3	0.076	0.025
Fipronil sulfide	1.90	0.010	0.0030
Fluconazole	6.80	0.011	0.0040
Hydrochlorothiazide	57.1	0.015	0.0050
Irbesartan	0.041	2.2	0.073
Ketoprofen	5.71	0.024	0.0080
Lamotrigine	2.86	0.23	0.075
Metoprolol	2.86	0.036	0.012
o-desmethylvenlafaxine	51.4	0.012	0.0040
Phenytoin	2.76	0.056	0.018
Primidone	6.67	0.011	0.0030
Valsartan	0.543	2.7	0.88
Valsartan acid	0.543	2.1	0.70

Els estudis de risc tant medi ambiental com per a la salut humana de TrOCs són de vital importància per conèixer la qualitat i poder usar les diferents matrius d'aigua urbana de manera correcte. D'altra banda, s'ha evidenciat la influència del riu Besòs en les mostres de pou analitzades en aquest capítol, on els TrOCs de risc medi ambiental a l'aigua subterrània ho eren també a l'aigua superficial. Per últim, monitoritzar l'aigua d'escorrentia urbana permet conèixer contaminacions de TrOCs de diferents aportacions, com ara TrOCs d'origen industrial. El següent capítol expandeix els coneixements exposats aquí per tota la plana de Barcelona.

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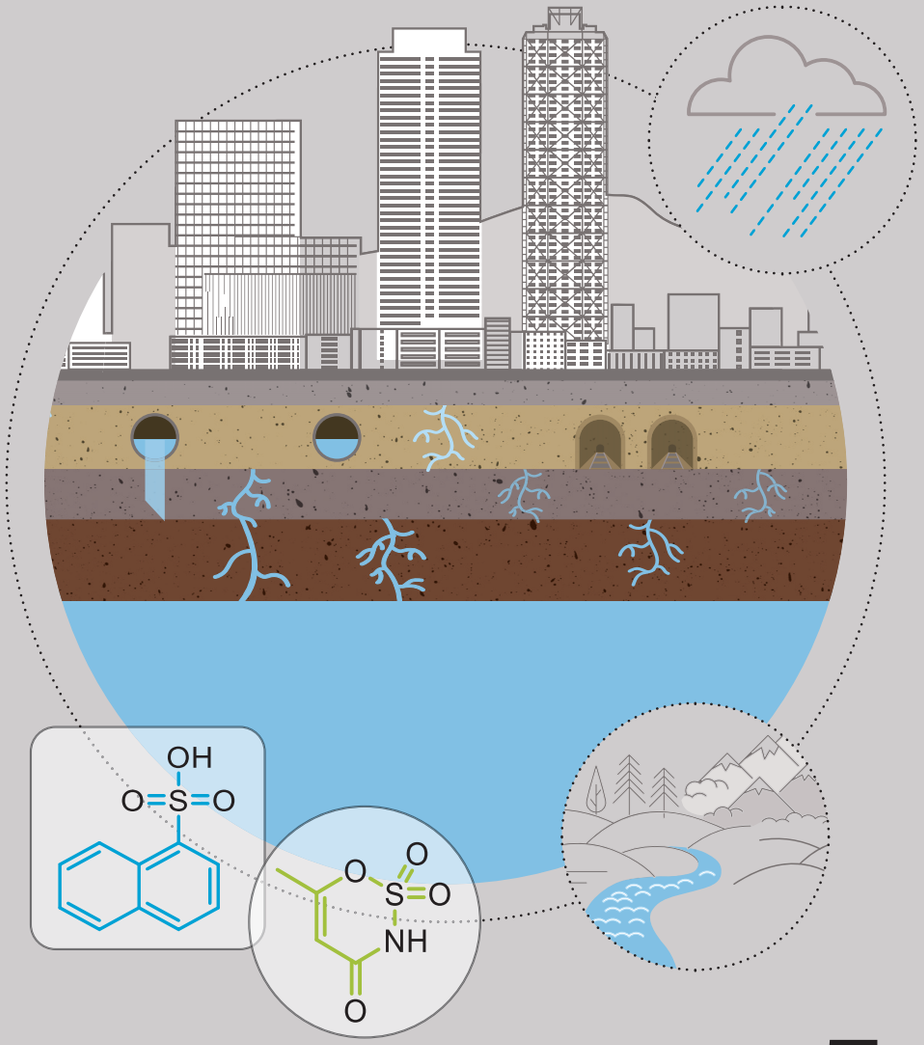
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Capítol



5.

Fonts de recàrrega i contaminació de l'aigua subterrània urbana

FONTS DE RECÀRREGA I CONTAMINACIÓ DE L'AIGUA SUBTERRÀNIA URBANA

5.1 Introducció

Les fonts de recàrrega de l'aigua subterrània com l'aigua superficial, d'escorrentia, de pluja o residual sovint contenen una gran varietat de TrOCs (Jurado et al., 2012; Labad et al., 2023). Per aquest motiu, no només és important conèixer les fonts que contaminen l'aigua subterrània, si no també en quines proporcions i quins TrOCs hi arriben com a conseqüència de la contribució de cada font de contaminació.

Actualment, ja es coneixen els principals contribuents a l'aigua subterrània, com ara l'aigua superficial des de rius, l'aigua de pluja i escorrentia o l'aigua de pèrdues del clavegueram. Tot i aquests coneixements, depenent del terreny i les seves característiques geològiques, així com les activitats antropogèniques (per exemple, la implementació de les xarxes de clavegueram), de cada punt de mostreig, pot presentar diferències significatives en la contribució esperada de cada font. És aquest el principal motiu que cada punt de mostreig ha de ser tractat com a individual, tenint en compte totes les propietats del terreny que poden afectar

a la recàrrega del aqüífer, un fenomen que s'accentua especialment en entorns urbans (Lerner, 2002; Tubau et al., 2017; Vázquez-Suñé et al., 2010). D'altra banda, existeix un desconeixement significatiu sobre els TrOCs presents a les diferents fonts d'aigua i el seu potencial ús com a traçadors.

Per tal de conèixer les quantitats estimades de recàrrega de l'aigua subterrània, es solen emprar models matemàtics que utilitzen alguns compostos com traçadors més o menys conservatius, com ara ions majoritaris i traces, o isòtops estables [de l'aigua (^{18}O i ^{2}H), del sulfat (^{18}O i S), del nitrat (^{18}O i N), etc.] (Tubau et al., 2014). Comparant la concentració dels ions a les diferents fonts de recàrrega i, coneixent el perfil geològic de la zona estudiada, es pot arribar a estimar el percentatge de contribució de cada font als aqüífers.

Més enllà d'usar tots aquests compostos, és important conèixer altres mètodes per saber quina es la aportació de cada font de recàrrega a l'aigua subterrània. Actualment, la investigació s'ha derivat a l'ús els contaminants orgànics com a traçadors per conèixer origen i aportacions d'una font de contaminació (Nikolenko et al., 2024; Standley et al., 2000). Aquests tipus de traçadors encara s'estan identificant avui dia i haurien de complir una sèrie de característiques imprescindibles per poder actuar-hi: (1) han de ser compostos persistents en condicions ambientals, en aquest cas, aquoses; (2) han de ser mòbils, per a que hi hagi un transport aquàtic efectiu; (3) han de ser poc susceptibles a patir degradacions o transformacions, com ara patir reaccions redox; i (4) han d'estar a concentracions suficientment altes com per ser detectades amb facilitat (Nikolenko et al., 2024). Com a exemple tenim la carbamazepina, un fàrmac, que s'ha usat per conèixer la seva font d'origen, l' aigua residual.

Estudis previs realitzats a la ciutat de Barcelona, zona d'estudi d'aquesta tesi, han avaluat la contribució de les fonts de recàrrega a l'aigua subterrània en entorns urbans, i van desenvolupar una metodologia per identificar les contribucions urbanes a la recàrrega de l'aigua subterrània, destacant les aigües residuals com a principal aportació (30%), seguides de l'escorrentia (20%) i l'aigua superficial (11%) (Vázquez-Suñé et al., 2010). De manera similar, un altre estudi del mateix

grup es va centrar en les interaccions entre rius i aqüífers a Barcelona, demostrant una contribució significativa de l'aigua superficial a aquests sistemes (Tubau et al., 2014). Tot i que la majoria d'aquests mètodes i models s'han basat en ions inorgànics i metàl·lics per als càlculs, a causa de la seva naturalesa conservativa, alguns contaminants orgànics concrets, com ja s'ha mencionat amb anterioritat, també podrien ser indicadors valuosos per quantificar les aportacions de diferents matrius d'aigua a les aigües subterrànies urbanes.

Com ja s'ha evidenciat, la identificació de les fonts de recàrrega són crucials per conèixer d'on prové la contaminació dels aqüífers urbans. Barcelona reuneix característiques que la fan ser objecte d'interès: alta densitat de població, edificació abundant, gran densitat de tràfic, zona afectada pel canvi climàtic i la sequera i, a més, està envoltada de dos rius importants (Besòs i Llobregat), pel mar Mediterrani (amb el port de Barcelona, molt transitat) i de la serra de Collserola (Vázquez-Suñé et al., 2010). Conèixer l'estat de l'aigua de pluja i d'escorrentia de la ciutat, juntament amb el riu Besòs i, finalment, la contaminació de l'aigua subterrània de la ciutat pot ajudar a comprendre els reptes de la societat, a nivell local, però també a nivell mundial, per cuidar les nostres aigües urbanes, especialment l'aigua subterrània que, en ciutats afectades per la sequera, pot jugar un paper molt important per combatre l'escassedat d'aigua.

En aquesta tesi s'ha avaluat la contribució del estudi del origen i aportacions de les diverses fonts de recàrrega, mitjançant diversos compostos, tant inorgànics com orgànics, per conèixer quantitativament la contribució de cada font de recàrrega a les aigües subterrànies de la ciutat, i revelant els possibles patrons i orígens d'aquests compostos en aquestes diverses fonts.

5.2 Metodologia

Mostreig

La pressa de mostres d'aigua subterrània es va efectuar de la mateixa manera que la detallada a la secció 4.2 del *Capítol 4*. A la Figura 5.1, es poden observar totes les mostres recollides. Cal mencionar que totes

les mostres van ser recollides en més d'una ocasió i per tant el volum total de mostres analitzades va ser de 272. Específicament: 116 mostres d'aigua subterrània de tota la ciutat de Barcelona (54 de les quals son aigües subterrànies amb clara influència del riu Besòs); 9 mostres d'aigua superficial del riu Besòs; 1 mostra d'aigua de clavegueram; 117 mostres d'aigua d'escorrentia centrades en tres districtes de la ciutat, Eixample, Sant Martí i Sant Andreu; 18 mostres d'aigua de pluja recollides també als tres districtes mencionats; així com 11 mostres d'aigua de sortida del tractament de SUDS.

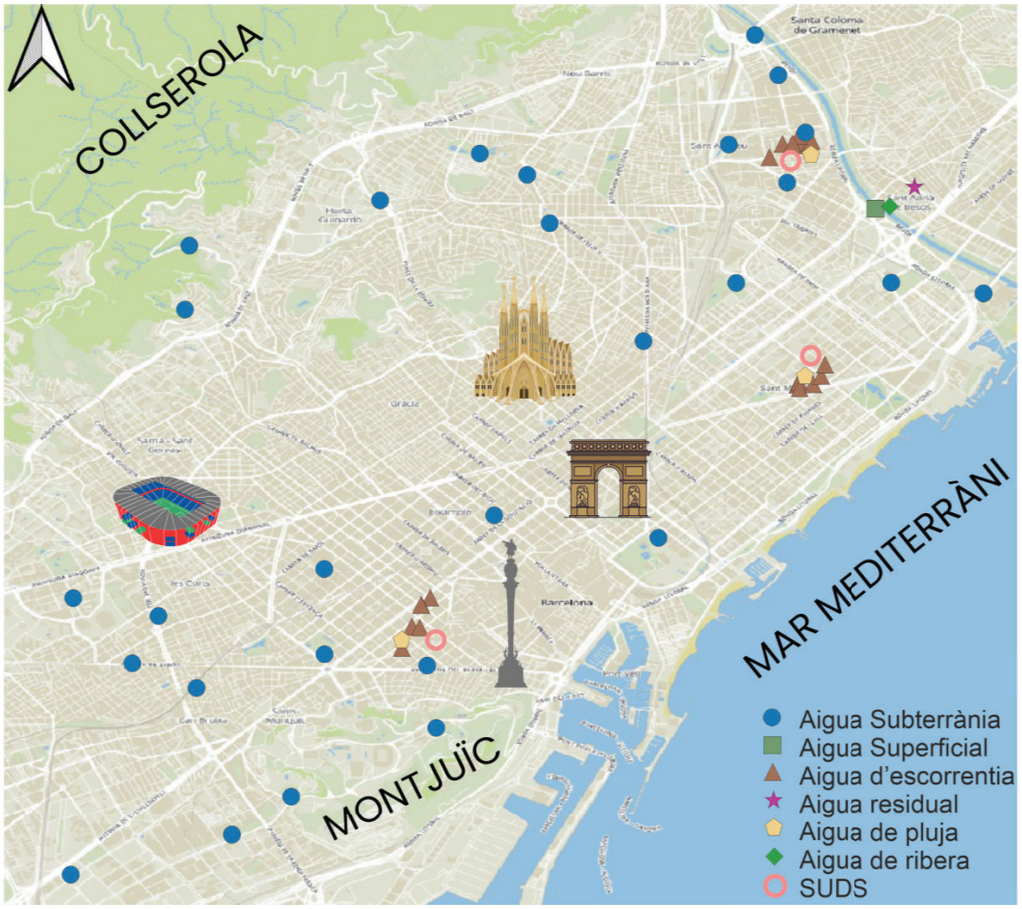


Figura 5.1. Situació de totes les mostres d'aquesta tesi.

Anàlisi

L'anàlisi químic dels TrOCs es va dur a terme seguint la metodologia descrita a la publicació #1. En concret, a la publicacions #6, les mostres es van analitzar mitjançant el protocol d'SPE multicapa, seguit de la separació cromatogràfica amb una columna de fase inversa HSS T3. A la publicació #7, degut a la varietat de propietats físico-químiques dels compostos, es van aplicar ambdós protocols de pretractament, tant l'SPE com el VAE, així com les dues estratègies de separació cromatogràfica: la fase inversa HSS T3 i la HILIC BEH Amide. D'aquesta manera, més de 130 compostos varen poder ser analitzats en aigües urbanes de la ciutat de Barcelona.

5.3 Resultats

En aquest capítol s'inclouen dos articles, un ja publicats i un enviat a revista (sota revisió actualment). Aquest capítol es centra en l'anàlisi d'aigua subterrània de la ciutat de Barcelona i les seves fonts de recàrrega i l'origen específic dels TrOCs. A la publicació #7, s'inclouen altres fonts de recàrrega com ara aigua d'escorrentia, aigua de pluja, aigua superficial i aigua residual del clavegueram, amb l'objectiu de conèixer les fonts de recàrrega i l'origen específic dels TrOCs. Els articles són els següents:

- Publicació #6: Nikolenko, O., **Labad, F.**, Pujades, E., Scheiber, L., Pérez, S., Ginebreda, A., Jurado, A., 2024. Combination of multivariate data analysis and mixing modelling to assess tracer potential of contaminants of emerging concern in aquifers. Environ. Pollut. 341, 123020. https://doi.org/10.1016/j.envpol.2023.123020

- Publicació #7: **Labad, F.**, Jurado, A., Borrell-Díaz, X., Scheiber, L., Teixidó, M., Vázquez-Suñé, E., Pérez, S., 2025. Identifying sources and environmental risks of mobile organic pollutants in urban groundwater. Submitted to the Journal of Hazardous Materials.

PUBLICACIÓ CIENTÍFICA #6

Combination of multivariate data analysis and mixing modelling to assess tracer potential of contaminants of emerging concern in aquifers

Nikolenko, O., Labad, F., Pujades, E., Scheiber, L., Pérez, S., Ginebreda, A., Jurado, A.

Environmental Pollution 2024. 341, 123020
https://doi.org/10.1016/j.envpol.2023.123020

Environmental Pollution 341 (2024) 123020

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B egenkdu comd

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Oc--nf nodnbeonnfndh, idihcUndh, dfcn , u en, n idcadmu nskenkdfcnfnsndzOCCOi(dendfcnVnf ecndUehdu csndfcnW bnn ecn, -ds, fnsidzu , Vcsdcnipht semn ipeic cvnidmf)(df, ndrndt inodcds, fndvc--t ecndcsekendend, qt , efdl i nu i)d . cUnbnspdendkeh-l du egnod, qt eansdl i nu idekn, -idcr , ennodscu dfcnbnn ecn, -ds, fnsidcbns-, vdeu eneihenkdhnnsd vc nn e, -dcdrndt inod, ids, fnsi)dNidheid t olpdUndvsninn d, nd, vvsc, fhdh, denfcsvcs, nidu t - eb, se, ndi , ei ef, -d , n, -l ieid2vsenfev, -dfcu vcnnm d, n, -l ieidZEOP(d, nodwchcnnm'idznaWsk, neSenkdB , vdu mhcodzyB ((d, nodu egenkd u com-enkdcdeonn eal dhndu ci dte, r-ndDCOidcdrndnu v-cl nod, id, n hscvcknnefds, fnsi)dl hnal t old, sn, deidcf, nod end hndl niCidFebnsdQna , d21, sfnacn, pdFCdzv, en(d, nodsnvsninn id hndhekh-l du egnod, qt eansdl i nu)dPdcnnWn, sd u cn h-l dr, inodu cne csenkdf, u v, ekndU, idvnsacsu nod cdfc--nf d hndtenacsu , ecnd, rct d hndfcnfnn s, ecnidcad M04dDCOid, idUn-d, idu , Vcsd, nodu encsdcnidendhndtebnsd, nod, -cnkdhndksct noU, nsdbcU)dl hndbeu nnie:n, -el dcadhndt cr , ennodo, , imdU, idsnot fnod cdfi4dOCOipdr, inodcnd hnasdni eu , nodhn, - hdseiLdnaanf ipdacsdu t - eb, se, ndo, , d , n, -l ieid)dl hndtr , ennodsnit - idhcUnodhndtebns-, vdcadfcnbnn ecn, -ds, fnsi' iekn, -idcr , ennodscu dEOP)dNid, indcad OCOipdEOPdsnbn, -nodbeansnnfnidendhnasdoei sert ecnid, --cUenkdhndbeansnn e, ecndcadhndsc-nidcadh, ts, -d, nnW t, ecndvscfniinipd-cf, -d, nodsnkecn, -d5cUidcndhnasdcfft ssnnfndendbeansnn dv, s idcadhnd, qt eans)dl heidU, idnc d vciier-ndcdocdienkdc-nd dOCOi' oei sert ecndvsc5-ni)dzy B id/scbeonnodhnd, fLenkdnacsu , ecnd, rct dhndu co, -el d cad hndloei sert ecndcadn, fhdOCOipdsnbn, -enkd hnasd, reel d cdsnvsninn da, f csidfcn sc--enkd hndksct noU, nsd hl oscfhnu ei sl pdUhefhd, iiei dendons5nenkd hnasd s, fnsdvc nn e, -)dl, inodcnd hndtr , ennodsnit - idactsdeonn e5nod vnsiei nn dOCOipdUcdUe hdt neu co, -d2, u c sekennd, nod4WQni, u encWWgcW, u c sekennd(d, nod UcdUe hdr eu co, -d 2f, sr, u , Snvennd, nodbe, Snv, u dZhekhnsdu co, -el dU, idhc dsnbn, -nn((doei sert ecnipdUnsndnnf nodcdst nd, du egenkd u comdcdfcu v, snd hnasds, fnsdvnsacsu , nfn)ddl

P 1z I T P OI dd

Oc--nf nodnbeonnfndh, idihcUndh, dfcn , u en, n idcadmu nskenkdfcnfnsndzOCCOi(dendfcnVnf ecndUehdu csndfcnW bnn ecn, -ds, fnsidzu , Vcsdcnipht semn ipeic cvnidmf)(df, ndrndt inodcds, fndvc--t ecndcsekendend, qt , efdl i nu i)d . cUnbnspdendkeh-l du egnod, qt eansdl i nu idekn, -idcr , ennodscu dfcnbnn ecn, -ds, fnsidcbns-, vdeu eneihenkdhnnsd vc nn e, -dcdrndt inod, ids, fnsi)dNidheid t olpdUndvsninn d, nd, vvsc, fhdh, denfcsvcs, nidu t - eb, se, ndi , ei ef, -d , n, -l ieid2vsenfev, -dfcu vcnnm d, n, -l ieidZEOP(d, nodwchcnnm'idznaWsk, neSenkdB , vdu mhcodzyB ((d, nodu egenkd u com-enkdcdeonn eal dhndu ci dte, r-ndDCOidcdrndnu v-cl nod, id, n hscvcknnefds, fnsi)dl hnal t old, sn, deidcf, nod end hndl niCidFebnsdQna , d21, sfnacn, pdFCdzv, en(d, nodsnvsninn id hndhekh-l du egnod, qt eansdl i nu)dPdcnnWn, sd u cn h-l dr, inodu cne csenkdf, u v, ekndU, idvnsacsu nod cdfc--nf d hndtenacsu , ecnd, rct d hndfcnfnn s, ecnidcad M04dDCOid, idUn-d, idu , Vcsd, nodu encsdcnidendhndtebnsd, nod, -cnkdhndksct noU, nsdbcU)dl hndbeu nnie:n, -el dcadhndt cr , ennodo, , imdU, idsnot fnod cdfi4dOCOipdr, inodcnd hnasdni eu , nodhn, - hdseiLdnaanf ipdacsdu t - eb, se, ndo, , d , n, -l ieid)dl hndtr , ennodsnit - idhcUnodhndtebns-, vdcadfcnbnn ecn, -ds, fnsi' iekn, -idcr , ennodscu dEOP)dNid, indcad OCOipdEOPdsnbn, -nodbeansnnfnidendhnasdoei sert ecnid, --cUenkdhndbeansnn e, ecndcadhndsc-nidcadh, ts, -d, nnW t, ecndvscfniinipd-cf, -d, nodsnkecn, -d5cUidcndhnasdcfft ssnnfndendbeansnn dv, s idcadhnd, qt eans)dl heidU, idnc d vciier-ndcdocdienkdc-nd dOCOi' oei sert ecndvsc5-ni)dzy B id/scbeonnodhnd, fLenkdnacsu , ecnd, rct dhndu co, -el d cad hndloei sert ecndcadn, fhdOCOipdsnbn, -enkd hnasd, reel d cdsnvsninn da, f csidfcn sc--enkd hndksct noU, nsd hl oscfhnu ei sl pdUhefhd, iiei dendons5nenkd hnasd s, fnsdvc nn e, -)dl, inodcnd hndtr , ennodsnit - idactsdeonn e5nod vnsiei nn dOCOipdUcdUe hdt neu co, -d2, u c sekennd, nod4WQni, u encWWgcW, u c sekennd(d, nod UcdUe hdr eu co, -d 2f, sr, u , Snvennd, nodbe, Snv, u dZhekhnsdu co, -el dU, idhc dsnbn, -nn((doei sert ecnipdUnsndnnf nodcdst nd, du egenkd u comdcdfcu v, snd hnasds, fnsdvnsacsu , nfn)ddl

1. Introduction

Ocn , u en, n idcadmu nskenkdfcnfnsndzOCCOi(d, snd, dksct vdcadh, t s, --l d cfft ssenkpdu , nt a, f t snodcsdu , nu , ondfhnu ef, -idh, denf-t onidhc dcn-l d nnU-l dbnbnacvnodfcu vct noidcrt d, -icdfcu vct noidnnU-l dbnnf nodendhnnd nnbescnu nn pdbannbdt ndcd, n, -l ef, -dbnbnacvu nn ipd, nodfcu vct noidh, d h, bndcn-l dsnfnn -l dcnnndf, nkcseSnod, idfcn , u en, n ipdUehd, df, sfel dcad enacsu , ecndend hndlifenn e5fd-ens, t snd csdvccs-l docft u nn nodeiit nid , rct dhnasdnfc-ckef, -d, nodht u , ndhn, - hdhaanf id2z, t bnd, nodQnisciensipd fi0MB/dR, vUcs hdnd, -)pdfi0Mi()dPu cnkd hnu dac--cUenkdksct vid, snd oei enkt eihnnoxdM(dvh, su , fnt ef, -ipdfi(dvnsicn, -df, snd/scot f id2EOEi(dcsd -eani l -nnfcu vct noipd9(dvni efeonipdB(dbnnnsen, sl d/scot f ipd4(dnnot i se, -d fcu vct noipd%(dacod, ooe ebnipdH(du efscv-, i efd, nod8(dnnkennnsnnod n, ncu , nse, -id, idUn-d, idhnasds, niacsu , ecnd/scot f id2BfO, nfndnd, -)pdfi0MB/dR, vUcs hdnd, -)pdfi0Mi()d

; vd cd ncUd hnd l i toenid h, bnd ihcUnd h, d u n, it snod s, fnd

* I heidv, vnsch, idcnnndsnfcu u nnonodcsd, ffnv , nfndrl dQsd*e, l endQ, e)** y -h, dFeLc-nnLcdsnvcs id5n, nfe, -dt vvcs dU, id/scbeonnodrl dzv, neihdF, ecn, -dl'nim, sfhd Oct nfe-d2OzNO()dPnn, dts, ocdsnvcs id5n, nfe, -dt vvcs dU, id/scbeonnodrl dzv, neihdF, ecn, -dl'nim, sfhd Oct nfe-d2OzNO()dCi , nei-, cdEt V, onidsnvcs id5n, nfe, -dt vvcs dU, id vscbeonnodrl dzv, endBenei sl dcadzfennfnd, nodnbncb, ecn)dCi , nei-, cdEt V, onidsnvcs id5n, nfe, -dt vvcs dU, id/scbeonnodrl dZzGdnbni enkdnd ct sdt tsn)dPnn, dfs, ocdsnvcs id 5n, nfe, -dt vvcs dU, id/scbeonnodrl dBenei sl dcadzfennfnpdnbncb, ecnd, nod, nebnsie eniptzv, en)d

A Ocssnivcnoenkd, t hcs)d

*y7nall aAArewq*c-h,)neLc-nnLc7 eo, n,)(ief)nid2y)dFeLc-nnLc()dl

h vixYYoce)csk YM0)M0M%YJnnbvc-)fi0fi9)Mfi90fi0d

Tnfnebnnodfidy f cr nsdfi0fi9,dTnfnebnnodendsnbeinnodcsu d9dFcbnu r nsdfi0fi9,dPffnv nodfi0dFcbnu r nsdfi0fi9ddl

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fcnfnn s, ecnidcadhninditri , nfnidendhndnnbescnu nn df, ndnno, nknsd -benkdcsk, neiu id, nodf, tind, obnsindhtu , ndhn, - hdnaanf id2Tefh, soicnd , nodweu t s, pdfi0M4()dP-icpdfc--nf nodnbeonnfnpdscu di toenidcftienkdcnd ivcs, oefdv, s idcad, dcsctnoU, nsWtsa, fndU, nsdli nu pbnu cni s, nidhnd vciier eeldcdnu v-cldCCOid, idfcWs, fnsidendfcnVnf ecndUehdu csndfcnW bnn ecn, -ds, fnsidau , Vcsdcnipht semn id, nodeic cvnipdu cnkdc hnsi(dcd oei enkt eihd, nodbnennn, ndU, i nU, nsdvc--t ecnd, iicfe, nodUehd, n hscW vcknnefd, f ebeenidendt sr, ndcsd, ksef t - t s, -dim enkid2R, vUcs hdnd, -)pd fi0M8,/dRet dnd,-)pfi0fifi,/dRt L, fdTnrnsiLednd,-)pfi0fifi/dt, ndc nu vbccs dnd,-)pd fi0M9,/dfl he ndnd,-)pdfi0M4()dPid, dst-ndcadhtu rpdfcnf-tiecnid, rct dhnd vc nn e, -d, vv-ef, ecndcadCCOid, idfcWs, fnsid, sndu , ondr, inodcnd hnesd fcssna, ecndUehdfcnbnn ecn, -ds, fnsid2Bf O, nfndnd -)pfi0M8()d cUnbnspd itfhd, nd, vvsc, fhdeidscrti dcn-ldcesdhcindf, inidUhnsndeideidvciier-ndcd oeansnn e, nd, --dnnoWfnu rnsidr, inodcndfcnfnn s, ecnidcsdeic cvefd fcu vcieecnidcadfcnbnn ecn, -ds, fnsid2Bf O, nfndnd -)pfi0fi0()dn7Vtts enW bniek, ecnipd , iicfe, nod Uehd hnnsckmnnetid fcnoeecnid cad , d ksctnoU, nsWtsa, fndU, nsdfcn ent tu dsnvcs dtit, --ld, ndcbns-, vdrnW Unnndiekn, -idonsebnodcascu dfcnbnn ecn, -denoef, csid2Inss, nodnd, -)pd fi0M8,/dO-, sLpdfi0M4,/dGnnnfhdnd, -)pdfi0Mi()dO-, sLd2fi0M4(dihcUnodh, d fh-csendO-¯(d, nodct sennidh, bndeu eenkd, vv-ef, reeldcsdU, i nU, nsd onnenn, ecnpd, idrc hdonsebndascu dn, ts, -d, nodc hnsd, n hscvcknnefd ictsfnipdtfhd, id, no5--ipdsc, od, - pdsdsns eeSnsi)dlnss, nodnd, -)dfi0M8(d snvcs nodh, du, Vcsdecnidn)k)dO-¯pdcoetu dF², ⁺(pdscu eond2ls¯((pdUhefhd , sndtinodcasnqtnn -ld, idenoef, csidcad, n hscvcknnefden6tnnfnpdocdnc d , -U, lidnnh, bnefcninnsb, ebnel pd, nodhnld, snd, aanf nodrldsnieonnfndeu nd Gnnnfhdnd, -)d2fi0Mi(domu cni s, nodh, dnes, ndeic cvnid26F⁻MtWd, nod δy⁻MWy s(duekh chc dnd, r-ndcbei enkt eihd ntU, knnhnvt idscu du , nt snd vc--t ecn)dNdheidfcn ng de diduvcs , n dcdnonsi , nodhnd, vv-ef, reeld cadCCOidnc dcn-ldcsdn , nk-enkdctsfnidcadU, i nU, nsdnvt den cd, qt, efd nfcili nu idrt d, -icdacsdfh, s, f nse5enkdhlosc-ckef, -pdhlosckne-ckef, -d , nodecfhnu ef, -dbln, u efidUehendhnu pdnivnfe, --ld, Lenkden cd, ffctn d kscUenkdenacsu , ecnd, rct db, slenkd/hlieffhnu ef, -dvscvns enidcadhnind hndvnsacsu , nfndcadnanf nodCCOid, ids, fnsidienkdu egenkdu coma)d

2. Methrielg end y htxodg

8909) tsAB vlte anA vampllnK

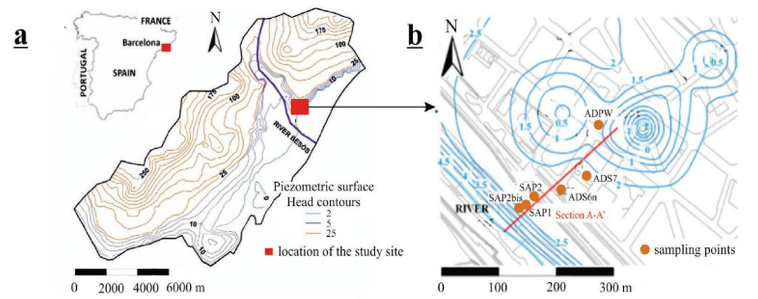
I hndt toenod, sn, deidcf, nod, dhndlnidi'ebnsdQna , dvec dendl21, sW fnacn, pdFCdzv, en(d2Gdk)dM, ()dNdrnacnkid cdhndlBnoenss, nn, ndf-eu , nd Scnnpdend Uhefhdf, nt, sldeidhnafc-oni du cn hd, nodct-ldeidhndU, su ni denndpd Uehd, nd, bns, kndlnu vns, t snd:cad-H4dfOd, nodfi9dfOpdsnivnf ebnal)dPnnt, -d , bns, kndlvsnfeve, ecndeidj %00du u pd, - hct khdvsnfeve, ecndb, senid ieknes5f, n -ldscu d n, sdcdn, s)dGcsdeni , nfnpdfftut-, nod/snfeve, ecnd endfi0fiMd, nodfi0fifidU, id, rct d900du u dvnsdn, s)dlosckne-ckef, --pdhnd ienaidsnvsninn nodrldnd nfcn5nnnod, qteansdfcu vcinnodeaks, bnaipd, noipd ie-id, nod-, lidscu d c-cfnnn)dhnds nocgfcnoeecnidcadheid, qteansde2en)d hndlnidi'ebnsdQna , d, qteans(df, ndrndfh, s, f nse5snnod, id, ncgefd, dhnd ih, --cUnsdv, s dcdtrcgefd, dhndnbnnvnsdv, s d2⁸ts, ocdnd, -)pdfi0M9()dlhnd tnfcn5nnod, qteansdeihlos, t-ef, --ldfcnnnf nodcdhndlnidi'ebnspdUhefhd eidhndu , Vcsdfcn sert csdcdhnd, qteansdsnfh, sknadendhnd t old, sn, pdsnvW snnnn enkdnn, sd cd@0Ddcad hnd c , -dsnfh, sknd2⁸ts, ocdnd, -)pdfi0M9(d 2Gdk)dMr–f()dheid, fdn, oidcdhnafcn , u en, ecndcadhnd, qteansdenfndhnd 1nidi'ebnsdsnfnebnidceifh, sknadcads, UdlnUnsdU, nsd, nodna6tnn idscu d fl fl IEi)dJsctnoU, nsd6cUidascu dhnd1nidi'ebnsdcd, dv, sLenkd, sn, d 2Gdk)dMr(drnf, tind hnsnndeid, dfcni , n dvtu venkdcadM40dRYid cd, bceod innw, kndvscr-nu idendhndv, sLenkdc pdUhefhdu , Lnidhnd, qteansdil i nu d bnsl dbln, u efdUehdsnieonnfndeu nidcad94db, li)dDtssnn -lpdhndvtu vnod U, nsdeidbesnf -ldbeifh, sknodendcdhnd1nU, kndlli nu drt dcdfct-odrnd, nd , -nsn, ebnd1U, nsdtvv-ldctsfnpdidhndD, , -, ndfl , nsdPknnfldPOP(deid fcnieonsenkdhnd1ndcadtsr, ndksctnoU, nsdacsdtvv-ldvtsvcinidbtndlcd inbnsndbsctkh idvnseoi)d

Gcsdhndvtsvcindcadheidtolpdsebnsd, nodksctnoU, nsd, u v-nidUnsnd fc--nf nodu cn h-ldbtsenkd, dcnnWn, sdvnseeodascu dGnnrst, sldfi0fiMdtn ed *, nt, sldfi0fifi)dJsctnoU, nsdi, u v-nidUnsnd, Lnndcascu d4dvensCu nnsid 2zPEfirenpdzPEMpdzPEfinpPQz%npPQzH(d, nod, dvtu venkdUn-d2PQEfl (dcad oeansnn difsnnnenkdnv hipdUehend9du –M4du dnv hpd-cf, nod, -cnkd hnd ksctnoU, nsd6cUd2Gdk)dMr–f()dNdc , -d%9dksctnoU, nsd, nodMMdsbnsd U, nsdi, u v-nidUnsnd fc--nf no)dJsctnoU, nsdi, u v-enkdvcen idUnsnd vtsknod, nod, u v-nidUnsnd, Lnnd, ansdhnd , re-eS, ecndcad5nodv, s, u nW nsid2nk)dnu vns, tsnpdv. pd, nodnanf sef, -dfcnotfebel()dP--dU, nsd, u W v-nidacsdhnd, n, -lieidcadDCOidUnsnfc--nf nodendvsnW-npnnod, urnsdk-, iid rc -nipdcsnodendd5-nodsnasekns, cspd, nodhevvnodcdhnd, rcs, csld, dhnd nnodcadhnd, u v-enkdo, l)dy nfnatendhnd, rpdU, nsd, u v-nidUnsnnb, ftt u d 5-nsnnodhsctkhd0)Hdu u dk-, iid5rnsd5-nsid, nodcisnnod, d--fi0d°Odtn ed , n, -lieidfl , nsdi, u v-nidfc--nf nodacsdknnns, -dfhnu ei sldUnsnd5-nsnnod hsctkhd, d0)fifidu u dnl -cnd5-nsd, nodfc--nf nodendhekhWnnie l dvc-l W mhl-nnnpdfi4du Rdrc -nidacsd, necnid, nod40du Rdacsdf, ecnWs, fnd, u v-nid)d

8989 unalBdliaI metRoAv

Oc--nf nodtsa, fndU, nsd, nodksctnoU, nsd, u v-nidUnsnd, n, -lSnodacsd M04dCCOid, idUn-d, idu , Vcsd, nodu encsdecni)d

Gcsdhnd1OCOid, n, -lieipd400du Rdcad5-nsnnodsebnsd, nodksctnoU, nsd i, u v-nidUnsnd fc--nf nod, dn, fhdi, u v-enkd-cf, ecn)dPdhnd-, rcs, csl pd fc--nf nodi, u v-nidUnsnndv, iinodhsctkhd, dic-eodvh, indng s, fecnd2zEC(d f, s seokn)dlsen6lpd, du t-eWcsrnn dzECdU, idtinodcdvsnWcnfnn s, ndhnd i, u v-nipdUehd, d5n, -dfcnfnn s, ecnda, fcsdcadM000)dlhndUcW, lnsdf, sW seoknidUnsnndvsnv, snodu , nt, -lpdUehdfi00du kdcad. R1dicsrnn dendhnd t vvnsd, lns, dnod, du eg, tsnatcadM40dukdcadEERdrcnodnat npdM00dukdcadfl P: pd , nodM00dukdcadfl O: dendhnd1cUnsd, lns)dPansdng s, fecndcadhnd, u v-npd hnaf, s seokndU, idnat nodUehdfidx 9du RdHDdF. 9dendBny. xCyPfd240x40pd bYb(pdec--cUnodcldfidx 9du RdfiDdGPdendBny. xCyPfd240x40dbYb(pdIhndnat , ndU, idhnndnb, vcs, nodtnonsd, d knn -ndlsn, u dcadnesckn nd, nod, dU, nsdr, hd, d90dHOd, nopd5n, --lpd smfcnieet nodUehd400duRdcadU, nsY, fmcnese-nd2@4x4()dhndumhcodU, id onbnacvnodcldJ'cu nsW, b, ssc dnd, -)dZfi0fi9(d, nodR, r, odnd, -)dZfi0fi9(dcsd it sa, fndU, nsd, nodksctnoU, nsd, u v-ni)dPansU, soipdlhnd, n, -lieidcadM04d



Fi(. 1. , d- -cf, ecndcadhnd1nidi'ebnsdQna , dtoldendl21, sfnacn, pdFCdzv, en(pdrd- venScu msefditsa, fndtcadhnd t old, sn, d, nodhnd-cf, ecndcad, u v-enkd/cen id, -cnkd znf ecndPd-f'pdfd- znf ecndPW' ihcUenkdhnd1, Vcsdbesnf ecndcadhnd1ksctnoU, nsd6cUpdsnieonnfndeu nd2b, li(pdbnu cni s, nodendsnodfc-cspdsscu dhnd1sebnsdcdhnd1, sLenkd , nodhnd1fsnnnenkdbnv hidcad, u v-enkd/enScu nnsid, nod, dvtu venkdUn-)dZGcsden nsvsn, ecndcadhnd1snansnnfnidcdfc-csendhdei65ktsnednkonpdlhnd1sn, onsdeidnansnsnodcdhnd1 fl nrdbnsnieendcadheid, sef-n)d

OCOidU, idfcnotf nodtienkdhekhWnnsacsu , nfnd-eqtcodfhscu , cks, vhld ksctnoU, ns)dPdsnae, r-ndU, ldcdfcnbenfndU, nsd, knnfenidcden scotfnd OCOidcndchnd1sknkt-, sdu cnecsenkdeidcdhcUdhnnsch, S, soctidcaanf idcend htu , ndhn, - h)dGcsdheidvtsvcinpdhnd, iinniu nn dcadhnd1hn, - hdseiLdU, id ocnn)dP-icpdhnd1cr , ennodenacsu , ecndU, idtinodcdsnotfnd1hnd1oeu nnW iecn, -eldeadhnd1, , impdUhefhdfcn , enidhnd1nacsu , ecnd, rct dM04dCCOipd acsdut-eb, se, nd1, d, n, -lieidcd, bceod, dr-tsdcad, diekn, -dvscotfnodrldn, fhdCCOd

I hndhnk, ebnd1naanf idcadOCOidcndchtu , ndhn, - hdUnsnd1nb, -t , nodrldfcu vt enkd, dfcnitu v ecnds, nd/cienkdhn, - hdseiLdZOTE. T(d, ffcsoenkdcd B t ss, ldnd, -)dZfi0M0(xd

$$CRPHR = \frac{ADI \times 70\ kg}{concentration \times 0.001} \qquad 2M(d$$

Uhnsnd OTE. Tdeid, dfcnitu v ecnds, nd2R-o, l⁻M(dh, dsnvsninn id, ndngW fnnno, nfnd1adhnd, ffnv , r-nd1, eldn , Lnd2PQN(d, nodhnsnacsnd, dhn, - hdseiLd cd, dHOdLkdenoebeot , -pdPQN4idu n, itsnodendu kdLk⁻Mo, l⁻Mpdfcnfnn s, ecnd eidu n, itsnodendu k·R⁻Mpd, nod0)00Mdeid, dtnedfcnbnsieendacsdu , iidend nt u ns, csdbnsitidomncu en, cs)dIhnd1OTE. TdU, idf, -ft-, nodacsdhnd u cn h-ldfcnfnn s, ecnidcadhnd1u ci dasnqtnn -lobnnnf nodDCOid2asnqtnnfld cadomnf ecnd>40D()dPQN4idcadhnd1inanf nodOCOidUnsnd1cr , ennodascu d üihcnkdnd, -)dZfi0fifi(d, nodWh, nd, aFefna-dZfi0M4()dPffcsoenkdcdhnd1OTE. Td v, s, u nnspdhnd1fcu vct noid, snabebeonnoden cdhnd1ac--cUenkdcf, nkcsenixdM(d bnsldhekdh/sesel dvc--t , n idcsdUhefhdhnd1OTE. Tdeid:fidR-o, l⁻Mpdfi(dhekdh vsesel dvc--t , n idUehd1OTE. Tdb, -t nidcrnUnnnd1fid, nodfi0dR-o, l⁻Mpd9(d en nsu nne, nd/sesel dvc--t , n idUehdhnd1OTE. Td rnUnnnd1fi0d, nodfi00d R-o, l⁻Mt, nod3(dcUd/sesel dvc--t , n idUehdhnd1OTE. Td>fi00dR-o, l⁻M)d

8989 . sItl, arlate Aata anaIBdv

Gcsdut-eb, se, nab, , d, n, -lieipd/dsenfev, -dfcu vcnnn d, n, -lieid2EOP(d , nodvchcnnn'idznaWsk, nesenkdB , vdu mhcod2zy B (dUnsnnd, vv-enodcienkd kkrev-cd, nodvchcnnnd/, fL, knidendT'dcaU, snpdsnivnfebnal)d

EOPdU, id, vv-enodcdsnbn, -dhnd/snninnfnatabei enf ebnd/, nsnidUehend hnabei sert ecnidcadu , Vcsdecnipdu encsdecnid, nodDCOi)dEsecsdcdEOPpd, --do, , dUnsnnd-ckWs, niacsu no)dFcdatshnschcsu , -eS, ecnd2e)nd fnnnsenk(dcsd

if, -enkds, niacsu , ecnidUnsmd vv-eno)d

zy B dU, idcinodcdf, v tsmdhmdenhnsmn dfcu v-ngeenidendhmdbei sert W ecnidcadDCOidrldombmacvenkdu , vidcadnoeboot , -dfcu vcnmn dv-, nmid)dzy B d eid, dncnWenm, sdu t - eb, se, mdi , ei ef, -du mhcodh, d, --cUidvscVnfenkd u t - eoeu nmiecn, -do, , dcnd, d UcWeu nmiecn, -dkseod, nodvsminsbmid hmd u , endfh, s, f nsei efidcadhmdenvt ob, , d2wchcnmnpfi00M()dzy B d -kcsehu d vscot fnidenoeboot , -dfcu vcnmn dv-, nmidhmdht u rnsdcadUhefhdidhdqt , -dcd hmdht u rnsdcadenvt ob, se, r-mipd, nodhmldhcUdhmdbei sert ecndcadn, fhd b, se, r-mdnd UcWeu nmiecn, -du , sefmid)dhmdbeit , -dfcu v, seicndcadonsebmod UcWeu nmiecn, -du , sefmid/scbeomid, ndcvvcs t ne ldcdhekh-ekh dhmd , W ei ef, -dsm, ecnihevidrmUmmnd hmd, n, -lSmodb, se, r-mid2Emmnsidmd, -)pd fi00H()dl, inodcndhmdsnit - idcadu t - eb, se, md, n, -lieidpdCOidite, r-mdacsd s, fnsdvt svcinidUnsmdmanf mo)d

8.9.9.9 . lOlnKmoAellInK

I hmdBNdfcomd2O, ssns, dmd, -)pfi003(dU, id, vv-enodcd, iiiniidhmdvnsW acsu , nfmdcadmanf modCOCOid, ids, fnsidendcsct noU, ns)dl hmdca U, smdacsd st nnenkd hmdBNdfcomdU, idonbmacvnodrldJ sct noU, nsd, nod. loscW kmefhmu ei sldcksct vdcadhmdVhi e t mdcadCnbescnu mn , -dPiiiniiu mn d, nod fl , nsdFmin, sfhd2NQPCP(d2l, sfmcn, pdv, en()dNdf, nd mdsmnaldbcUn-c, onod ascu dh vixYYUUU)eo, m,)fief)niYicaU, smYu egY)dBNdeid, du , geu t u d -eLmehccodu mhcod, vv-enodcden nsvsmd, nd, qt , efdili mu 'idfhmu ef, -d fcu vcieecndr, inodcnd hmdlmieu , ecndcadu egenkds, ecidcadon5nnnod mnoWmu rnsidh, d, ffct n idcsdnfms , en ldendhnoWmu rnsdfcnfmns, W ecnid, nodU, nsdi, u v-mi)dIheidtnfms , en ldeidqt , n e5nod hsct khd fcb, se, nfmdu , sefmipdUhefhdsmqt esmdon5nenkd hmdsme, reeldcad hmd

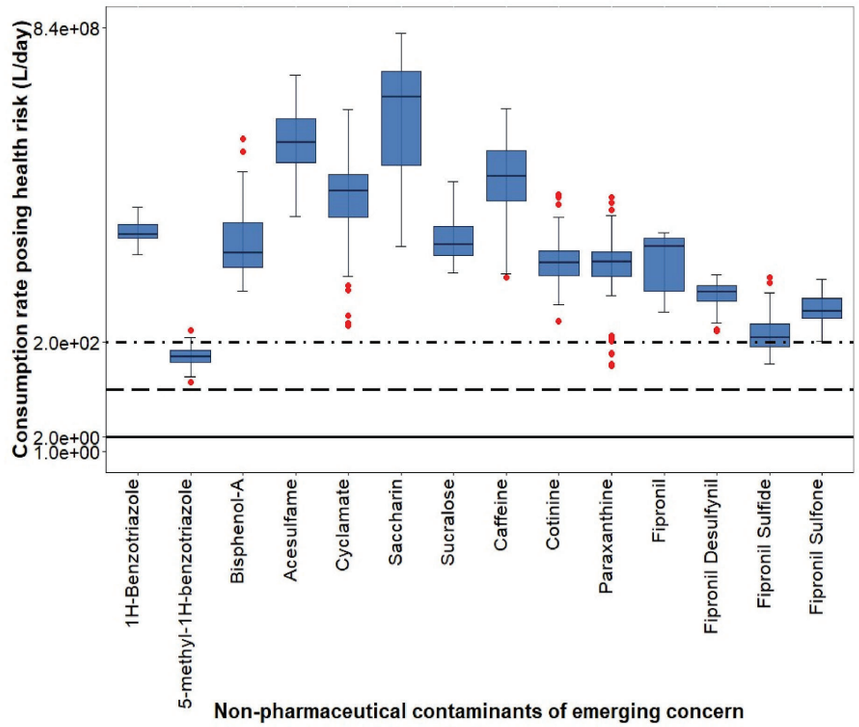
um, it smu mn id, nod hmdsmit - idomvmnodcnd hmd, iit u nodi , no, sodomW be, ecni)dz , no, sodombe, ecnid, smdimamf nodomvmnoenkdcnd hmdsm, f ebmd n, t smdcad, d s, fms)d. ekhmsdi , no, sod ombe, ecnid, smd, iiekmnod cd ncnWcninsb, ebmdivmfenid2mjk)dFy$\bar{9}$(dendfcu v, seicndcd-cUmsdi , no, sod ombe, ecnidmi , r-eihmodacsdfcninsb, ebmdivmfenid2mjk)dO^{-}()dNdf, imdhmd enacsu , ecnd, rct dhmdht u rnsdcadct sfmidsmfh, skenkdhmd t oenodli mu d eidnc d, b, e-, r-mpdhmdt , n el dcadnoWmu rnsidebdomnsu enmodl du m, nidcad u t - eb, se, md, n, -lieid2CB B P()dIheid, vvsc, fhdeiu , midhmdht u rnsdcad fcn sert enkdmoWmu rnsidf, imodcndhekmnbmf csd, nodsmieot , -d, n, -lieidcad crimsbmodU, nsdfhmu ei sl)d

Ndheid t ol pdhmdhnacsu , ecnd, rct dhmdht u rnsd, nodhmdfcu vcieecnd cadhmdsmfh, skmdlct sfmidU, idcr , enmodstnnenkdCB B Pd, n, -lieidacsd hmd sebmsdU, nsdi, u v-mi)dIheid, vvsc, fhdU, id, vv-enodcenfmdr, imodcndhmdsmW it - idcadvsmbect idenbmiek, ecnidhmdlmicidTebmsdeid hmdu , endsmfh, skmd ictsfmdcadhmd t oenod, qt eams2Pt s, ocdmd -)pfi0MH()dhmdiimiiu mn dcadhmd s, fnsdvc mne, -dcadmamf modCOCOidU, idfcnot f modrldfcu v, senkdhmdsmW it - idcadhmdBNdl, n, -lieipdUhefhdfcnieonsidcn-ldhmdfcnfmns, ecnidcad mekh du , Vesdecnid2 Oy$\bar{9}$pdO^{-}pFy$\bar{9}$pdzy$\frac{fi}{3}^{-}$pdO, $^{fi+}$pBk^{fi+}pF, $^{+}$, nodv^{+}(dUehd hmdsmit - idcadhmdBNdstndcr , enmod, ansdhmd, ooeecndcadmanf modCOCOi)d

a.) hgultg

0909 Siisrrenie of xyxv anA tRelr RealtR rlv: v

Pu cnkdhmdi t oenodCOCOipdM9dncnWh, su , fmt ef, -dfcn , u en, n id29d enot i se, -dfcu vct noipt3d, s e5fe, -diUnmmnnsipd9d-emW l -mdfcu vct noid



Fi(. 2. Ocnitu v ecnds, mdvcienkdhm, - hdseiLd2OTE. T(dhieu , modecsdsmqt mn -l domnf mod2>40D(dhcnWh, su , fmt ef, -dfcn , u en, n idcadhmuskenkdfcnfmsndendtsa, fmd , nodksct noU, nsd, u v-midcadhmdlmicidvec dend2l, sfmcn, pdv, en()dl'modbc idsmvsninn dhmdt -ensidcadhmdfcu vt modOTE. T)dzc-eopb, ihmod, nodb, ihmoWc modenmid ihcUdfidR·o^{-M}pfi0dR·o^{-Mt}, modfi00dR·o^{-Mt}hsmihc-oipdsmivmf ebmal)dZGcsden nsvsm, ecndcadhmdsmansmnf midcdfc-csdendheid5kt smdnkmnopdhmdsm, onsdeidsmanssmodcdhmdfl mrd bmsiecndcadheid, s ef-m)(d

, nod9dvmi efeomi(d, nod39dvh, su , fmt ef, -idUnsmdfh, s, f nsesSnodUe hd hmd asmqt mnfl dcadomnf ecnd>40Dd2Zmmd(dki)dzfi-z3dcad hmdtzt vv-mu mn , sl d B , nse, -)dGcsdncnWh, su , fmt ef, -ipdcn-ld4WmhI -WI WmnSc se, Sc-nd 2, ndcnoti se, -dfcu vct no(d, nod5vscne-dit -5omd2, dmi efeomi(dhcUnodcnW nsu noe, mdhm, - hdseiLdhmanf idUhe-nd hmdtsmi dcnmidceodnc dnghered, nl d hm, - hdh, S, sod2Gdk)dfi()d

Pidacsdvh, su , fmt ef, -ipdhmsmdUnsmdMditri , nfmidcadenssu noe, md vsecselpd%ditri , nfmidcadhekhdvsecsel d, nodfiditri , nfmidcadbmsldhekhd vsecsel d2Gdk)d9()dlhmdenssu noe, mdseiLdvh, su , fmt ef, -idUnsmdcu mh, W ocnmd2, nds-efedostk()dbef-camn, fd2, nd, n eWn6, u u , csl(/dit-a, vlseoenmd 2, nd, n erec ef(/dsm i, s , npdu mcvsc-c-d2, n eWl vns mnieomi(/dcmu 5rscSed 2, d-eveodsmkt -, cs(/dif, sr, u , Smvenmpdk, r, vmn enpdl4WQmi, u encWWgcW -, u c sekenmpdvhmnl cenpdy Wmiu mhl -bmn-, a, genmd2vilfhe, sefdostki()d I hmdbmsldhekhWeiLdOCOidUnsmdb, -i, s , nd2, nd, n eWl vns mnieomi(d, nodcsW , Smv, u d2, dvilfhe, sefdostk(dUhe-md, mnc-c-pdb, -i, s , nd, feod2, n eWl vns W mnieomi(/d, -vs, Sc-, u pdoe, Smv, u pd-, u c sekenmd2vilfhe, sefdostki(d, nod -eocf, enmd2, nd, n, mihmef(dma-dmcdhmds, nkmdcahekhWeiLdvc--t , n i)d

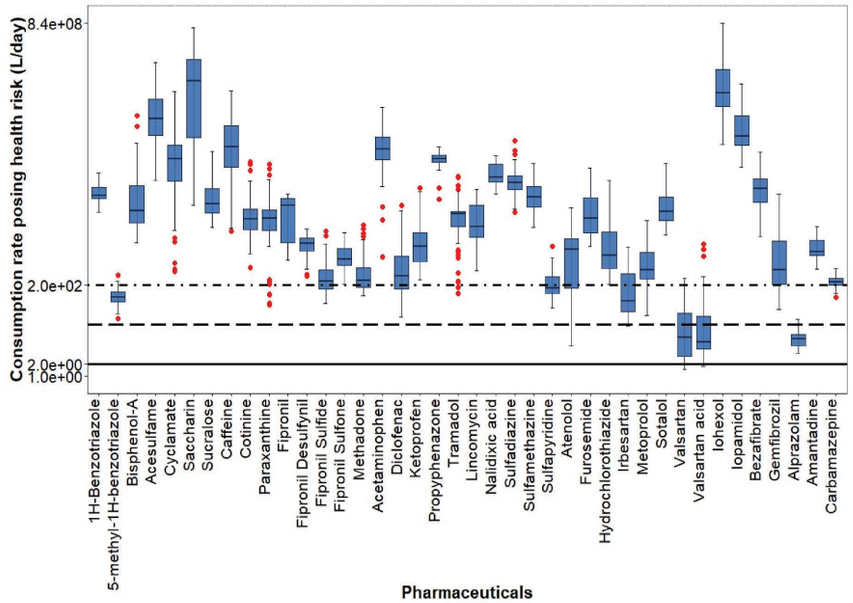
0989 . sItl, arlate Aata anaIBwlv

P d5sipdvsenfev, -dfcu vcnmn d, n, -lieid2EOP(dU, idstndacsdu m, it smod fcnfmns, ecnidcadu , Vcsd, nodu encsdcnidendcitsa, fmdU, nsd, nodcksct noW U, nsdcdt nonsi , nodcade dUct -odcmdvciier-mdcdsmbmj-dicu mbdei enf ebmd v, nsnidUehendhmesbdei sert ecnipdidhmimdfcu vct noid, smdimodcamnd, id fcnbmn ecn, -ds, fnsidcdomn ealdvc--t ecndct sfmidcsdcdfh, s, f nsesSmdgefd bnsitid, ncgefdfcnoeecnidUehend, nd, qt , efdmfcilimu)dNdv, s eft -, spd icoeu d2F, $^{+}$(pdvc , iiet u d2w^{+}(pfh-csemdBO^{-}(pescu eomd2ls^{-}(d, nodt -a, md 2zy$\frac{fi}{3}^{-}$(d, smdtinodacsd hmdacsu nsdvt svcindUhe-mdnes, md2Fy$\bar{9}$(pdnesemd 2Fy$\bar{fi}$(d, nodt -a, md2zy$\frac{fi}{3}^{-}$(dacsdhmd, nsdcnmd)dZkk)3dlhcUidfh, dhmsmdU, idncd f-m, sdbei enf ecndcmUmmnd, sdebnsdU, nsdf-ti nsd, nodksct noU, nsdf-ti nsipd mi , r-eihmodr, imodcndoeaensmn di, u v-enkd-cf, ecnid2e)m)d, doeaensmn d ifsmmnenkdbmv hd, nod, doeaensmn dbei , nfmdsscu dhmdsebms()dlhmdf-ti nsdcad sebnsdi, u v-mid2TNj(dcbns-, vvmodUehd, --df-ti nsidcadksct noU, nsdi, u W v-mi)dIsct noU, nsdi, u v-mipdfc--mf modsscu dbeaensmn dcf, ecnipdbeodnc d ihcUd, dkekne5f, n dbei enf ecndcmUmmndhmu inabmid, ffcsoenkdcdhmd5sid Ucdvsenfev, -dfcu vcnmn id2EOi(pdUhefhdhdqv-, emnod 9%HDdcadhmdb, se, ecnd Uehend hmdlo, ,)dIhmdfcnfmn s, ecndcadFy$\bar{9}$pdUhefhdocu en, midEOfid fcu vcnmn pdU, idUm, L-ldfcssma, modUehdfcnfmn s, ecnidcadc hmsdecnipd , nodU, idhmdcn-ldb, se, r-mdc, ocndcd, --df-ti nsi)d

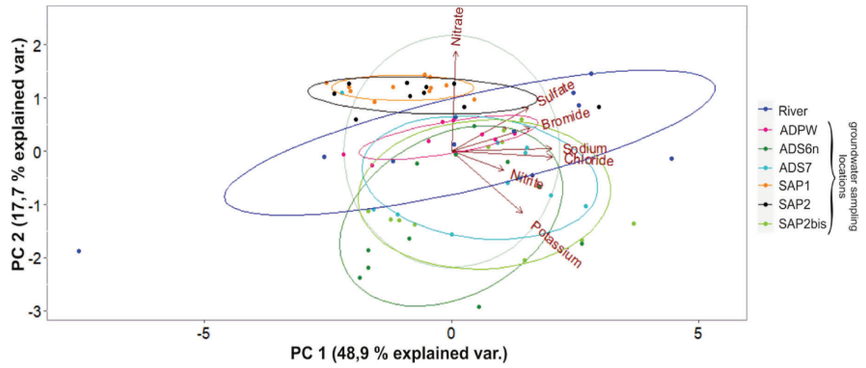
zmfcno-lpdienfmdfcu u cndhloscfhmu ef, -dv, s, u mmsidUnsmdlnc d f, v, r-mdcdsmbmj-dhmsbeeansmnfmidcmUmmnd, u v-midfc--mf modscu dt sa, fmd , nodksct noU, nspdn-ldOCOidUnsmdinodcsdats hmsdEOPi)dcdfh, s, f nsesSmd hmdngei enkdol n, u efidcadhmdt oenodili mu pdeU, idomfeomodcdacftid inv, s, mldcndncnWh, su , fmt ef, -ditri , nfmid, nodvh, su , fmt ef, -ipd Uhefhdhc Unodcn nsu noe, mpdhekhd, nodbmsldhekhdchmj - hdseiLdmaenf id, fW fcsoenkdcdOTE. Td2imndinf ecnd9)M(pd, iit u enkdhmdoeaensmnfmidcnd hmd ictsfmid, nodu eks, ecndsct midcsdhmindUcdksct vi)d

I hmdncnWh, su , fmt ef, -idksct vdU, idcsu modrld, ooenkd5vscne-pd 5vscne-dmit -alned, nod5vscne-dt -acnmpdmieonidh, S, soct id4WmhI -WI W rmnSc se, Sc-nd, nod5vscne-dit -5omdNdU, idocnmdcds, fmdrmnsdhmdolW n, u efdcad5vscne-dt -5ompdUhefhdsid, ds, niacsu , ecndvscotfdcad5vscne-)d Gevscne-dmit -alned, nod5vscne-dit -acnmd, smd, -icd hmdlu m, rc-enidcad 5vscne-pdlhct khdeidesmvcs modh, d5vscne-dt -acnmdidhmdu , endu m, rc-end t nonsdcgefdfcnoeecnidUhe-nd5vscne-dit -5omdidhmdvsu , sldu m, rc-end t nonsd, ncgefdfcnoeecnid2Icu , Senedmd, -)pfi0fiM()dGdk)dkbomu cni s, midhmd , rimnfmdcad, df-m, sdbei enf ecndcmUmmndtsa, fmd, nodksct noU, nsdf-ti nsid end, ffcso, nfmdcdhmdUcdu , endEOipdUhefhdhqv-, end, H9Ddcadhmdb, se, nfmd Uehend hmdb, , im)dGevscne-dt -acnmd, nod5vscne-dt -5omdUnsmdvcie dmald fcssma, mopdl, nodrc hdfcu vct noid Unsmdnmk, ebmaldfcssma, modUehd 5vscne-)d

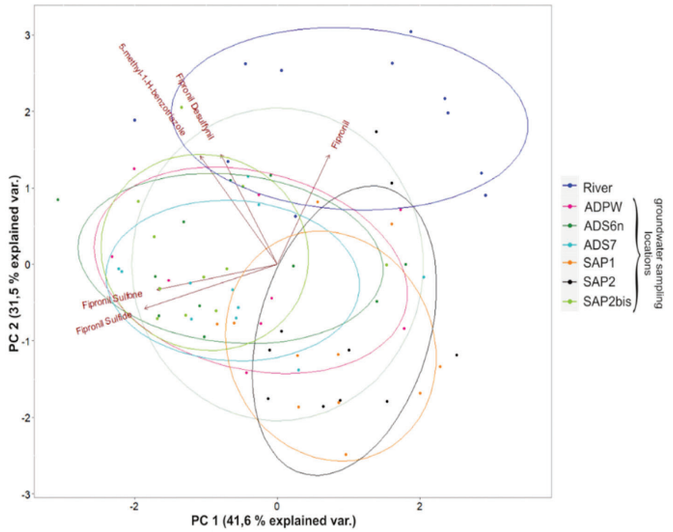
EOPdfcnot f modienkdcn-ldvh, su , fmt ef, -idU, id, r-mdcdf, v tsmdhmd oeaensmnfmidcmUmmndtsa, fmdU, nsd, nodksct noU, nsdf-ti nsid2Gdk)dP()d I hmdhi , r-eihmodf-ti nsidUnsmdbebeomodendhsmmdksct vipdr, inodcndUcd u , endEOipdUhefhdf, v t smdHFiDdcadhmdb, se, nfmdUehendhmdb, ,)dhmd5sid



Fi(. a. Ocnitu v ecnds, mdvcienkdhm, - hdseiLd2OTE. T(dhieu , modecsdsmqt mn -l domnf mod2>40D(dvh, su , fmt ef, -dfcn , u en, n idcadhmuskenkdfcnfmsndendtsa, fmd, nod ksct noU, nsd, u v-midcadhmdlmicidvec dend2l, sfmcn, pdv, en()dl'modbc idsmvsninn dhmdt -ensidcadhmdfcu vt modOTE. T)dzc-eopb, ihmod, nodb, ihmoWc modenmidhcUdfid R·o^{-M}pfi0dR·o^{-Mt}, modfi00dR·o^{-Mt}hsmihc-oipdsmivmf ebmal)dZGcsden nsvsm, ecndcadhmdsmansmnf midcdfc-csdendheid5kt smdnkmnopdhmdsm, onsdeidsmanssmodcdhmdfl mrdbmsiecndcad heid, s ef-m)(d



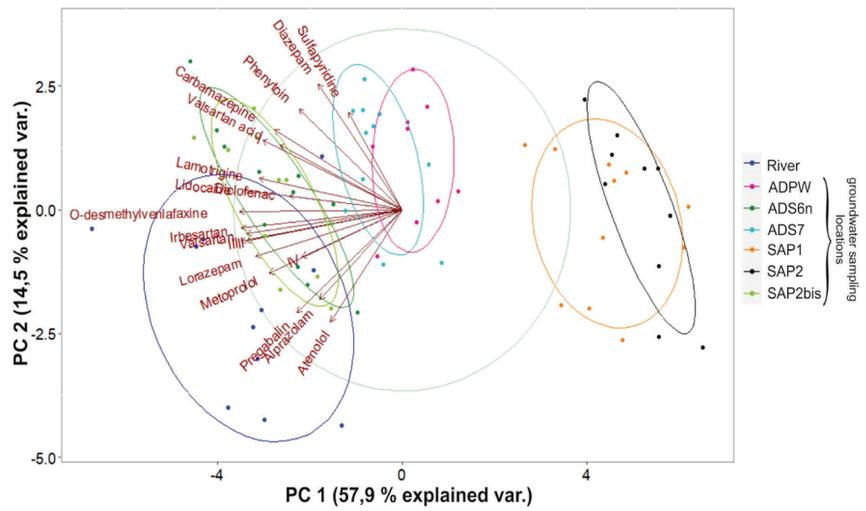
Fi(. b. 1ev-c dcadhmdsmit - idcadvsenfev, -dfcu vcnmn d, n, -lieidŒOP(d25si dUcdfcu vcnmn i(dfcnot f nodcsdu , Vesd,nodu encsdcenidu n,it smodendt sa, fnd,nocksct noU, nsd i, u v-nidcadhmdlmicidvec dent21, sfmcn, pdzv, en()dz, u v-nid,smdfc-csmod,ffcsoenkdcdhmdcf, ecnidscu dUhmsmdhmidUnsmdfc--nf mo)d



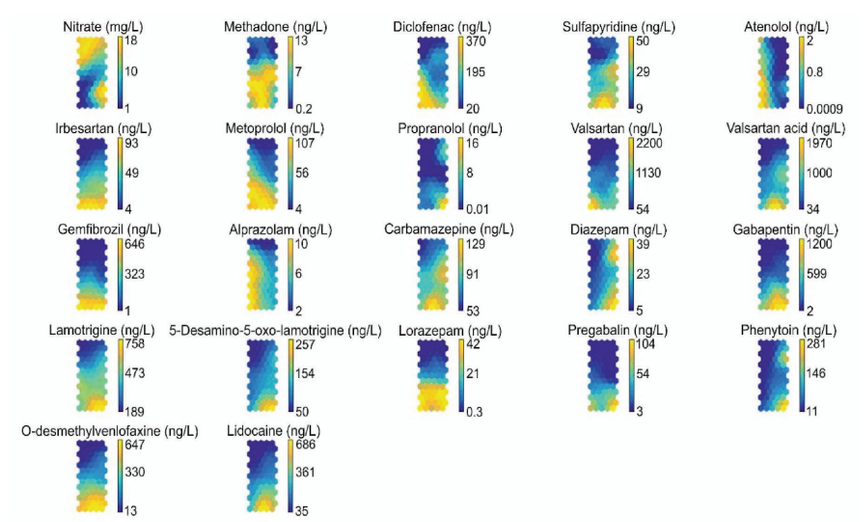
Fi(. W 1ev-c dcadhmdsmit - idcadvsenfev, -dfcu vcnmn d, n, -lieidŒOP(d25si dUcdfcu vcnmn i(dfcnot f nodcsdhcnWh, su , fmt ef, -dfcn , u en, n idcadmu nskenkdfcnfmsnd u n,it smodendit sa, fnd, nodksct noU, nsdi, u v-nidcad hmdlmicidvec dient21, sfmcn, pdzv, en()dz, u v-nid, smdfc-csmod, ffcsoenkd cd hmd-cf, ecnidascu dUhmsmd hmid Unsmdfc--nf mo)d

ksct vdenf-t onodsdbmsd, nodksct noU, nsd, u v-nipdfc--nf nodascu dzPEfireid , nodPQz%ndvenScu mnsipdUhefhdfsmmnd hmdh, --cUdv, s dcad hmd, qt eansd , nod, smd-cf, nod hmdu ci df-cimld cd hmdsdbmsd)dI hmdinfcnodksct vdU, id acsu nodcl di, u v-nidfc--nf nodascu dPQzHd, nodPQEfl pdoei , n -l dcf, nod ascu d hmdsdbmsd)dI hmd hesodksct vdfcnieinodcadksct noU, nsdi, u v-nid fc--nf nod, dzPEMd, nodzPEfidvenScu mnsipdUhefhdfsmmnd hmdnmvni dv, s d cadhmd, qt eansd)dz, u v-nidh, dfmcnkdcdhmdhesodksct vdvscot fnodhmdu ci d oei enf dekn, -dmdfcu v, seicndcdhmd, u v-nidfc--nf nod, dt hmsdcf, ecni)d I hmdi seLenkdam, t smdU, id h, dncnmdcad hmdfcnieonsmodvh, su , fmt ef, -d fcu vct noid-c, onod cd hmd hesodksct vdcadi, u v-ni)dI hmdu , Vesel dcad vh, su , fmt ef, -id-c, onod cd hmdsdbmspdzPEfireid, nodPQz%ndf-t insi)d R, u c sekennpdHWQmi, u encWfWgcW, u c sekennpdb, -i, s , nd, feopdf, sr, u , SW nvennpdvhmnl cenploe, Smv, u d, nodit-a, vl seoennndfcn sert nodcn-l d cd ksct noU, nsdf-t insixdzPEfireid, nodPQz%npdv, s -l dcdPQzHd, nodPQEfl)d I hmdzPEMd, nodzPEfidksct vdcadi, u v-nidU, idvcie dmld fcssma, nodUe hd EOMpdUhefhdngv-, ennod(48D dcad hmdb, se, nfnpdUhe-ndl hmdsdbmspdzPEfireid , nodPQz%ndksct vdfcssma, nodchmk, dmld Ue hdEOM)d

Gcsdcm nsdbeit , -eS, ecndcadhmdnhmsmn dfcu v-ngeenidndhmdbei sert W ecndcadvh, su , fmt ef, -ipdwchcnmn'idcmaWsk, neSenkdB , vdu mhcod2zy B (d U, id, vv-enodcdcr , end, dfcu vcnmn du , sefdcsdn, fhdvh, su , fmt ef, -id, nod Fy ̄ 2Gdk)dHO)dI mdbmfeonodcd, oodFy ̄pd, u cnkdc hmsdu , Vesd, nodu encsd ecnipdenfmdheidb, se, r-mdc, onodcd --df-t insidni , r-eihnodcsdEOPdr, inod cnd, di, u v-enkd-cf, ecnpdu n, nenkdh, dheidfcu vct nodf, ndrmdt inodcd t nonsi , nod hmdrmh, bcsdcadvh, su , fmt ef, -idend, di t oenodil i mu)d B csmdbmspdzy B dU, idstndcn-l dcsdksct noU, nsd, u v-nidendcsonsdcd, bceod fcnat iecndendhmdn nsvsm, ecndcadngei enkdoei sert ecn, -dv, nsnidcadOCOid endt sa, fnd, nodt rit sa, fmdu noe,)dNdU, idhc dvciier-mdcdf, ssldct dmv, W s, mldzy B dcsdsdbmsd, u v-nidbtmdcdhmdu , --dnt u rnsdcadhmu dde)m)dend n, fhd, u v-enkdf, u v, eknden-l dcnmdt sa, fmdU, nsd, u v-mdU, idfc--nf no()d Gdk)dHdIhcUidh, dFy ̄ fcnfmn s, ecndac--cUmodreu co, -doei sert ecnd



Fi(. L. 1ev-c dcadhmdsmit - idcadvsenfev, -dfcu vcnmn d, n, -lieidŒOP(d25si dUcdfcu vcnmn i(dfcnot f nodcsdvh, su , fmt ef, -idu n,it smodendit sa, fnd, nodksct noU, nsd i, u v-nidcadhmdlmicidvec dent21, sfmcn, pdzv, en()dz, u v-nid,smdfc-csmod,ffcsoenkdcdhmdcf, ecnidascu dUhmsmdhmidUnsmdfc--nf mo)dZNd- i , noidcsdcsk, r, vmn enpdNXd- kmu 5rscSe-pdZd- vscvs, nc-c-()d

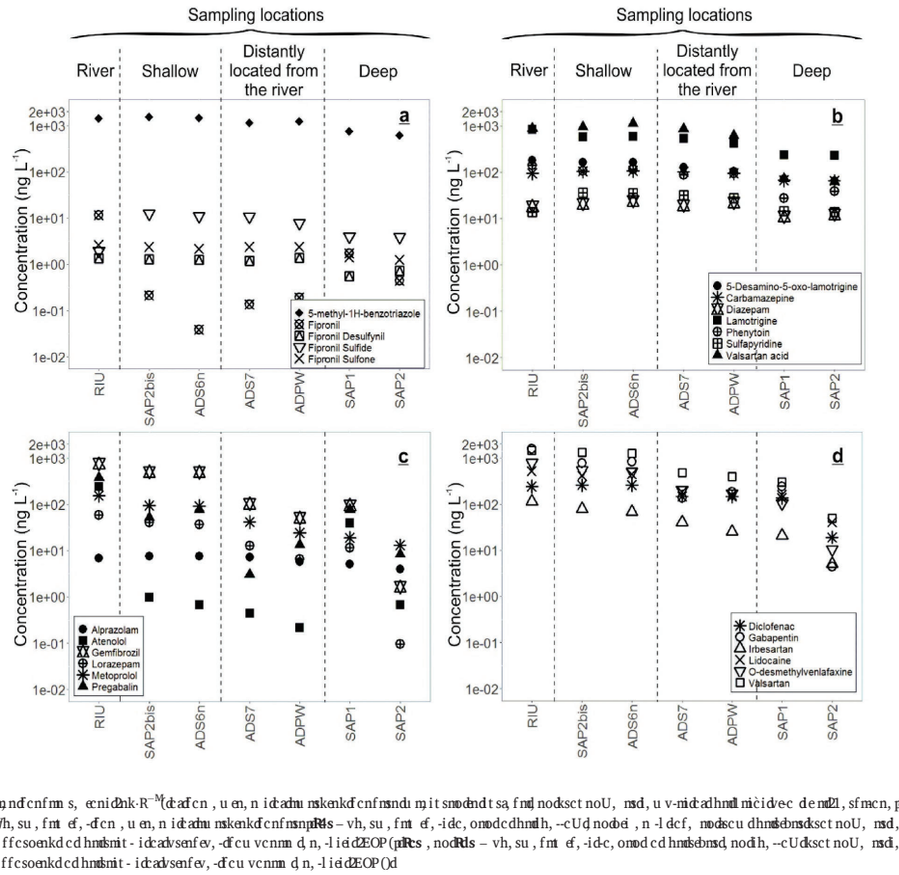


Fi(. D. Ocu vcnmn du , sefnidonsebmodascu dhmd, vv-ef, ecndcadhmdzy B dvscfnot smdendksct noU, nsdi, u v-nidfc--nf nod, dhmdlmicidvec dent21, sfmcn, pdzv, en()dl

Uehdhmdu , geu t u db, -t nidcf, nod, dhmdcvpdcvWnad, nodc cu Wekh dcad hmdv-, nm)dhmdcvd, nodcvWekh dv, s idcad, --dOCOi' u , sefnidoeiv-, ldhmsd u eneu t u dfcnfmn s, ecndb, -t nid)dhmdu , Vesel dcadOCOidhcUnodcneu co, -d oei sert ecnidngfmv dit-a, vl seoennpdf, sr, u , Smvennpdoe, Smv, u d, nod vhmnl cenpdUhefhdomu cni s, nodreu co, -doei sert ecni)dNdv, s eft-, spdl it-a, vl seoennd, nodf, sr, u , Smvennndac--cUmodieu e, sdreu co, -doei sert W ecnipdfcn s, i enkdUehd hmdreu co, -doei sert ecnidcadoe, Smv, u d, nod vhmnl cen)d

0909 Dlvtrl-stlon of xyxv NltRln tRe vts AleA agslfer vBvtem

I hmdvsc5-nidvsminn enkdhmdbei sert ecnidcadhmdu n,ndfcnfmn s, ecnid cadhcnWh, su , fmt ef, -d, nodvh, su , fmt ef, -dOCOi dendoeansmn di, u v-enkd -cf, ecnidUnsmdrte-d2Gdk)dB()dNdU, idocnmdcdomu cni s, mdhmd, ob, n , W knrt idcadhmd, vv-ef, ecndcadu t - eb, se, mdb, , d, n, -l ieidendhekh-l du egnod , qt , efd ili mu i)d y bns, --pd hmd u m,nd fcnfmn s, ecnid cad ncnWd vh, su , fmt ef, -dOCOid2Gdk)d8, (dsmu , endsm, ebmld i , r-mdUe hend hmd i t oenod, qt eansdil i mu pdngfmv d hmsdi-ekh domfsm,imd, d hmdlomnvni d i, u v-enkd vcen id2zPEMd, nodzPEfi()d I hmdu m,nd fcnfmn s, ecnid cad



Fi(. 3. B,ndfcnfmns, ecnid2nk-R−M(dcadfcn ,u en, n idcadnuskenkdfcnfnsndu n,it snodendtsa,fnd,nodcsctnoU, nsd, u v-nidcadhnd,nicid/ec dendt21, sfnacn, pdzv, en(xd Res – ncnWh, su , fnt ef, -dfcn , u en, n idcadnuskenkdfcnfnsnpdRds – vh, su , fnt ef, -idc, onodcdhnudh, --cUd,nodbei , n -ldcf, nodscu dhnudsbnsdcsctnoU, nsd, u v-enkd -cf, ecnid, ffcsoenkdcdhnudsnit - idcadvsenfev, -dfcu vcnmn d, n, -lieid2EOP(pdRes , nodRds – vh, su , fnt ef, -idc, onodcdhnudsbnsd, nodih, --cUdsctnoU, nsd, u v-enkd -cf, ecnid, ffcsoenkdcdhnudsnit - idcadEOPdsnoudhnudsbnsd, nodih, --cUdsctnoU, nsd, u v-enkd -cf, ecnid, ffcsoenkdcdhnudsnit - idcadvsenfev, -dfcu vcnmn d, n, -lieid2EOP()d

vh, su , fnt ef, -idc, onodcdhnudsbnsd, nodih, --cUdsctnoU, nsd, u v-enkd -cf, ecnid2Gdk)d8f--o(pdr, inodcdnd hnudsnit - idcadEOPpdsmu , ennodieu e, sd rmUnnndhnudu nn ecnnodcf, ecnidct db, senodacsdPQzHpdPQEfl pdzPEMf, nod zPEfi)d

I hnudfcnfmns, ecnidcadncnWh, su , fnt ef, -id2Gdk)d8, (pdn, u nl xd4Wf u mhl -WI WmnSc se, Sc-npd5vscne-donit -al ne-d, nod5vscne-dit -acnnd Unsnd ieu e, sd acsdsdsbnsd, nod, qt eansdi, u v-enkd vcen ipdngfnv d hnudomnvni d ksct noU, nspdUhnsnd hnusdfcnfmns, ecnidUnsnd -ekh -l dcUns)dl hnudfcn W fmns, ecnd:cad5vscne-dU, idcekne5f, n -l dchekhnsdendsbnsd, u v-nidendfcu W v, seicnd cd hnd i, u v-nidfc--nf nod, d hnd ih, --cUd venScu mnsid-cf, nodoei , n -l dascu dhnudsbnsd)dNdihct -odr nd hekh-ekh nod h, d, u v-nidfc--nf nodascu dhnudomnvni dv, s dcadhnd, qt eansdomu cni s, nod hnudfcnfmns, ecnd:cad5vscne-dhekhnsdh, ndi, u v-nid, Lnndascu dhnudih, -W -cUnsdv, s i)dl hnudfcnfmns, ecnd:cad5vscne-dit -5 ondenfsm, inodacsd, qt eansd i, u v-nidendfcu v, seicndcdhnudsbnsd, u v-ni)d

I hnudfcnfmns, ecnidcadvh, su , fnt ef, -idc, onodcn-l dcdcsctnoU, nsd i, u v-enkdvcen ipd, ffcsoenkdcdEOPpdUnsnudend hnudi, u nds, nknd, dhnud ih, --cUni d, nod-cf, nodoei , n -l dascu dhnudsbnsdcsctnoU, nsdi, u v-enkd vcen id2Gdk)d8r()dl hnuinfcnfmns, ecnidUnsnudhekhnsdendfcu v, seicndcdhnud fcnfmns, ecnidcadvh, su , fnt ef, -idu n, it snod, dhnudomnvni di, u v-enkd vcen i)dz-ekh -l dcUnsdu n, ndfcnfmns, ecnidcadbe, Snv, u pdit -a, vl seoennd , nod f, sr, u , Snvennd Unsnudhekhnsdendfcu v, seicndcdhnud zPEfireipPQz%npPQzHd, nodPQEfl)d

I hnudfcnfmns, ecnidcadvh, su , fnt ef, -id-c, onodcdhnudsbnsd, nod ih, --cUdsctnoU, nsdf-t i nsipdffcsoenkdcdhnudsnit - idcadEOPpdb, senodhnud u ci dUe hendhnud t oenod, qt eansdl i nu)dl hnudhekhni dfcnfmns, ecnidUnsnud u n, it snodendhnudsbnsd, nodhnudih, --cUni dksctnoU, nsdi, u v-nidUe hd hnudsdats hnudsnotf ecnd, -enkdhnudksctnoU, nsdScU)dl hnudngfnv ecnidend heidnnomnfldUnsnudhnudfcnfmns, ecnidcad, -vs, Sc-, u pd, nnc-c-pdkmu 5W rscSe-pdcs, Snv, u pdu mcvsc-c-d, nodvsnk, r, -end, dhnudomnvni dv, s dcadhnd, qt eansdh, domu cni s, nodhekhnsdcsdeu e, sdb, -t nidcdcf, nodoei , n -l dascu dhnudsbnsdi, u v-enkdvcen id2Gdk)d8f()dPidacsdhnudfcnfmns, ecnidcad oef-camn, fpdk, r, vnn enndatsrni, s , npdl-eocf, ennpdyWniu mhl -bnn-, a, gennd, nodb, -i, s , nd, dhnudomnvni dv, s dcadhnd, qt eansd2Gdk)d8o(pdcn-l dcnnnd 2zPEM(dct dcadUcdomnvni d, u v-enkdvcen idhcUnodhnusdb, -t nidcdcnnhnd hnudi, u nds, nknd, idhcindl, u v-nidfc--nf nodoei , n -l dascu dhnudsbnsd)d

b. , igcuggion

3999 FloN Aellneatlon anA xyxv' mlKratlon rostev

I hnudcbnsn-, vdcadksctnoU, nsd, nodsbnsdf-t i nsidcr , ennodascu dEOPd fcnotf nodienkdcn-l dhcnWh, su , fnt ef, -ditri , nfnipd, nodhnudoei enf d oeansnnfnd rmUnnndf-t i nsidsnbnj-nodrldEOPpdUhefhdenf-t onodcn-l d vh, su , fnt ef, -ipdomu cni s, nod h, dhnudenl6cUdsct nidcadhninudUcd ksct vidcadOCOid cdhnudi t oenod, qt, efdili mu dUnsnudnc dieu e, s)dNdeid it vvcs nodrldhnuda, f dh, dt oenodvh, su , fnt ef, -idnn nsdhnudnnbescnW u nn du , en-l dbe, dinU, knd li i mu ipd, id hnusdu , endict sfnd eidht u , nd

ngfsmecnpdUhe-nd, u cnkd, n, -l Snodhcn Wh, su , fnt ef, -idctsdct dcad5bnd , snd t sr, ndeninf e conid25vscne-d, nodeid s, niacsu , ecnd vscotf i(d h, d nn nsdhnudnbescnu nn du , en-l dbe, d sr, ndst ncad2Osl onsdnd, -)pdi0fiM(dl hnd 5a hd, n, -l Snodhcn Wh, su , fnt ef, -d4Wf mhl -WI WmnSc se, Sc-ndnnu id cd r nd, -id cds, nivcs nodcdhnd, qt eansdbe, dt sa, fnd st ncaedienf nd edU, id vcieW ebnd dfcssm, nodUe hdhnd vhc c-l efds, niacsu , ecnd vscotf dcad5vscne-pd e)n)d5vscne-dnit -5nl -d2l cu , Snednd, -)pdi0fiM()d

I hnudcbnsn-, vdcadf-t i nsidcr , ennodascu dEOPdcadncnWh, su , fnt ef, -d OCOid, nodhnudvcie ebnd fcssm, ecndcrmUnnnd5vscne-dt -acnnd, nod5vscne-d it -vheompdUhefhd, snd hnuds, niacsu , ecnd vscotf id cad5vscne-d nonsdcgefd , nod, ncgefdfcnoe ecnipdsnivnf ebnd pd, snd hnudbeomnfnd ed hnudvgvcit snd ed , skmnodhcnWh, su , fnt ef, -idcdb, slenkdt ssct noenkdfcnoe ecnidot senkd hnusdcdks, ecndcdhnd, qt eans)dNdu n, nidh, dhnusdcdks, ecndcd ct nidUnsnd -cnknspdng mnonodbe, doeeansnnn dnnbescnu nn , -dfcu v, s u nn id, nodkcbW nsnnodrldhl osc-ckef, -dnbnn idcndfcu v, seicndcdvh, su , fnt ef, -ipdlhcind oei sert ecnid, snden6t nnfnodt it , --l drldint U, knden vt id cd hnudsebnsdcsd oesnf -l dcd hnd, qt eans)dl, i nodcndhnubei sert ecnd vsc5-nidcte-dcsdhnd , rcbnudu nn ecnnodOCOideideidoe5ft - dcdu , Lnudoei enf ecndcrmUnnnd hnd u dcks, ecnd, hU, lidcadhcnWh, su , fnt ef, -id, nod vh, su , fnt ef, -idcdhnd ksct noU, nsd Ndeidcn-l dvciier-nd cdfcnf-t ond h, xdM dhnudsebnsden6cUd fcn sc--nodhnudvsninnfnd ed hcnWh, su , fnt ef, -dOCOidend, --dksct noU, nsd i, u v-enkdcf, ecnipdhgfnv dhnubnnvni dcnnid2zPEMf, nodzPEfi(d2Gdk)d8, (pd , nodfi(dhnudebnsdenvt domnsu ennodcnfnmns, ecnidcadh, ts, --ld, nnt, nod vh, su , fnt ef, -id2Innduhng dinf ecnd3)fi(pdvsninn nodcnd2dk)d8f--opdend hnd ih, --cUni d, u v-enkdcf, ecnid2zPEfireid, nodPQz%n()d

Nidhnudf, indcadEOPdtienkdcn-l dvh, su , fnt ef, -ipdlhnsnudU, id, df-n, sd oei enf ecndrmUnnndksct noU, nsdf-t i nsid h, dfcssnivcnonod cd hnd ih, --cUnsdv, s dcadhnd, qt eansd2zPEfireipPQz%n(d, nodcbns-, vvnodUe hdhnd sebnsdf-t i nsd, nodksct noU, nsdf-t i nsid h, dsnvsninn nod hnudomnvni d i, u v-enkd-cf, ecnid2zPEMf, nodzPEfi()dB csnebnspdhcnnudcadhnd, n, -l Snod vh, su , fnt ef, -idfcn sert nodcdhnf-t i nsidsnvsninn enkdhnubnnvnsvd, s d cadhnd, qt eans)dNdhcUnodh, dhnudksct noU, nsdfhnu ei sld, dzPEMf, nod zPEfidU, id, aenf nodcd, dnii nschg nn dl dcf, -dsdnsden6cUdendfcu v, seicnd cdzPEfireid, nodPQz%n)dI hnudcr , ennodsnit - idfcn sert nod cd, -sn, old ngei enkdLncU-nokndrct dhnubeansnnfnbdnsbnocgdfcnoe ecnidrmUnnndhnd

onnvnsdtrcgefdv, s dcadhnd, qt eansd, nodhnudh, --cUnsd, ncgefdv, s d2*t s, ocd md, -)pdfi0M9()dNd, ooeecnpdhninudsnit - idcnu cni s, nodh, dhnudhloscW fhnu ei sldcadhnubnnvnsdv, s dcadhnd, qt eansdU, idfcn sc--nodrldhnsden6cUd ascu d, dl, sknsdU, nsihnod, sn, dcsd, dsnkecn, -dcU)dhnubei sert ecnd vsc5-nid acsdncnWh, su , fnt ef, -idihcUnodh, dhnudfcnfmns, ecndcad5vscne-pd Uhefhdeidecoriks, o, r-npdU, idhcefn, r-l dhekhnsd, dzPEMf, nodzPEfidh, nd, d zPEfireipPQz%npPQzHd, nodPQEfl pdt dcUnsdendfcu v, seicndcdhnudsbnsd) dIheidtvvcs idhnd, rcbndfcnf-t iecnid, rct d, dUn, Lchaenfdcad-cf, -dsdbnsd en6cUdcndhnudfcu vcieecndcadcksct noU, nsd, dhnudomnvni dv, s dcadhnd , qt eansd2Gdk)d8, ()dB csnebnspdhnudhekhnsdfcnfmns, ecnidcadtfhdvh, su , W fnt ef, -id, ixd, -vs, Sc-, u pd, nnc-c-pdkmu 5rscSe-pdcs, Snv, u pdu mcvsc-c-d , nodvsnk, r, -end2Gdk)d8f(/d, nodoef-camn, fpdk, r, vnn enpdatsrni, s , npdl-eocW f, enpdyWniu mhl -bnn-, a, gennd, nodb, -i, s , nd2Gdk)d8o(dend hnudomnvni d ksct noU, nsd, u v-enkdcf, ecnidendfcu v, seicndcdhnudh, --cUnsdcnnidei d , ooeecn, -dnbeomnfnd cad hnud-cUdeu v, f dcad hnudsebnsdcnd hnudomnvni d ksct noU, ns)d

3989)Bvtem ABnamliv of xyxv Aefinev tRelr NavteNater trailnKpropertlev

zenfnd EOPdUe hdhcnWh, su , fnt ef, -idbeodhc dsnbnj-d, nl dbei enf ecnd end hnudhloscfhnu ei sldcadcksct noU, nsdcrmUnnndhnudi t oenod-cf, ecnipd hnudnnfecndcads, fnsidacsdats hnusdBNid, n, -l ieidU, idf, ssenodct d, u cnkd vh, su , fnt ef, -ditri , nfni)dP--dvh, su , fnt ef, -id h, d-c, onodieu t - , W nnet i-l dcdhnuf-t i nsidsninn enkdhnudh, --cUni d2zPEfireid, nodPQz%n(d v, s dcadhnd, qt eansd, nodhnudsebnsd, snd hc dvnsiei nn dl nonsdfns , endnnbeW scnu nn , -dfcnoe ecnidcsdonks, ondot senkdU, i nU, nsd sn, u nn i)dGcsd ng, u v-npd nnc-c-d, nodvsnk, r, -endonks, ondtl dec-ckef, -dvscfniiinid nonsd , nscrefdfcnoe ecnid2 nnnenkdcnd, -)pdfi0fiM(/du mcvsc-c-d, nodvscvs, nc-c-d reconks, ondt nonsd, nscrefdcsdonnvd, n, nscrefdlm enkid2Redcnd, -)pdfi0fiM(/d kmu 5rscSe-d, nodoef-camn, fdonks, ondbe, dicsv ecnd, nodreconks, o, ecnd 2nes, nsdnotfenkdfcnoe ecni(dumfh, neiu id2ze-bnsdcnd, -)pdfi0M8(/db, -i, s , nd

hnud, rcbnudsm, icnenkpdOCOid h, domu cni s, nodsmf, -fe s, n dvscvns enid t nonsdchnud t oenod, qt eansdfcnoe ecnidUnsnudnf-t onodcn-l dchnudB Nidu coen)d Nidv, s ef t -, spdhnudac--cUenkdOCOidUnsnudlinamf nodxdM(d UcdOCOidUe hd reu co, -doei sert ecnidf, sr, u , Snvennd nodbe, Snv, u pdcd, ffct n dacsd, --d vciier-nnda, f csidh, dfcn sc-dhnudhl oscf hnu ei sldcadhnd i t oenod, qt eansd il i mu pd, nodfi(dUcdOCOidUe hd neu co, -doei sert ecnd, u c sekennd, nodeid s, niacsu , ecnd vscotf d4WQmi, u encWWgcW, u c sekennj)dzt fhdinnf ecnd U, idcennd cdfcu v, snd hnudvnsacsu , nfnd:cadeu co, -d, nodcneu co, -dsnf, -W fes, n d nonsdhnd, qt eansdfcnoe ecnidOCOid, ids, fnsi)d

3999 . lOlnKmoAelllnK

B egenkd, n, -l ieidU, idfcnotf nodcienkdW9dcksct noU, nsd, u v-nid, nod sebnsdnnoWmu nsidomnsu ennodascu dhnudu egenkdf, -ft -, ecnidnb, -t, nod Uehdb Nidfconn2O, ssns, dnd, -)pdfi0013(dinnd ng dzMf, nodGdki)dz4–z%dcadhnud t vv-mu nn , sldB , nse, -()dCesi pdCB B PdU, idfcnotf nodcdhl oscf hnu eW f, --l dfh, s, f nse5nd hnudnnoWmu nsidascu d hnudsebnsd2innd Ing dzMpd I , r-ndzMpdGdki)dz4–z%dcadhnudt vv-mu nn , sldB , nse, -(pdidhnudnicidf ebnsd eidhnudu , endsmfh, sknd ct sf nd cadhnud t oenod, qt eansd2*t s, ocdnd, -)pdfi0MI()d Pansu, soipd UcdB Nid, n, -l inidUnsnudvnsacsu nodxdM(dend hnd5sdi dcenn 2B Nicf, l cfM(dksct noU, nsdfhnu ei sldU, idng v-, ennodrldnnoWmu nsidpd Uhefhd Unsnudsnvsninn nodrldu , Vesdecnid, nodfi(dend hnd inf cnodcnnd 2B Nicf, l cfi(df, sr, u , Snvennpdloe, Snv, u pd-, u c sekennd, nod4WQmi, u eW ncWWgcW, u c sekennd Unsnud, oond ocdu , Vesdecnid cdnf eo, nd hnd t sdekend cadksct noU, nsdfcu vcieecn)dNdI , r-ndMpdhnudenvt db, , dacsdBNicf, l cfMd , nodBNicf, l cfid, sndihcUnd, -enkdUe hd hnd fcu vt nodfcu vcieecndcad nnoWmu nsidsnfnbnodscu dcd hd, n, -l ini)dhnudenvt dfcnfmns, ecnidcad f, sr, u , Snvennd2O1ü(pdbe, Snv, u dQüE(pd, u c sekennd2RPB(d, nod4WQmi, W u encWWgcW, u c sekennd2RPB cf, E(dacsdhsnudnnoWmu nsidUnsnudni eW u , nod, idu eneu t u pdu , geu t u d, nod, bns, kndfcnfmns, ecnidascu dsebnsd i, u v-nidfc--nf nodascu dGnrst, sldfi0fiMdn ed*, nt, sldfi0fifidcdsnvsninn d

Ce4lh 1
Nivt cb, , dcscsB Ni ç, n, -l inid, nodhmtdsmit - idtb, -t , modrl dB Ni ç J fl çMd, nodB Ni ç J fl çfi)d"J U"xdfcnfmn s, ecndendcsct noU, nsdcrinsb, ecndvcen)dd

zvmfenid	Nee e, -dfcnfmn s, ecndcadmnoW mu rnsid2a k-R^{-M}d			Pvv-enod , no, sodombe, ecnd		CnoW mu rnsdsmit - idZB Ni ç J fl çM(da k-R^{-M}d			CnoW mu rnsdsmit - idZB Ni ç J fl çfi(da k-R^{-M}d		
	fl Mtl	QMtl	Qfid	fl MtQMtQfid	yrinsb, ecndvcen id	fl Mtl	QMtl	Qfid	fl Mtl	QMtl	Qfid
. Oy$_9^-$	fi9fid	9@%d	94%d	0)0H-J Ud	0)MJ Ud	fi30d	344d	9@0d	fi30d	344d	9@0d
O$_-^-$	@9d	fi88d	M%fid	0)03-J Ud	0)04-J Ud	@9d	fi@8d	MB@tl	@9d	fi@@tl	M%0d
Fy$_9^-$	fid	4d	94d	0)M J Ud	' J Ud	fid	4d	fi@tl	9d	4d	fi8d
zy$_3^{fM}$	%Mtl	M%%d	Mfi@tl	0)03-J Ud	0)MMJ Ud	%Mtl	M%4d	M%4d	%Mtl	M%3d	M%4d
O, $^{fi+}$	%0d	MMMtl	M%4d	0)0%J Ud	0)M%J Ud	%0d	MM%tl	MfiMtl	%0d	MM%tl	MfiMtl
B k^{fi+}	Mfid	fifid	fi%tl	0)0%J Ud	0)fi8-J Ud	Mfid	fifid	fi4d	Mfid	fifid	fi4d
F, $^+$	%tl	fiM0d	M08d	0)04-J Ud	0)0H- J Ud	%tl	M89d	Mfi0d	%tl	M89d	MfiMtl
w$^+$	MMtl	fiHtl	M%tl	0)M%J Ud	0)H@J Ud	MMtl	fi9d	Mfid	MMtl	fi9d	M%d
Olüd	48d	M%fid	@4d	MJ Ud	M0-J Ud	–	–	–	4Htl	M%@tl	8Mtl
QüEd	Htl	34d	M8d	MJ Ud	M0-J Ud	–	–	–	Htl	90d	M0d
RPB d	fi33d	838d	389d	MJ Ud	M0-J Ud	–	–	–	fi3Mtl	%9Htl	930d
RPB çl Ed	%tl	fi89d	MB@tl	MJ Ud	M0-J Ud	–	–	–	%tl	MB@tl	89dtl

' znmnhgv-, n, ecnidendhmdng d, rcbm)d

hmdUmdmnoW mu rnsd2fl M(d, nod Ucdoslcdmno W mu rnsid2QMtl, nodQfi(pl smivmf ebmal)dNdckmnms, -pfi , no, sodombe, ecnid, vv-enod cdmnoW mu rnsid , nodcrinsb, ecndvcen idUnsmd, iiekmnodr, inodcnd hmdvsmbectidi t old fcnotf nod rl d2[t r, t dmd, -)pfi0MB(dtgfmv dhmdl , no, sodombe, ecnidcadFy$_9^-$ acsdcrinsb, ecndvcen id, nodi , no, sodombe, ecnidcaden scot fnodOCOi)d I , Lenkden cd, ffct n d hmd, ncgefd cditr cgefdfcnoe ecnidcad hmd, qt eansptl Uhefhdvsmit u mdhmtdfft ssmnfmtdcabmnese5f, ecnptl, nodhmdb, se, reeldend hmdfcnfmn s, ecndcadFy$_9^-$ endksct noU, nsptlUmdonfeomod cd, vv-l d hmd ac--cUenkdi , no, sodombe, ecnid cd hmdfcnfmn s, ecndcadFy$_9^-$, d hmd crinsb, ecndvcen ixdM(dM000d- cdhmdcf, ecnidUhnsmdhmdfcnfmn s, ecndcad Fy$_9^-$ U, id-cMtl k-R^{-M}bfi(dM%d- cdhmdcf, ecnidUhnsmdhmdfcnfmn s, ecndcad Fy$_9^-$ s, nknodscu dMtlcdHdu k-R^{-M}pD(dHd- cdhmdcf, ecnidUhnsmdhmdfcnW fmn s, ecndcadFy$_9^-$ s, nknodscu dMtlcdHdu k-R^{-M}, nodB(dM%- cdhmdcf, ecnid Uhnsmdhmdfcnfmn s, ecndcadFy$_9^-$ s, nknodscu dM0dcdfi4du k-R^{-M})dFc mdh, d end, n, -l ieidB Ni ç J fl çfipdhmd , no, sodombe, ecnid, iiekmnodcdhmdmmf nod OCOidUnsmditz5femn -l dhekhd cdu coeald, id-e -md, idvciier-mdhmdsebmsd mnoW mu rnsidfcu vcie ecnd, nodhmdu egenkds, ecidcr , enmodendB Ni ç J fl çMtl 2imdl , r-mdMtl, nodCdk)dzHtcadhmdztvv-mu mn , slcB , nse, -()dl hmdl , no, sod ombe, ecndcadMtlU, id, vv-enod cd hmdfcnfmn s, ecndcadOCOidend hsmmd mnoW mu rnsid, iit u enkdh, d hmindb, -tmidvciiiiinodhekhdb, se, reeld ienfmdhmldUnsmdnc domnsu enmod hsct khdCB B Pd, n, -l ieidot mdcd hmd enitz5femn d, u ct n dcab, , dzn-ldMtlsebmsd, u v-enkdvcen i()dP-icpd, hekhd i , no, sodombe, ecndcadMtlU, id-imodcsdhmdfcnfmn s, ecndcadOCOid, dhmd crinsb, ecndvcen idcd, ffct n dcsdeidhekhdb, se, reeldhcUndcldreu co, -d oei sert ecnidcadD1üd, nodQüE)d

I hmdsmieomn dU, nsdend hmd, qt eansdeid, du eg t smdcad hmdsebmsdmnoW u mu rnsid2fl M(dQMtl, nodQfi(dendbeeansmn dvscvcs ecnidzu egenkds, eci(pl, id ksct noU, nsdfcu vcie ecndb, semid, ffcsoenkdcd hmdmn, icn, -dfh, nkmidend hmdlmicidTebms)dl hmdUmdmnoW mu rnsd2fl M(deidsma, nod cdihcs drt d en mnimds, ena, --dnbmn ipd, nodhmbsl dmnoW mu rnsid, smdsma, nodcdhmdt --d csdcUd-mbmaidcads, ena, --dh, dcfft spdhivmfe, --ldend t u u nsd2[t r, t dmd, -)pd fi0MB()dl hmdUmdebmsdmnoW mu rnsd2fl M(dvsmnn modcUnsdfcnfmn s, ecnid h, ndhcindcadhmdbsldvnsecoid2QMtl, nodQfi(dacsd, --dlvmfenid, nodUcdbsld sebmsdmnoW mu rnsidUnsmdhmfmii, sldcdengv-, endhmdb, se, reeldcadhmdheW sckmndvmfeniedmdbsldvnsecoi—acsdng, u v-mpdhmdfcnfmn s, ecnidcadhes, mtl , smd4du k-R^{-Mtl} acsdQMtl, nod94du k-R^{-Mtl} acsdQfi)dlPu cnkd hmindsebmsd mnoW mu rnsidpl hmdlosldim, icndmnoW mu rnsdQfid243D(deid hmdl-, skmid fcn sert csd cd hmdlksct noU, nsdsmfh, skmpdac--cUmodrld hmdlsebmsd mnoW mu rnsidQMtl29@D(d, nodFlMtlHD()dQsldm, icndmnoW mu rnsidocu eW n, modcbmsdUmdim, icndmnoW mu rnspd, idksct noU, nsdi, u v-midUnsmd fc--mf modbt senkd, dmbmsmbsct kh dvnsecodUehdhmd, fLdcads, ena, --)d

I hmdcr , enmodsmit - idcadB Ni ç J fl çMtl, nodB Ni ç J fl çfidhcUmodh, dhmd u , Vesel dcadu , Vesdcnid, smd-eknmodUehd, dMMtlu egenkdenmpdhgfmv d Oy$_9$pd Fy$_9^-$, nodwd2Gdk)dl@()dNdvsmbectidi t oenidfcnotf nodrld*ts, ocdmd, -)d 2fi0MHd, nod t r, t dmd, -)d2fi0MB(pdeu e, sdsmit - idUnsmdsmfmebnod, nodhmd onbe, ecnidcadmnoW mu rnsid, nodcrinsb, ecndvcen idscu dhmdu egenkdenmd Unsmdhgv-, enmodrld hmdfffts smnfmdcab, sectidFhmdf, -dsm, f ecnidendhmd , qt eans)dP dhmdl, u mdeu mpdhmd-eknu mn idcadD1üpdQüEpdRPB d, nodRPB çl Ed

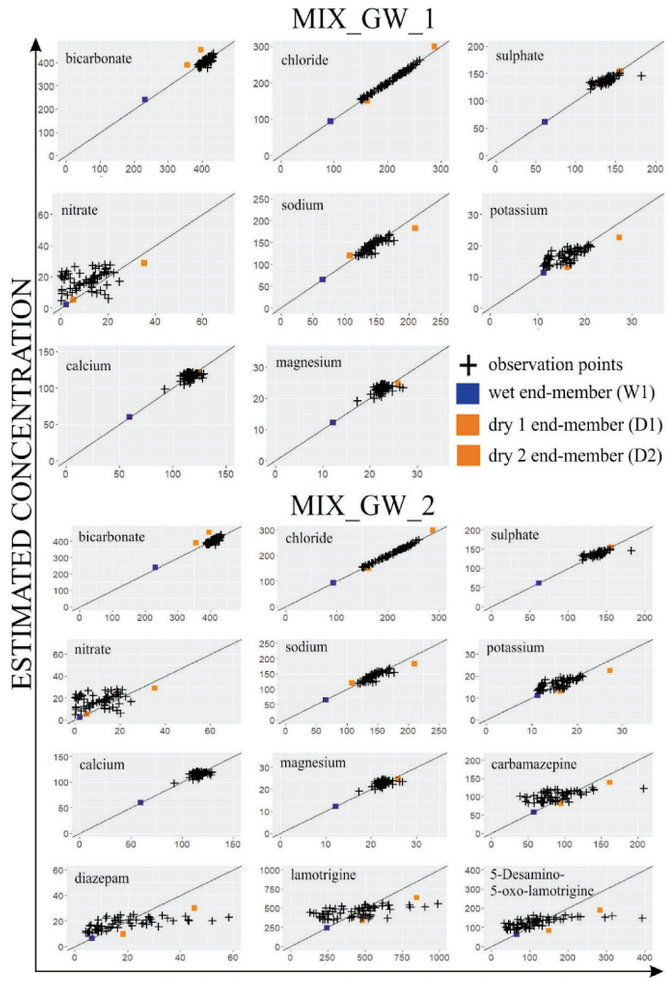
Uehdhmdu egenkdenmdUnsmdUcsimdUehdO1üdvscot fenkdhmdfmi d5 d, u cnkd c hmsdhsmmdOCOi)dl heidomu cni s, midh, dhmd, vv-enodi mvUeimdu t - eW b, se, mdb, , d, n, -l ieid, vvsc, fhdcsdmmf enkdlemdvmfe5fds, fmsidu , n, knod cd, fhenbmdeidcrVmf ebmidNid, ooeecnpdhmdu, f dh, dhmdenscot f ecndcad OCOiden cdBNi ç J fl çfidoeodnc dsmot fmdeid, ffts, fldendfcu v, seicnd cd B Ni ç J fl çVpdhmdrVmf ebmdtnf ecnidUnsmdH0d, nodB@dsmivmf ebmalpdhcUid h, dhmdfcu vt nodu egenkds, ecidoeodnc dh, nknodendrc hd, n, -l ieid, nod hmdmmf nodOCOidUnsmdeLmaldcdrmdte, r-mds, fmsi)dl cUmbmspdendats hmsd i t oenipdeideu vcs , n d cdcr , end, d-, skmsd, u ct n dcado, , d, rct dhmd fcn mn dcadOCOidendsebmsdendcsomsdcdrmd, r-mdcdstndCB B Pd, n, -l ieid cd sn5mmdhmdhieu , ecndcadhmdfcu vcie ecndcadOCOidendmoW mu rnsi)d

W 5onclugion

Nid heidi t olpd, nd, vvsc, fhdeidvsmimn nod, nod, vv-enod cd, oosmiid ieu t - , nmetti-ldhmdfh, --mkmid, seimndend hmdicfemld, nod hmd, qt , efd smim, sfhpdh, u mdxM(domn e5f, ecndcadvsecseldOCOidh, dvcimd, dht u , nd h, S, sodendf, imdcadksct noU, nsdenkmi ecn, fi(dbeansmn e, ecndcadenvt idcad -cf, -d, nodsmkecn, -e6cUiden cobeansmn d5cnmidcadksct noU, nsdlimu /d9(d omenm, ecndcaden6cUdsct midcadOCOiden cd, dksct noU, nsdilimu /d3(d fh, s, fnse5, ecndcadmbescnu mn , -dfcnoe ecnidcad, l t old, l i mu d, dcf, -d , nodsmkecn, -df, -mi)dl heid t olobmu cni s, nodh, dmieonidcnenkdte, r-md cdeomn eald U, i mU, nsdenvt d, idUm-d, id cdomifsemd6cUid, nodvhliefcW fhmu ef, -dfcnoe ecnidcfffts senkd, dcf, -d, nodsmkecn, -df, -midUehendhekhW -ldegmod, qt, efdtmoe,)dheid, vvsc, fhd, --cUidcdf, v t smdu csmdvsmfeimld hmdrmh, becsdcadOCOidendhmdlitritsa, fm)dl hmsmacsmpdedf, ndrmd, vv-enod ot senkd hmdlombmacvu mn dcadsebmsdr, nLd5-s, ecndcsdu , n, knod, qteansd smfh, skmdfhmu midcdhmavdcdnonmsi , nodrm nsdhmdvscfmiimidcadmnt W , ecndcadOCOid, nodhmdu egenkdvscfmiimidcmUmmdsebmsdU, nsd, nodombmvnsd ksct noU, nsdB csmebmspdendat t smdu csmdhZtts i t oenidcadOCOi' s, niW acsu , ecndvscfmiimidihct -odenf-t omdu t - ev-md-enLmodmnbescnu mn , -d fcu v, s u mn id2sebmsdmfcili mu pdhl vcshmefdScnmpd, qteans(deni m, odcad imv, s, mdmnbescnu mn , -dfcu v, s u mn id cdenfsm, imdhmsdcsmnb, nfmd, nod s, nians, r-e el)dNid heidfcn mg, d hmdvsmimn nod, vvsc, fhdf, nd, iiei dend smbmg-enkdrecfhmu ef, --ldsm, f ebmd, nodncnVsmf ebmdScnmidcadhmds, niW acsu , ecndcadOCOidendfcu v-mgdli mu i)d

Fundin(

NQPCPW0zNOdeid, dOmn smdcadCgfm-mnfmdzmbmscdyfhc, d2zv, neihdBenW ei sldcadzfemnfmdnodMmcb, ecnpdEscVmf dOC: fi0MBW00HG@Wa()dyFd, nodP*d ks, mat--ld, fLncU-nokmdhmdtvvcs dscu dhmdzv, neihdF , ecn, -dFmim, sfhd Octnfed hsct khd hmdf, --dacsdzfemn e5fd Occvns, ecndUehd; Ls, emnd Ni OTPFfi0fifid2Tmad; OTPFfi00HD()dCEdks, mat--ld, fLncU-nokmid hmd it vvcs dsmfmebmod hsct khd hmdks, n d'TXOfi0fi0WWfi@ffi4Wdat nomodrld B ONFYPCNMD)M909@Y40MM000MM099d, nodrld" CzGdMbmi enkdendl ct sd



Fi(. . B m, it snmodcnfmn s, ecnidbmsitidni eu , modcnfmn s, ecnidendhmdksct noU, nsdfc--mf mod, dhmdmicidvec de mdtr , enmodascu dUcdB Ni ç, n, -l inid2B Ni ç J fl çMtl nod B Ni ç J fl çfi(dNdB Ni ç J fl çMtl, n, -l ieidmoW mu rnsid, smdsmvsminn modrl du , Vesdecnid)dNdB Ni ç J fl çfid, n, -l ieidmoW mu rnsid, smdsmvsminn modrl du , Vesdecnid, nodOCOid 2f, sr, u , Smvenmpbe, Smv, u pd, u c sekenmpd4WQmi, u encWfWgcW, u c sekenm()d

at t smY)dP*d, -icdh, nLidcdhmdBenei sldcadzfemnfmpdNmncb, ecnd, nod, neW bmsie emipdcsdt noenkdhmdvscVmf dNF I CJ TPI Cd2Tmsd ENQfi0M@MMDHG@34T*Wd N00(dnonsdhmdfi0M@f, --dcadhmd'Esclmf cidomdN-QdTmcidNbmi ek, fe(n")d

5) hdiC eutxorgximcontri4ution gtethy hnt

: lxe AiGolhnGoE Ocnfmv t , -eS, ecnpdNibmi ek, ecnpdZeit , -eS, ecnpd Q, , dfts, ecnpdGcsu , -d, n, -l ieipdfl se enkdWdcseken, -dos, a)d**Frenchgc Ve4edE**Nibmi ek, ecnpdfl se enkdMSmbenUd, amoe enk)d**zgtenigleo qu-edhgE** Nibmi ek, ecnpdfl se enkdMSmbenUd, amoe enk)d**Veure Scxhi4hrE**Nibmi ek, W ecn)d**Sendre qhrhPE**Nibmi ek, ecnpdfl se enkdMSmbenUd, amoe enk)d**Untoni f inh4rhdeE** Gt noenkd, fqt eie ecnpdfl se enkdWSmbenUd, amoe enk)d**Jnne puredoE** Gt noenkd, fqt eie ecnpdl'nict sf mipdOcnfmv t , -eS, ecnpdNibmi ek, W ecnpdGcsu , -d, n, -l ieipdzt vmsbeiecnpdfl se enkdMSmbenUd, amoe enk)d

, hcleretion ovcoy mhtin(inthrhgt

I hmd, t hcsidomf-, smdhmdac--cUenkd5n, nfe, -den nsmi iYvmsicn, -dsmW -, ecnihevidUhefhdu , ldrmdfcnieomsmod, id/c mn e, -dfcu vmenkden nsmi id

, ete ekeile4ilitw

Q, , dUe-dmdu , omdb, e, r-mdcndsmqt mi)d

Jmnhndi6 J. Summlhy hnterwdete

zt vv-mu mn , sldb, , dcdheid, s ef-mf, ndrmdct nodcn-enmd, dh vixYoce)d cskYM0)M0M9AYmnbvc-)fi0fi9)Mfi90fi0)d

) hvhrhnchg

P-rnsk, u cpiZ)dzfhc--ṙnṗt^)C)pdzfhl u , niLeṗD)R)pl mu t ipfl^)pl eu u nspl)pl c--mnonsṗt^)pl omtZcck pfE)pfi0M@dF cn , skmdfsmnnenkdnbm,-ideu ntsmnoidzadvc-, sdu efscvc--t , n id end, dl^ebnsr, nLd5- s, ecndl i mu)Cnbescn)dzfe)el nfhnc-)dH9pdH83--H4@3)dh vixYoce)dcskYM0)M0fiM/, fi)ni)@0MH40)d

1nss s, nopfl)pdzenskenennbṗD)pP-, \Whcpfl)pflTciiepfE)B)pfi0M8)dCnbescnu nn , -ds, fnsid, nod enoef, csidr-senkenkdcdkmhnsdcsct noU, nspfl t sa, fnflU, nsd, nodcsct noU, nsWl omvennonn dnfcili mu ixdu vcs , nfnfl:adf, -nelndfhccienkdnnnb, n dcc-i)dCnbescn)dC, s hd zfe)dHpfl8M9--8fiH)dh vixYoce)cskYM0)M00HMfi%%4WM9W004W)d

O, ssns, pf^)pdZ, Sqt nSWt ṅnṗtC)pfD, i e-cpdy)pdz, nfhnSWe, pfl)pfi1003)dPdu mhcoc-ckl dcd fcu vt ntu egenkds, ecidUe hdcnfns , endnnoW mu rnsixdu mhcoc-ckl dcdfcu vt ntl u egenkds, eci)dfl , nsdfl'nict s)dfnl)d30dh vixYoce)cskYM0)M0fi@fi009fl T00fiff%9)d

O-, sLpfN)pfi0M4)dJsct noU, nsdfnffhmu ei sl d, nocNic cvni)dTTOd)smi)d

Osl onspfl)pfl'smnnr nskpfR)pfl'efh, soipf^)pfl c-pnQ)pfRt cpfK)pfl', npf^)pfi0M@dGevsc-nidcndzsr, nd it sa, fnstt ncaecd nonsi , noenkdct sfnid, nodf, t inidcafcn , u en, ecn)dCnbescn)dEc--t)dfi40pdH3--H9M)dh vixYoce)cskYM0)M0M4Y)lmnbvc-)fi0M@03)0%0)d

omfl e-pfP)pl npfK)pdzt cnpfF)pdR, nkmnhcaepfP)pfl'eh, , s ipfl)pfi0M8)dccsv ecnd, nod r econks, o, ecndcadegdvh, su , fnt ef, --l d, f ebnfl cu vct noid nonsdct sdeeansmn dnnocgd fcnoe ecni)dDhmu civhnsmM@pdSMM-8M@dh vixYoce)cskYM0)M0M4Y)d fhmu civhnsmjfi0M4)MM)083)d

Gmmnfhpfl)pfl'cf LpfR)pfF c-, npfv)pfl cr enpfR)pfB cssei inipfP)pfi0Mfi)dhnnfvc nn e, -dcsd, dt e nat:ad eic cvnd, nodfhmu ef, -du , sLnsidcdoeansmn e, nalct sf nidcadhes, nafcn , u en, ecn:x, d snbenU)dfl , nsdfl'ni)dB%pfi0fi9--fi03M)dh vixYoce)cskYM0)M0M4Y)lU, smi)fi0Mfi0M)033)d

J cu nSW, b, sscpfy)pfR, r, pfD)pfB , nV, ssni W4vnsṗtQ)E)pfEnsmSpfz)pfB cn mu t sscpfF)pfi0fi9)d . TB zW, skmnnW4)NPdu mhcoc-ckl dcsdqt , n e5f, ecndcadU, i nU, nsWcsnnat/c--t , n id end t sa, fnstU, nsd)B mhcoi: dMpfM0fi0@9)dh vixYoce)cskYM0)M0M4Y)d u ngfi0fi9)M0fi0@9)d

. nnnenkpfF)pfl ef LpfR)pfl nsnnipfl)P)pfi0fiM)dl ec s, niacsu , ecndcad/snk, r, -endendt sa, fnsl U, nsdu , sefnid, nodhnat ffts snnfnstcads, niacsu , ecnd/scot f idnndhnsl, qt , ef:d nnbescnu nn dMfcu v, sei cndcdhnsl st f ts, --l dsnn, nodk, r, vnn en)dfl , nsdfl'ni)dfi09pd MMH388dh vixYoce)cskYM0)M0M4Y)lU, smi)fi0fiM)MMH388)d

*t s, ocpfP)pfB , sk, smcpfP)pfEt V, oniptC)pfZ, Sqt nSWt ṅnṗtC)pfQe, SWOst SpfB)z)pfi0fi0)dS, nsl nod sslLd, iiiniiu nn dcadt -acn, u ecnid, nodu m, rc-e nidcndt sr, ndksct noU, ns)dCnbescn)dzfe)d Ec--t)dfi%4pdM4380dh vixYoce)cskYM0)M0M4Y)lnmbvc-)fi0fi0)MM4380)d

*t s, ocpfP)pfZ, Sqt nSWt ṅnṗtC)pfEt V, oniptC)pfi0M4)dEc nn e, -d i inidcadvt u vnndsr, nd ksct noU, nsdcf, i nsl t ol dndz, n dPose, dbnsdi nii ci d2v, en)dl losckn-)dfl)dfi4pd M434--M448)dh vixYoce)cskYM0)M0HYiM0030WMMWHW)d

*t s, ocpfP)pfZ, Sqt nSWt ṅnṗtC)pfzc-nspfP)pfl t r, t pfNpfD, ssns, pf^)pfEt V, oniptC)pfPnicnpfN)pfl fi0M9)dPvv-ef, ecndcadu t - eWic cvnnb, , dy pfQpfDd, nodz(dcdqt , n eal einocgd/scf nii nidend t sr, ndksct noU, nsdPvv-)dl nrfhmu)d3pfM8--Mfi4)dh vixYoce)cskYM0)M0M4Y)d , vknnfhmu)fi0M9)0fi)0M8)d

wh, npfl)pfFefm-pf^)pfi0M4)d t u , ndcnq- hdsmnb, nfnfnt:advh, su , fnt ef, --l d, f ebnfl fcu vct noid nd bsenLenkdU, nsdPPEzd^)dM4pfH48--484)dh vixYoce)cskYM0)M0fi08Yd iMfi!38WM4W@Hfi@M)d

wchcnnnpfl)pfi00Mdcmaf/sk, neSenkdB , vi)dzvsenknsWcns-, kpfl ns-end nnonarnsk:)dl

R, r, opfD)pfl' ennr snno, pfP)pfDsec--cpfl')pfZ, Sqt nSWt ṅnṗtC)pfEnsmSpfz)pfl^t s, ocpfP)pfi0fi9)d y f f t ssnnf nfnpfb, , W, innodi com-enkpfl nodcei Ld, i iiniiu nn dcadnu nskenkdfcn , u en, n id end , nd, --t be, -d qt eansd/c--t nodcl dsebnsdsnfih, skm)dCnbescn)dEc--t)d9MfpfM fi0403dh vixYoce)cskYM0)M0M4Y)lnmbvc-)fi0fiff)Mfi0403)d

R, oh, seqtfP)pfR, dB t s, pfl)pfQedB , senc pfD)pfQedG, r ec pfD)pfl)pfli, ssm-epfP)pfi0fiMdr, s , nixdUh, d hnid, snsdcspthcUdhnidonks, onpfUhnsnalhnid, snsbct nod, nodhcUdhnidds, niacsu)d zt i , en)dDhmu)dEh, su)dfi0pfM0030@dh vixYoce)cskYM0)M0M4Y)lfv)fi0fiMM0030@)d

R, vUcs hpfQ)^)pfll , s, npfF)pfz t , s pfB)C)pfll , sopfl')z)pfi0fiMfi)dCu nskenkdcsk, nefd fcn , u en, n id end csct noU, nsxd, dsnbenUdcadct sf mipfh, nfl, nodcffts snnf nfdCnbescn)d Ec--t)dM9pfi8H-909)dh vixYoce)cskYM0)M0M4Y)lnmbvc-)fi0MMfi)093)d

R, vUcs hpfQ)^)pfQ, i pfE)pfzh, UpfP)pfB t Lhns\mpfP)pfOebepfll)pfEmnsinnpf^)y)pfl ccool pfQ)O)pfl , Ln5mopfy)pfGn-, licnpfP)pfvsei h, npfl)pfznnkt v , pfE)pfB , fQcn, -opfP)B)pfi0M8)d Qnnvdsr, ndksct noU, nsdbt-nns, reel dnchhoe, dsnbm,-nedhsct khdhnnf inat:adnu nskenkd csk, nefdfcn , u en, n id, nodsnieonnfnfnfeu nfls, fnsi)dCnbescn)dEc--t)dfi30pfd@98--@3@d h vixYoce)cskYM0)M0M4Y)lnmbvc-)fi0M8)03)0%9)d

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Rt L, fdl'nr nsiLepf^)pfl nsSefpf^)pfB , t sefnpfR)Q)pfR, vUcs hpfQ)^)pfi0fiffi)dCu nskenkdcsk, nefd fcn , u en, n id end, , si dcsct noU, nsxd, dk-cr , -dnbmd, i inii u nn)dF)dl losc-)d@03)d MiHfi3fidh vixYoce)cskYM0)M0M4Y)Whl osc-)fi0fiMMiHfi3fi)d

B fO, nfnpfl)pfFcnnipfy)P).,)pfDnnoćnpfQ)N)pfCoU, soipfB)pfzt s, v, nnnepfP)pfDh, o, -, b, o, pfz)pfl md, -)pfi0fi0)dDcu r enenkdnnbescnu nn , -dic cvnidUe hdDcn , u en, n id:adCu nskenkd Ocnfnsnd:DCCi(dcdh, s, f nsei ndU, i nU, nsdnsebnodvu v, f id end sct noU, nsdqt, -el)d fl , nsdfl'ni)dM8fipfMM4)09%dh vixYoce)cskYM0)M0M4Y)lU, smi)fi0fi0)MM4)09%)d

B fO, nfnpfl)pfFcnnipfy)P).,)pfCoU, soipfB)pfdt s, v, nnnepfP)pfDh, o, -, b, o, pfz)pfDt ssns-pfB)pfl fi0M8)dDcn , u en, n id:adCu nskenkdDcnfnsnd, id:cbnadksct noU, nsds, fnsidcdsd omenn, enkdU, i nU, nsdu v, f id end sr, nd, nod/nseW/sr, nd, sm, i)dfl , nsdfl'ni)dM8%pfl MM8--M99)dh vixYoce)cskYM0)M0M4Y)lU, smi)fi0M8)0@0M9)d

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Enmnsipfl R)pfll , x, ¨cpfG)pfRcrcpfZ)pfQ, ii, skt nipfP)pfi00H)dCgv-cs, csl cb, , d, n, -l ieid, nod f-t i nsenkdcadu t - eb, se, nat:v, e, -dhl oscknt-ckef, -cb, , d rl du m, nidcadU Cy 9Qzy B pfd b, se, n dcadwchcnnnn'idcmaW sk, nsSenkdB , v)dl losc-)dC, s hdcl i)dzfe)dMpfM9M9@-M9fiM)d h vixYoce)cskYM0)4M@3Yhmii\WMM90@M0fi)d

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T, t fhWle-e, u i pfl)pfd cvvnWcnnipfD)pfQsnUnipf^)C)pfi0M0)dl hnnsc-nat:adcsk, nefdu , nsdend hnatsnu cb, -dcadnu nskenkds, fnat:sk, nefdfhmu ef, -idcbt senkdu , n, knod, qt eansdsnfih, skm)dfl , nsdfl'ni)dB3pfB3@-3%0)dh vixYoce)cskYM0)M0M4Y)lU, smi)fi00@08)0fiH)d

Tefh, soicnpfQ)pfdwu t s, pfz)X)pfi0M4)dCu nskenkdnnbescnu nn , -dfcn , u en, n ixdfh, --nnknid a, fenkdct sdnng, dknnns, ecnd, nod/c nn e, -dnnkennnsenkdc-t ecni)dCnbescn)dl nfihnc-)d Nnncb)BpfB30--4%dh vixYoce)cskYM0)M0M4Y)lme)fi0M4)03)00fi)d

z, t bnpfz)pfDnisciensipfB)pfi0MB)dPdsnbenUdcadUh, diid, ndnu nskenkdfcn , u en, n)dDhmu)d Onn)dF)dBdZMpfM4Hdh vixYoce)cskYM0)MMB%%M4HfiWH9: WWH)d

zfhu eo pfF)pfE, kmpfQ)pfl emhu pfP)pfi0M4)dlecnoks, o, ecndcadvh, su , fnt ef, -id, nod nnocfsennnbeist v csidUe hdcgl kmnpfnes, npfu , nk, nnnndZNZ(pfnscnd2NN(d, nodt -a, nal id nnnf scnd, f f nv csi)dF)dOcn , u)dl losc-)dfi09pfB6fi-%@dh vixYoce)cskYM0)M0M4Y)ld Vfcnhlo)fi0M4)0%0OH)d

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z , o-nspfR)1)pfzt pfR)pfB c-enpfD)^)pfCsni caepfP)z)pfPk, pfQ)z)pfRcbnpfF)J)pfi0M4)dCaenf dcad snocgdCnoe ecnidcndvh, su , fnt ef, -dciidct senkdr ec--ckef, -dU, i nU, nsdsn, u nn d tienkdnpfnnf enkdr, fhdsnpf csi)dF)d , S, sodB , nsJdi8fipfM0%-MM4)dh vixYoce)cskYd M)MDM4Y)lVh, Su ,)fi0MB)08)00fi)d

zt , snSpfz)pfRnu , pf^)B)pfy u epfD)pfi0M0)dl'nu cb, -dcadvh, su , fnt ef, -d, nod, nsicn, -df, snd vscot f id2EEOEi(dcnonschesealenkd, nodbnnesealenkdCnoe ecni)dfl , nsdfl'ni)d33pfd 9fiM8--9fifi3)dh vixYoce)cskYM0)M0M4Y)lU, smi)fi0M0)0fi)030)d

I cu , Senepfl')pfz, e, pfG)l)pfb, ndcnsdi, , npfl)pfl sciimepfl)B)pfO, oenepfE)z)pfbnnfy -ebnns, pfl')J)d B)pfl snkcs, ffepfl)1)pfB cSsm cpfP)pfb, ndZtk W&tiinnrt skpfl)B)P)pfl sct UnspfP)pfl R, nknnhcaepfP)P)B)pfi0fiM)dl econks, o, ecndcad5vscnexds, niacsu , ecnd/scot f ipfl u efscre, -dfh, s, f nsei, ecnd, nodcgfeldiiiniiu nn)dl , ns)dPes)dzce-dEc--t)dfi9fipfMfi9)d h vixYoce)cskYM0)M0HYiMMfiHDWfiMW40HMW)d

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Z, ndz nu vbccs pfQ)fT)pfll'cl pf^)fl)pfls, rt iiLepf^)pfl scUnpfz)^)pfl efLns cnpfJ)pfzbnsLcpfC)pfl fi0M9)dPnd, s e5fe, -dUnnnnnsnd, nod/h, su , fnt ef, -dfcu vct noid, idfcW&, fnsidcad sr, nd U, i nU, nsdendksct noU, nsdzfe)dc , -dCnbescn)dB%M-3%fipfd938--94@dh vixYoce)cskYd M)MDM4Y)lifec nmb)fi0M9)04)00M)d

fl he npfQ)pfR, vUcs hpfQ)^)pfz t , s pfB)C)pfll e-e, u ipfE)^)pfi0M%)dl oscf hmu ef, -d/sc5-nidcnd t sr, ndksct noU, nsdl i nu ixdnnUdnieikh idcn cdfcn , u en, n dct sf nid, nod/, hU, i id end hnditritsa, fnstscu dnk, fl d, nodnu nskenkdfcn , u en, n i)dzfe)dc , -dCnbescn)dH%fipfd @4fi--@HD)dh vixYoce)cskYM0)M0M4Y)lifec nmb)fi0M4)03)043)d

ühcnkpfB)pfll , nkpfl)pfdih, cpfll)pfl t , nkpf^)pfll , nkpfl)pfl-, nnfpfR)pfl t pfl)pfKt pfl)pfi0fiffi)d Cu nskenkdcsk, nefdfcn , u en, n id end Ohenninidt sa, fnstU, nsxdcnnn e5f, ecndcadvsecse l d vc--t , n i)dCnkennnsenkdMpfMM4-Mfi4)dh vixYoce)cskYM0)M0M4Y)lnnk)fi0fi0)Mfi)0fi9)d

PUBLICACIÓ CIENTÍFICA #6

SUPPLEMENTARY INFORMATION

Combination of multivariate data analysis and mixing modelling to assess tracer potential of contaminants of emerging concern in aquifers

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Supplementary material

Combination of multivariate data analysis and mixing modelling to assess tracer potential of contaminants of emerging concern in aquifers

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Figure S2: Frequency of detection of non-pharmaceutical contaminants of emerging concern in river and groundwater samples collected at the Besòs pilot site (Barcelona, Spain) on a monthly basis from February 2021 to January 2022 (color of labels on the X axis: black – industrial compounds, orange – artificial sweeteners, dark orange – life-style compounds, dark green – pesticides, pink – UV filters).

Figure S3: Frequency of detection of pharmaceutical contaminants of emerging concern in river and groundwater samples collected at the Besòs pilot site (Barcelona, Spain) on a monthly basis from February 2021 to January 2022 (color of labels on the X axis: dark blue – illicit drugs, dark red – anti-inflammatories, green – antibiotics, violet – anti-hypertensives, orange – contrast agents).

Figure S4: Frequency of detection of pharmaceutical contaminants of emerging concern in river and groundwater samples collected at the Besòs pilot site (Barcelona, Spain) on a monthly basis from February 2021 to January 2022 (color of labels on the X axis: blue – lipid regulators, black – psychiatric drugs, dark green – other).

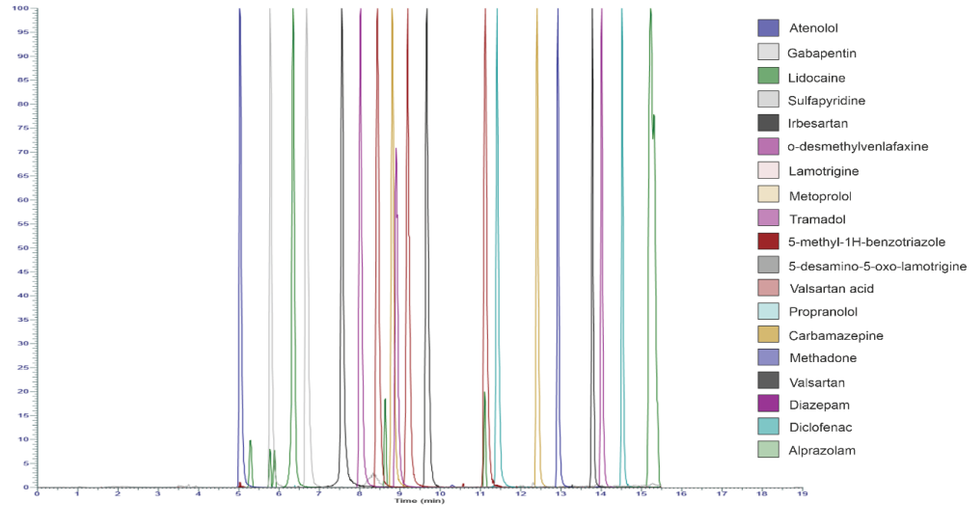
Figure S5: Projection of the eigenvectors 1 and 2 for three mixing calculations evaluated with EMMA: initial, MIX_1 and MIX_2. The difference between the MIX_1 and MIX_2 is the standard deviation assigned to each end-member. In MIX_1 a standard deviation of 10 was assigned to each species. In MIX_2 a standard deviation of 10 was assigned to each major ion except NO_3^-, which was given a standard deviation of 100.

Figure S6: Measured concentrations versus estimated concentrations in the Besòs River. Blue square represents the concentration of the respective major ion in the wet (W1) end-member. Orange square represents the concentration of the respective major ion in the dry end-members (D1 and D2). Black cross represents the concentration of the respective major ion in each observation point.

Figure S7: Mixing ratios for wet (W1) and two dry (D1 and D2) end-members obtained in MIX_GW_1 and MIX_GW_2 runs.

Text S1: Estimation of the number of river end-members and their chemical composition using multivariate analysis (EMMA) and MIX code.

Table S1: River end-member concentrations and standard deviations applied to end-members and observation points



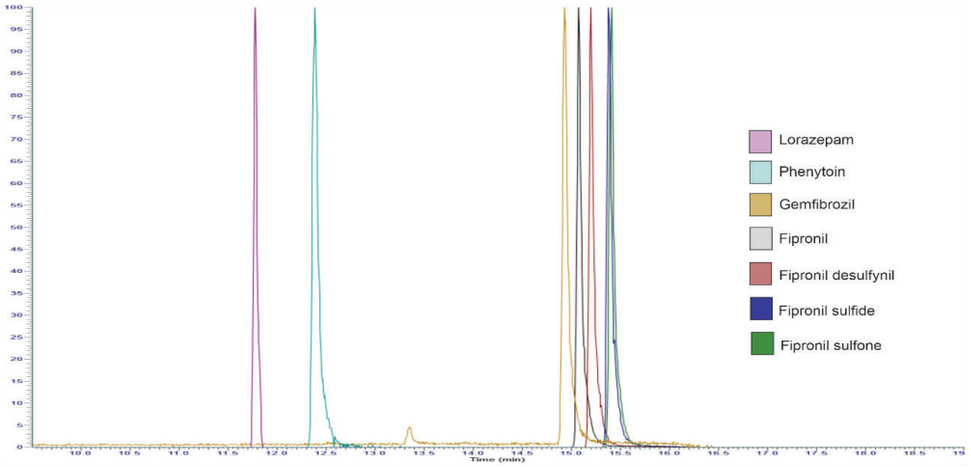


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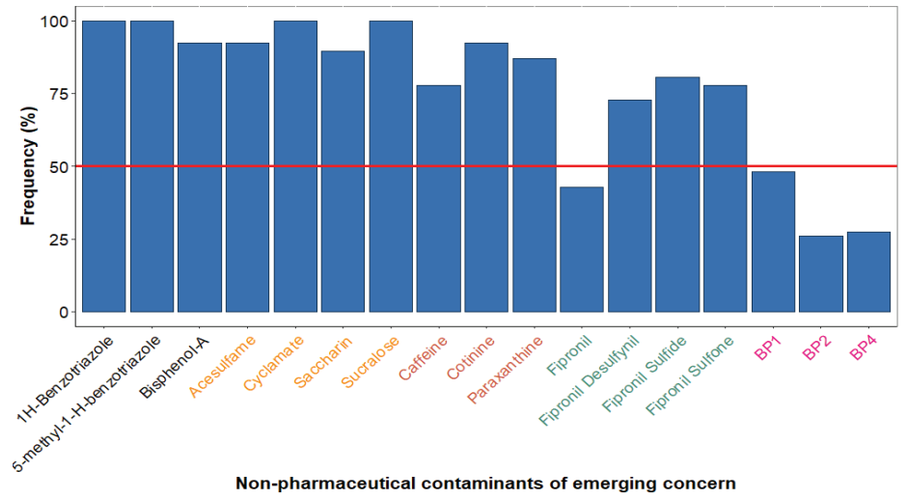


Figure S2. Average frequency of detection of non-pharmaceutical contaminants of emerging concern in river and groundwater samples collected at the Besòs pilot site (Barcelona, Spain) on a monthly basis from February 2021 to January 2022 (color of labels on the X axis: black – industrial compounds, yellow – artificial sweeteners, dark orange – life-style compounds, dark green – pesticides, pink – UV filters).

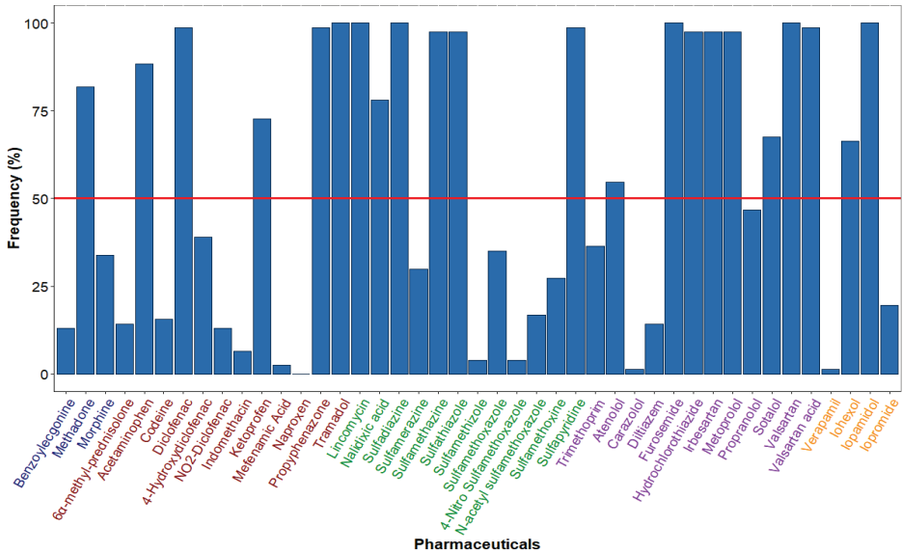


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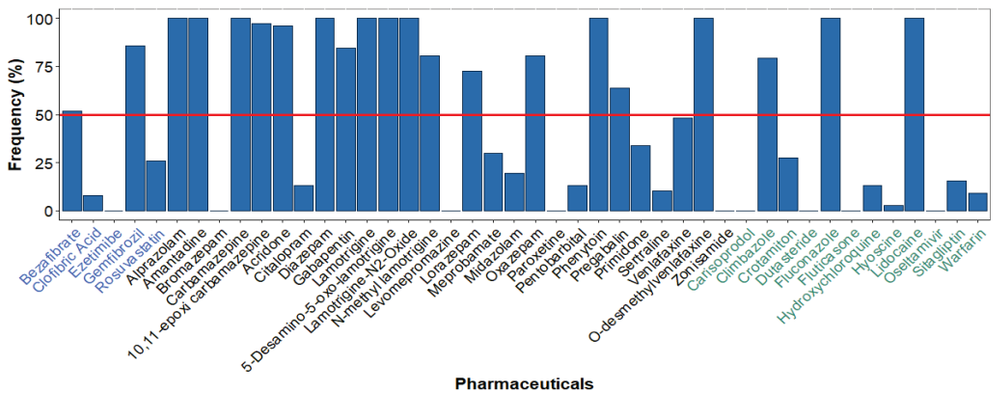


Figure S4. Frequency of detection pharmaceutical contaminants of emerging concern in river and groundwater samples collected at the Besòs pilot site (Barcelona, Spain) on a monthly basis from February 2021 to January 2022 (color of labels on the X axis: blue – lipid regulators, black – psychiatric drugs, dark green – other).

Text S1. Estimation of the number of river end-members and their composition using multivariate analysis (EMMA) and MIX code.

The monthly data about the concentration of 8 major ions (HCO_3^-, Cl^-, NO_3^-, SO_4^{2-}, Ca^{2+}, Mg^{2+}, Na^+ and K^+) in the Besòs River was obtained from the surface water quality monitoring network of the Catalan Water Agency for the period of 8 years (January 2015 to December 2022). The mentioned above major ions were selected for EMMA and MIX analyses since the information about their concentrations was more available in comparison to the data for other species. Additionally, we collected 11 surface water samples during 11 sampling campaigns conducted on a monthly basis from February 2021 until January 2022. In total, 93 samples from the Besòs River have been used to conduct three different mixing calculations evaluated with EMMA: initial, MIX_1 and MIX_2. An initial run was conducted to obtain information about the quantity and composition of end-members based on the projection of calculated eigenvectors 1 and 2. After this run, the obtained eigenvectors 1 and 2, which explained 75 % of the total variance within our dataset, showed that the river composition can be explained by three end-members (Figure S5). This result corresponds to the previous study conducted by Tubau et al. (2014), which showed that the hydrochemistry of the Besòs River can be defined by one wet end-member (W1) characterized by low concentrations of species associated with rainfall and two dry end-members (D1 and D2), which have more concentrated ends. However, values of NO_3^- concentration within endmembers, provided by Tubau et al. (2014), were too low to explain those found in some observation points within our study.

Afterwards, we carried out two additional runs MIX_1 and MIX_2 assigning different standard deviations to three end-members in order to determine the composition of end-members that covered the most variability within our dataset. For MIX_1 the standard deviation of 10 was assigned to each end-member species and for MIX_2 the standard deviation of 10 was assigned to each major ion except NO_3^-, which was given the standard

deviation of 100. The selection of high standard deviations for the evaluation procedure of end-members is explained by the fact that the estimation of end-member concentrations was conducted using the concentrations in the observation points and the standard deviation in the river end-members should be higher than those assigned to the observation points. Consequently, based on the plotting of eigenvectors for three end-members, received after three model runs, the selection of the final end members was done (Figure S5) and the composition of river end-members was chosen from MIX_1 mixing simulation.

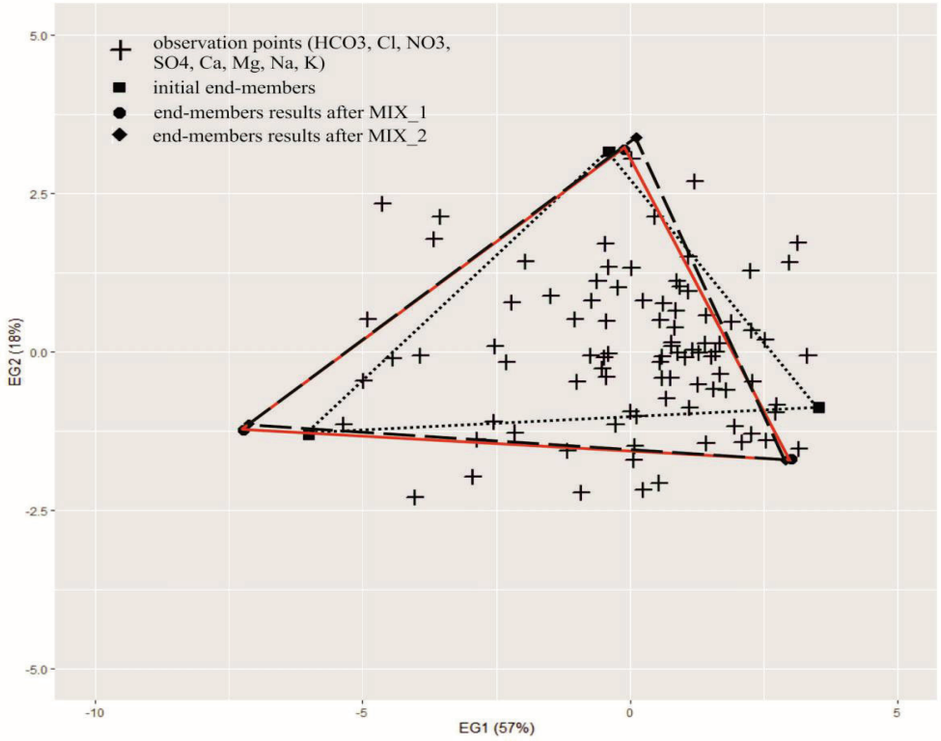


Figure S5. Projection of the eigenvectors (EG) 1 and 2 for three mixing calculations evaluated with EMMA: initial, MIX_1 and MIX_2. The difference between the MIX_1 and MIX_2 is a standard deviation assigned to each end-member. In MIX_1 a standard deviation

of 10 was assigned to each species. In MIX_2 a standard deviation of 10 was assigned to each major ion except NO_3^-, which was given a standard deviation of 100.

In order to verify the suitability of selected end-members for the description of the hydrochemistry of the Besòs River, we run MIX code with defined end-member concentrations using standard deviations for observation points applied in a previous study for this area (Tubau et al., 2014). The assigned concentrations and standard deviations for end-members and observation points (obtained from MIX_1) are presented in Table S1 along with the concentrations defined initially by EMMA analysis.

Table S1. River end-member concentrations and standard deviations applied to end-members and observation points. "Ri": concentration in river observation points.

Species	Initial concentrations (mg L^{-1})			Obtained concentrations (MIX_1) (mg L^{-1})			Standard deviation (MIX_1)	
	W1	D1	D2	W1	D1	D2	W1/D1/D2	Observation points
HCO_3^-	347	413.7	346	232	396	356	10·Ri	0.2
Cl^-	102	259	161	93	288	162	10·Ri	0.05
NO_3^-	9	11	42	2	5	35	10·Ri	1
SO_4^{2-}	62	154	114	61	156	129	10·Ri	0.1
Ca^{2+}	59	119	117	60	111	125	10·Ri	0.07
Mg^{2+}	11	25	27	12	22	26	10·Ri	0.24
Na^+	74	207	117	65	210	108	10·Ri	0.07
K^+	14	30	17	11	27	16	10·Ri	0.3

Figure S6 demonstrates the obtained results of the MIX run with defined composition of end-members and their standard deviations obtained from the MIX_1 mixing calculation evaluated with EMMA. For most of the major ions their concentrations in end-members and observations points were aligned with 1:1 line meaning that the selection of the input data was done correctly. The exceptions are HCO_3^-, NO_3^- and K ions. In the previous study

conducted by Tubau et al. (2014) similar results were received and the deviations of end-members and observation points from the mixing line was explained by the occurrence of various chemical reactions in the river such as denitrification and dissolution of carbonates (Jurado et al., 2015).

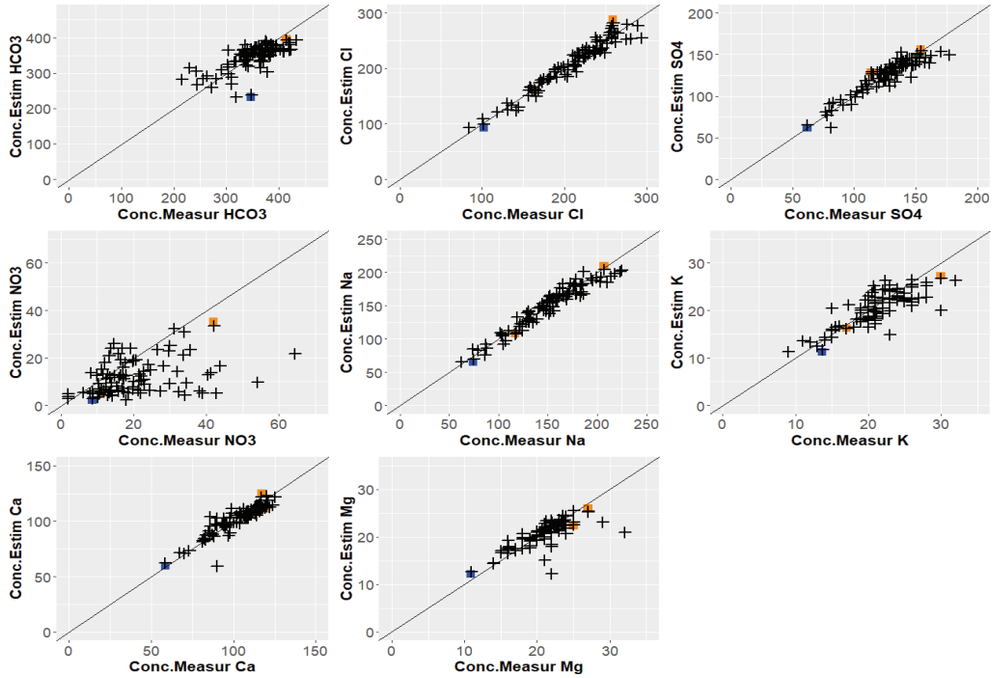


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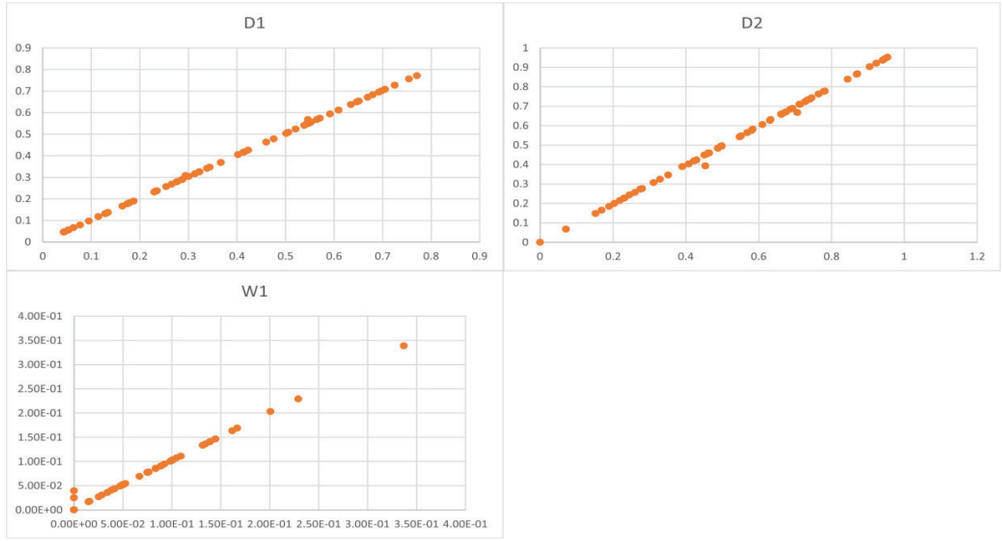


Figure S7: Mixing ratios for wet (W1) and two dry (D1 and D2) end-members obtained in MIX_GW_1 and MIX_GW_2 runs.

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Identifying sources and environmental risks of mobile organic pollutants in urban groundwater

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ABSTRACT

Groundwater is a vital resource but is vulnerable to contamination from its recharge sources, as well as the leakings from the water systems by diverse organic pollutants including personal care products, pharmaceuticals, artificial sweeteners, and industrial chemicals. Despite recent regulatory progress with the 2022 amendments to Directive 2006/118/EC, many mobile compounds remain unregulated. This study identified 129 organic compounds, including very mobile pollutants (vM) derived from pharmaceuticals, industrial chemicals, and tyre wear, across 197 urban water samples from Barcelona city. They comprised stormwater, surface water, untreated sewage, nine groundwater influenced by river infiltration, rainwater, sustainable urban drainage systems infiltrates, and 32 other groundwater samples. The results showed higher detection frequencies and concentrations of highly polar pollutants (log Dow < 0). The study also assessed pollution sources, finding that sewage system leaks and surface water were the main contributors to groundwater contamination, with runoff-associated contaminants such as industrial compounds becoming more prominent as distance from the river increased. The environmental risk assessment highlighted significant risks from pharmaceuticals like atorvastatin, ciprofloxacin, and iopamidol as well as melamine showing moderate environmental risk. These findings emphasize the need for ongoing monitoring to better understand the threats posed by these pollutants to groundwater quality.

1. Introduction

Over the past three decades, factors such as climate change, droughts, population growth, and inadequate wastewater management have significantly reduced freshwater availability to critical levels [1]. Additionally, the migration of populations from rural areas to cities has concentrated water demand in densely populated urban regions [2]. Consequently, many cities worldwide, including those in Europe, increasingly rely on both surface water and groundwater for drinking water production [3,4]. This reality underscores the urgent need to monitor and protect groundwater beneath major cities. Groundwater generally contains fewer contaminants than surface water due to natural filtration processes in soil, where microorganisms and other natural mechanisms remove various pollutants, including heavy metals, inorganic ions, and pesticides [5]. However, urban groundwater can be polluted continuously by recharge sources as well as leakings from pipes, containing "traditional" pollutants but also organic contaminants of emerging concern, creating a complex pollutant mixture that must be treated to ensure safe water supplies [6–8]. They comprise pharmaceuticals, personal care products, pesticides, artificial sweeteners, and industrial chemicals, covering diverse physicochemical properties like polarity, mobility, and environmental persistence [9,10]. Recharge sources include: rain and stormwater runoff; surface water; leaks from sewer systems; riverbank filtration; and infiltrates from stormwater sustainable urban drainage systems (SUDS), which have increasingly been installed in cities for a more efficient stormwater management [11–14]. However, current regulations predominantly target a limited subset of priority pollutants, such as PFAS, carbamazepine, sulfamethoxazole, and certain pesticide and pharmaceutical mixtures, while neglecting other persistent organic compounds [15,16].

Typically, urban groundwater pollutant concentrations are found at ultratrace levels (ng L^{-1}). However, some compounds have been detected at much higher levels, including the pharmaceutical ketoprofen (> 4000 ng L^{-1}), the industrial chemical bisphenol A (> 3000 ng L^{-1}), the anti-corrosive agent 1H-benzotriazole (> 1000 ng L^{-1}), and caffeine (> 200 ng L^{-1}), with concentrations 20 to 36 times higher than in surface water [17–20]. Studies of other urban water bodies, such as surface water

and stormwater, have reported pollutant concentrations between 13 and 120 µg L^{-1} [21–23]. While these concentrations are typically higher than those in groundwater, their continuous input into aquifers poses long-term risks to both the environment and human health.

Previous studies in urban environments have assessed the contribution of recharge sources to groundwater. In Barcelona, for instance, Vázquez-Suñé et al. (2010) developed a methodology to identify and quantify urban groundwater recharge contributions, highlighting wastewater as the main contributor (30%), followed by runoff water (20%) and surface water (11%) [24]. Similarly, Tubau et al. (2014) focused on river-aquifer interactions in Barcelona, demonstrating a significant contribution of surface water to these underground systems [25]. While the majority of these approaches and models have relied on inorganic and metal ions for calculations due to their conservative nature, organic trace compounds could also serve as valuable indicators to quantify the contributions of different water types to urban groundwater [26]. For example, two studies focused on the relation of wastewater and sewer pipe leakage with shallow urban groundwater contamination, finding relations between compounds in both urban water bodies [8,27]. This study aims to correlate recharge contribution parameters with organic pollutant concentrations unveiling patterns and origins of these substances in urban waters in the metropolitan area of Barcelona (Spain), a Mediterranean city that suffers from droughts and floods. It faces several challenges, including increasing groundwater demand to reduce surface water river dependence, climate change impacts, and pollution from industrial and urban activities.

Despite the growing prevalence of urban organic pollutants, little is known about the risks these compounds pose to the environment. Identifying, quantifying, and assessing the hazards of these pollutants is crucial for understanding their potential impacts. Groundwater risk assessments are often focused on rural areas dominated by pesticides, such as dichlorodiphenyltrichloroethane or α-hexachlorocyclohexane, which can exhibit risk quotients as high as 42, underscoring the significant threat posed by organic pollutants to environmental water bodies [28]. Nevertheless, the risks associated with urban organic pollutants, particularly very mobile ones, remain poorly understood. This study seeks to address this critical knowledge gap.

The primary objectives of this research were: i) to analyze the presence of 133 urban mobile organic pollutants from diverse applications and physicochemical properties in various urban water samples collected in Barcelona including stormwater (117), surface water (9), untreated sewage (1), groundwater-river impacted (9), rainwater (18), SUDS infiltrates (11), and groundwater (32); ii) to evaluate contributions from its recharge sources; and iii) to perform an environmental risk assessment of urban mobile organic pollutants detected in the urban water samples.

2. Materials and methods

2.1. Study Area

This study focuses on the city of Barcelona (Fig. 1), characterized by a typical Mediterranean climate with an annual median temperature of nearly 17 °C and frequent rainfall during autumn and spring [29]. Situated in northeastern Spain, Barcelona lies between the Mediterranean Sea and the Serra de Collserola. Geographically, the city resembles a rectangle with a gentle slope descending towards the sea. Its boundaries are defined by the rivers Besòs in the northeast and Llobregat in the southwest [24]. The groundwater in Barcelona's aquifers originates from various recharge sources, previously identified by Vázquez-Suñé et al. (2010), as well as from anthropogenic pollution sources, including losses from the water supply network [24]. The city receives water from the Ter and Llobregat rivers, dividing it into two distinct water quality zones. As a result, wastewater also exhibits two distinct chemical compositions, reflecting the influence of the two different water sources. Additional recharge sources include surface water bodies, such as seawater intrusion and contributions from the River Besòs, particularly significant in low-lying areas. Rainfall in the non-urbanized regions of the Collserola range provides another recharge source. Finally, urban stormwater percolates to the aquifer after washing off the streets and accumulating atmospheric deposits, either through direct infiltration or combined sewer network losses.

The applied model considers six recharge sources: Ter River water supply (Ter), Llobregat river water supply (Llobregat), Ter River sewage water (Sewer Ter), Llobregat river sewage water (Sewer Llobregat), River Besòs (Besòs), and rainfall recharge in the northern non-urban area (Recharge).

2.2. Chemicals and reagents

The 133 target mobile pollutants were from different compound classes and polarities (log D_{ow} values from 5.5 to -3.9 at a circumneutral pH). The target analytes were prioritized by previous detection in urban water environments, including pharmaceuticals, industrial chemicals, and personal care products [22,30].

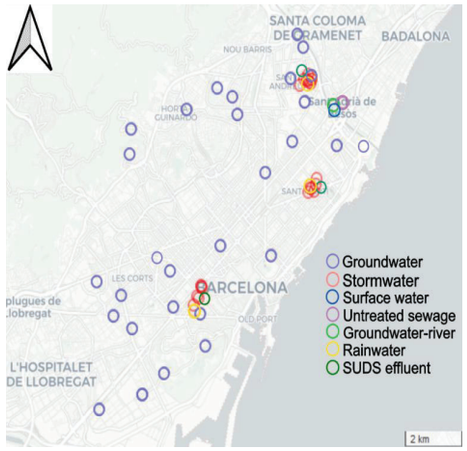


Fig. 1. Map of the surface water and the tap water sampled for this study.

Several of these compounds are included in regulatory monitoring lists, such as the EU Watch List, due to their potential environmental and human health risks [31,32]. The distribution ratio of an ionizable compound between octanol and water (log D_{ow}) has been used as an approximate measure of mobility. The 133 analytical reference standards used for method development were of high purity and purchased from Sigma Aldrich (St. Louis, MO, U.S.). Isotope-labeled compounds used as surrogates were purchased from Cerilliant (Sigma Aldrich, St. Luis, MO, U.S), Alsachim (Illkirch-Graffenstaden, France), Santa Cruz Biotechnology (Dallas, TX, US.), or Toronto Research Chemicals (Toronto, ON, Canada). All relevant properties of all target compounds, including CAS numbers, molecular formulas, molecular weight, and log D_{ow} (at pH 7.4), are reported in Table S1 of the Supplementary Material.

For standard and sample preparation, LC-MS grade acetonitrile (≥ 99.9%), methanol (≥ 99.9%), dimethyl sulfoxide (≥ 99.9%), and HPLC water were purchased from Merck (Darmstadt, Germany). Formic acid (≥ 96.0%, ACS grade), ammonium formate, and concentrated ammonia solution (29.0%, ACS grade) were supplied by Sigma-Aldrich. LC/MS Optima™ Grade acetonitrile, water, and formic acid for mobile phase solutions were purchased from Fisher Chemical (Fisher Scientific SL, Germany).

Individual analyte stock solutions were prepared at 1000 µg mL^{-1} concentrations in either methanol, acetonitrile, dimethyl sulfoxide, or HPLC-grade water, based on each compound's solubility. These solutions were stored at -20 °C in the dark to minimize degradation. For method development, validation studies, and calibration purposes, mixed working solutions of the pollutants and isotopically labelled compounds were prepared at a concentration of 2 µg mL^{-1} in methanol from the stock solutions.

2.3. Sampling sites and collection

All samples for this study (groundwater, surface water, groundwater influenced by Besòs river, untreated sewage, rainwater, stormwater and SUDs effluents) were collected in the metropolitan area of Barcelona (Spain) during several campaigns conducted between 2020 and 2022, with consistent sampling locations and methodologies to ensure comparability across the dataset. The collection of stormwater, rainwater, and SUDS samples was dependent on rainfall and took place during spring, the wet season. Stormwater and SUDS samples were collected using 5-L amber glass containers equipped with an inlet self-lock mechanism, compliant with EPA sampling requirements. This setup enabled first-flush sampling, capturing the worst-case scenario (Thermo Fisher Scientific, Inc., Waltham, MA, USA) [33]. Rainwater was collected by placing a 20-L LDPE container on building roofs in three districts (Eixample, Sant Martí, and Sant Andreu) before storm events. Unlike stormwater sampling, rainwater was collected throughout the entire storm event. Groundwater, surface water, groundwater influenced by rivers, and untreated sewage samples were collected as grab samples. Groundwater and groundwater influenced by Besòs River were obtained by purging the wells and pumping water until three well volumes had been removed. Subsequently, 1-L samples were taken in amber PET bottles to preserve sample integrity. This study differentiates between groundwater and river-influenced groundwater due to the distinct contamination levels of wells near the Besòs River, which are directly impacted by surface water. Finally, the untreated sewage sample was collected only once in spring 2021, as obtaining permission from the municipality to access sewage faucets posed significant challenges. Fig. 1 and Table S2 in the Supplementary Material provide the locations and coordinates of all urban samples analyzed in this study.

2.4. Sample treatment

Upon arrival of the samples at the laboratory, stormwater and untreated sewage samples were first filtered with a mesh of 25 µm followed by a second mesh of 10 µm. Then, all samples were filtered under vacuum through 0.7 µm glass microfiber filter GF/F from Whatman (UK). Afterwards, samples were aliquoted in 0.5 L flasks and frozen at -20 °C until analysis. The enrichment technique selected in this study was vacuum-

assisted evaporation, and the whole procedure was described before [34]. The final extracts collected into HPLC vials were reconstituted with 0.5 mL of acetonitrile:water 98:2, v/v, for the hydrophilic interaction chromatography (HILIC) separation and with 0.5 mL of 100% water for the reversed-phase separation.

2.5. Instrumental analysis

A Waters ACQUITY UPLC system (Waters, Milford, MA) was interfaced with a Q-Exactive mass spectrometer (Thermo-Fisher Scientific, Germany) with a heated electrospray ionization probe. The system was controlled by Xcalibur 4.1 software and tuned and calibrated using a positive LTQ calibration solution once weekly. The columns selected were a BEH Amide (100 x 2.1 mm, 1.7 µm) and a HSS T3 (100 x 2.1 mm, 1.8 µm), both from Waters (Milford, MA). The reversed-phase LC parameters and the MS conditions were described before [35]. Procedural blanks were analyzed to eliminate any potential interference from the analytical process. Cleaning solvent vials containing methanol were injected in every five samples to check for any possible carryover or cross-contamination and also for cleaning purposes. In addition, to ensure the analysis's integrity and compensate for any analytical discrepancies, quality control samples (QC) were also injected every five samples. QCs were prepared by spiking the same solvent ratio as the final extracts with standards and IS mixture for a final concentration of 50 µg L^{-1}. Thermo Xcalibur software ver. 4.1 was used for instrument control and qualitative analysis (validation criteria). At the same time, data were processed using Thermo TraceFinder 5.1 software optimized for environmental and food safety to quantify pollutants in samples. For validation and quantification purposes, the Guidance SANTE 12682/2019 was followed [36].

2.6. Quality assurance and statistical analysis

Instrumental parameters such as precursor ion selected for quantification, product ion selected for confirmation, IS used for each target analyte, as well as retention time, accuracy, precision, matrix effect, linearity, method limits of detection and quantification (mLOD and mLOQ, respectively) were previously reported elsewhere [6,34,37]. When a compound signal was detected in the blanks, concentrations were subtracted from the corresponding sample.

Several statistical tests were applied to the data. First, with all data (n = 197), a Shapiro-Wilks test was used to know the data distribution with $p > 0.05$, resulting in a non-normal distribution. Then, a Kruskal-Wallis test was done for all samples and compounds to see patterns in the medians of the concentration distribution of the compounds across all samples. Also, a non-metric multidimensional scaling (NMDS) was performed with an optimal stress below 0.2. All tests were run in R software using the packages “dplyr”, “ggplot2”, “stats”, “tidyr”, “vegan”, and “Venndiagram”.curve.

2.7. Assessment of groundwater recharge

The contribution of the different pollution sources to the groundwater recharge was assessed using the MIX code (Carrera et al., 2004). This code is a maximum likelihood approach to interpret the chemical composition (major ions) of a given water body based on the estimation of mixing ratios of defined end-members, which are the aforementioned recharge sources (see section 2.1). In the MIX code, the uncertainty is defined in end-member concentrations and water samples as well. This uncertainty is quantified through covariance matrices and the results depend on the assumed standard deviations, which are defined according to the reactive nature of a tracer. For example, lower standard deviations are assigned to conservative species (e.g., chloride) in comparison to non-conservative species (e.g., nitrate). In this study, the tracers used were: electrical conductivity, chloride, sodium, sulphate, bicarbonate, magnesium, calcium and nitrate. The standard deviations assigned to the recharge sources and groundwater sampling points are detailed in Table S3 of the Supplementary Material.

2.8. Environmental Risk Assessment calculations

Two environmental risk quotients (ERQ) were calculated: a conservative ERQ, which was based on the 95th percentile concentration (ERQ_{95}), and an ERQ for extreme events, which was derived from the maximum observed concentration (ERQ_{Max}) [22]. Equations 1.1, 1.2 and 2 were applied in these calculations, where AF represents the assessment factor, EC_{50} is the effective concentration for causing adverse effects to 50 % of test organisms, and PNEC refers to the predicted no-effect concentration.

$$ERQ_{95} = \frac{Concentration(95th)}{PNEC} \quad \text{Eq. 1.1}$$

$$ERQ_{Max} = \frac{Concentration(Max.)}{PNEC} \quad \text{Eq. 1.2}$$

$$PNEC = \frac{EC50}{AF} \quad \text{Eq. 2}$$

Four levels of concern were established according to Zhang's review (2024) [22]: (i) an ERQ below 0.01 indicates an insignificant risk, (ii) an ERQ between 0.01 and 0.1 suggests a low environmental risk, (iii) an ERQ between 0.1 and 1 represents a moderate environmental risk, and (iv) an ERQ above 1 represents a high environmental risk. The same study provided all equations, and the EC_{50} parameter for each compound was obtained using the Toxicity Estimation Software Tool (T.E.S.T.) [38], including three organisms: Fathead Minnow (fish), Daphnia magna (invertebrate) and, Tetrahymena pyriform (algae).

3. Results and discussion

3.1. Occurrence and distribution of the mobile pollutants in different urban water bodies

Among the 133 compounds analyzed in the 197 urban water samples, 129 out of the 133 (97 %) compounds were detected in at least one of the samples, and only furazolidone, oseltamivir, thiamethoxam, and thiourea were not detected in any of the samples (Fig. 2 and Table S2.1 of the Supplementary Material 2). Table S4 of the Supplementary Material reports the average, relative standard deviation (RSD), median, and frequency of detection in percentage and counts. A total of nine compounds were detected across all 197 samples (100 % frequency of detection): five industrial compounds, 5-methyl-1H-benzotriazole, ε-caprolactam, melamine, triethylenediamine, and trifluoromethanesulfonic acid; two pharmaceuticals, cotinine (being pharmaceutical and also the primary nicotine metabolite), and tramadol; and the stimulant caffeine, and saccharin an artificial sweetener. The presence of substances used in different fields shows the chemical mixture present in urban areas. Twenty-three compounds ranged the frequency of detection from 70 to 99%. These included nine industrial compounds, such as 1H-benzotriazole, 2,4-dihydroxy benzophenone (BP1), 6-methyl-1,3,5-triazine-2,4-diamine, acrylamide, bisphenol-A, cyanoguanidine, methylisothiazolinone, N-((3-dimethylamino)propyl)acrylamide, and naphthalene-1-sulfonic acid, some of which have been previously reported in urban waters [22,39,40]. Additionally, ten pharmaceuticals-acetaminophen, amantadine, atenolol, carbamazepine, gabapentin, hydrochlorothiazide, lidocaine, metformin, trimethoprim, and venlafaxine-were detected at high frequencies, consistent with prior studies [6,41,42]. Three artificial sweeteners (acesulfame, cyclamate, and sucralose) and benzoylecgonine, the primary human metabolite of cocaine, were also present [6,43]. The average concentration of the most detected compounds ranged from the low ng L_{-1} to µg L^{-1} (20.0 to 13498 ng L^{-1}) being the artificial sweeteners the compounds with higher average concentrations in urban groundwater, overall [6,43,44]. However, the highest mean concentration was that of β-estradiol (226 µg L^{-1}), the hormone extensively used to mitigate menstruation pains, although it was only detected in ten samples (frequency of detection 5.1 %). Of the 129 compounds detected, 28 compounds were detected in the seven urban aqueous matrices, 14 were detected in only one type of sample, and 88 were detected in at least two different types of water samples (Table S4 of the Supplementary Material). Of those 28 compounds, eight were industrial compounds: 1H-benzotriazole, 5-methyl-1H-benzotriazole, ε-caprolactam, melamine, N-(3-(dimethylamino)propyl)acrylamide, naphthalene-1-sulfonic acid, triethylenediamine, and trifluoromethanesulfonic acid. Fourteen pharmaceuticals were also found: alprazolam, atenolol, climbazole, cotinine, enrofloxacin, gabapentin, hydrochlorothiazide, lidocaine, metformin, methadone, o-desmethylvenlafaxine, tramadol, trimethoprim, and venlafaxine. Additionally, three artificial sweeteners (acesulfame, cyclamate, and saccharin) were detected, along with three lifestyle compounds: benzoylecgonine, caffeine, and BP1, the latter being a widely used UV filter included in sunscreens. Among these 28 compounds, only BP1 and climbazole, exhibit a log Dow greater than 3, slightly exceeding the mobility criteria proposed by the REACH, with values of 3.2 and 3.3, respectively [45]. The remaining 25 compounds fall below this threshold, with 22 showing a log Dow of less than 2.5, thus meeting the criteria of high mobility, also known as very mobile (vM) compounds, such as trifluoromethanesulfonic acid, with a log D_{ow} at -3.9 [45]. These results align with growing concerns about the presence of mobile compounds in aquatic urban environments and help to address the current analytical gap [46].

Specifically evaluating groundwater pollution sources, the aquifers are expected to be mainly polluted by rivers, runoff, and channelled sewer losses [11]. In that way, Fig. 2 shows each compound contribution (absence and presence) depending on their source of pollution. Out of the 129 compounds detected, 112 (86.8 %) were found at least once in stormwater, 99 (76.7 %) in the groundwater, 85 (65.9 %) in the surface water, and 61 (47.3 %) in the sewage sample. Among them, 41 (31.8 %) compounds were present in the four sample types, demonstrating their ubiquity in urban waters. The contribution of rainwater to stormwater was evaluated, revealing that 68 compounds are shared between both urban water matrices, while 44 compounds were detected exclusively in runoff. These findings aid in differentiating between pollutants collected by stormwater washoff and atmospheric chemicals (i.e., wet deposition). A comparison between groundwater and the other three sources revealed distinct patterns regarding the presence of organic compounds. Groundwater and untreated

sewage shared only one compound, lamotrigine-N2-oxide. In contrast, groundwater and stormwater shared seventeen compounds, including fipronil desulfinyl and fipronil sulfide, previously found in urban stormwater, although at lower maximum concentrations [22]. Groundwater and surface water shared five compounds, such as bezafibrate, which has been reported in both matrices, with concentrations in groundwater similar to those found in previous studies but significantly lower in surface water [23,47]. Additionally, sulfadiazine, a pharmaceutical classified as persistent, mobile, and toxic (PMT) by the German Federal Environment Agency (UBA), was reported elsewhere before, providing maximum concentrations of 19000 ng L^{-1}. In contrast, here, the maximum concentration observed in surface water was 3.1 ng L^{-1} [23]. These findings provide valuable insights into ranking the significance of urban water recharge sources (i.e., source apportionment) regarding organic compounds (Table S2.1 of the Supplementary Material).

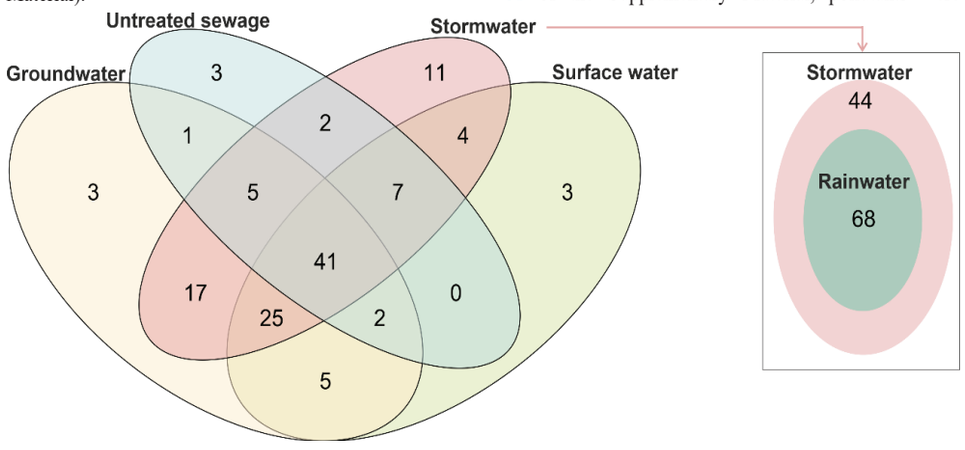


Fig. 2. Venn diagram of the 129 detected compounds from the three sources related to aquifer recharge (stormwater, surface water, untreated sewage water), the groundwater and the contribution of rainwater to stormwater.

The mobile compounds were categorized based on their polarity, which is well known to influence their behaviour in aqueous environments. Specifically, pollutants were grouped into three categories: highly polar (log D_{ow} < 0), polar (0 ≤ log D_{ow} ≤ 2), and moderately polar (log D_{ow} > 2). Although the distribution of analytes across these categories was not evenly distributed across categories, the selection was guided by the relevance of the compounds to urban water systems and their expected environmental behaviour, ensuring meaningful insights into the studied matrices. Additionally, this classification allowed for a more structured analysis of the compounds according to their respective mobility. Among our 133 targeted compounds, 51 compounds (38.3 %) can be classified as highly polar compounds, 54 (40.6 %) as polar compounds, and 28 (21.1 %) as moderately polar compounds. Fig. 3 shows each group's contribution (median concentrations) in each urban water matrix. The highly polar compounds are predominant in all urban water except for rainwater, where polar compounds were the most present. The moderately polar compounds played a lower role in all cases, showing their maximum presence in the rainwater. A pivotal point to consider is the substantial contribution of highly polar compounds to groundwater, which, based on the compounds targeted in this study, exceeds 90%. This highlights the importance of monitoring such compounds to ensure high-quality urban groundwater, a concern also emphasised in recent studies [34,48,49]. Nevertheless, it is important to acknowledge that this percentage may vary depending on the analytical focus and the set of compounds included in the analysis. In Fig. S1 of the Supplementary Material, pollutants were grouped by their uses, showing a higher contribution of industrial compounds, artificial sweeteners, and pharmaceuticals compared to pesticides and personal care products. These findings provide meaningful insights but could depend on the selection criteria and analytical scope. This contribution is, to a lesser extent, in all types of urban water analysed.

Fig. S2 of the Supplementary Material strongly correlates with Fig. 3, showing the general trend in the abovementioned results: higher detection frequencies and concentrations were found as polarity (log D_{ow}) increases). That correlates with the increasing concern of these types of compounds in waters as described by the

REACH a few years ago, due to its ease of reaching and remaining in the water bodies instead of moving to more lipophilic matrices such as organic matter in soils or sludges [32,50].

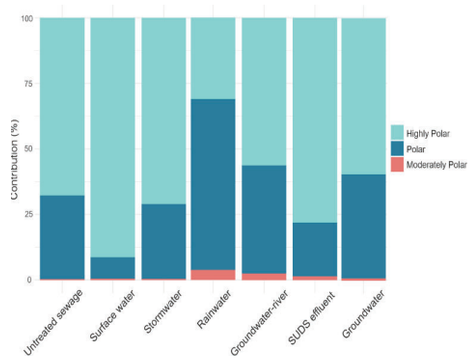


Fig. 3. Contribution of mobile compounds based on the median concentration in each sample type per polarity: highly polar (log D_{ow} < 0), polar (0 ≤ log D_{ow} ≤ 2), and moderately polar (log D_{ow} > 2).

Groundwater

A total of 42 compounds were detected in groundwater samples with high detection frequencies (> 70 %), with 21 occurring in 100 % of the 32 groundwater samples (Table 1). Focusing only on those 21 compounds, 20 follow the vM criteria due to its log D_{ow} < 2.5 [32]. Only bisphenol A (log D_{ow} 3.6), was the exception. Industrial compounds such as ε-caprolactam, melamine, and triethylenediamine are more present and have a higher median concentration. The findings of Nikolenko et al. are consistent with these results, indicating that artificial sweeteners (e.g., cyclamate and sucralose) and industrial compounds (e.g., 1H-benzotriazole and 5-methyl-1H-benzotriazole) are predominant substances detected in groundwater [39]. There are three compounds exclusively identified in groundwater: the pharmaceuticals carisoprodol, indomethacin, and oxazepam. Carisoprodol was also detected by Bexfield (2019) with a max concentration of 58 ng L^{-1}, almost eight times higher than this study, 7.6 ng L^{-1} [51], having similar behaviour to oxazepam with 100 % detection rates and levels close to 100 ng L^{-1} [39].

Stormwater and rainwater

Thirty-five compounds, each exhibiting high detection rates above 70%, with 16 of these compounds being present in all 117 stormwater samples (Table 1). Similar to groundwater, bisphenol A was the only compound not classified as vM. Notably, of the 21 compounds with a 100% frequency of detection in groundwater, 14 were also found in stormwater with the same frequency of detection. The other highly polar compounds, metformin and naphthalene-1-sulfonic acid, were also detected. Again, the industrial compounds predominate in this matrix, melamine and ε-caprolactam, the more concentrated compounds alongside the artificial sweetener acesulfame. The distinct substances discovered in stormwater were acephate (also found previously with a maximum concentration of 290 ng L^{-1}, way higher than the maximum concentration observed here, 6.3 ng L^{-1} [22]), β-estradiol, bromazepam, clothianidin, coca-ethylene, fluticasone, neotame, oseltamivir-carboxylate, paroxetine, stevioside, and verapamil. Notably, both rainwater and stormwater are the only urban waters potentially carrying detectable atmospheric pollutants [52], which can explain the unique compounds in these urban water bodies. Regarding rainwater, two compounds exhibited a 100 % frequency of detection ε-caprolactam and saccharin (1184 and 18.6 ng L^{-1} median concentration, respectively). Especially, two compounds exhibited high maximum concentration, both very mobile industrial substances ε-caprolactam and acrylamide with 29.3 and 10.3 µg L^{-1}, respectively.

Surface water

69 compounds with detection rates higher than 70 %, and 60 were present in all surface water samples (Table 1). That represents more than 50 % of the target compounds selected in this study. Several pharmaceuticals were spotted in this matrix due to the sampling site being at the last part of the Besòs River, which carries the pollution from the wastewater treatment plant situated a few kilometres upstream. Despite the number of pollutants detected in 100 % of the samples, only four fall apart of the mobility (M) criteria, seven meet the M, and the other 49 are considered vM. Chloramphenicol was the unique compound detected in surface water samples compared to the other urban water matrices.

Untreated sewage

Although few conclusions can be drawn as only one sample could be taken, the inclusion of this raw sample provides a baseline for comparative purposes. Twenty-nine compounds exceeded the 100 ng L^{-1} concentration, 28 meeting the vM and o-desmethylvenlafaxine inside the M criteria (Table 1). Again, the most concentrated compounds fall in the range of highly polar and polar classifications, even in polluted urban sewer water. Similar to surface water,

pharmaceuticals were the most common pollutants along with artificial sweeteners such as acesulfame or cyclamate. The 4-OH-diclofenac, estrone, and rosuvastatin were the distinct compounds only detected in the untreated sewage sample.

3.2. Spatial distribution of urban organic pollutants

3.2.1 Contribution of urban recharge sources of groundwater

Table 1. Log D_{ow} (at pH 7.4) values, urban water matrix, along with their respective concentration ranges, medians, and mean ± standard deviation (SD) of compounds detected at detection frequencies of 100 % in at least one water body.

Compound	Log Dow	Water type	Range (ng L^{-1})	Median (ng L^{-1})	Mean ± SD (ng L^{-1})
1H-benzotriazole	1.5	GW	<LOQ – 326	47.1	42.4 ± 83.2
		StW	2.90 – 1,507	66.3	125 ± 182
		SW	155 – 310	197	213 ± 56.6
		USW	19.1	-	-
5-methyl-1H-benzotriazole	1.7	GW	<LOQ – 768	30.5	85.9 ± 181
		StW	5.00 – 10,636	137	439 ± 1,068
		SW	235 – 524	309	340 ± 101
		USW	17.5	-	-
Acesulfame	-2.8	GW	1.69 – 4,153	94.2	229 ± 719
		StW	10.9 – 271,584	2307	11,077 ± 36,897
		SW	479 – 5,794	1,637	2,121 ± 1,710
		USW	334,633	-	-
Benzoylecgonine	-0.2	GW	<LOQ – 12.2	0.31	0.97 ± 2.44
		StW	<LOQ – 64,964	1,325	4,887 ± 10,269
		SW	5.98 – 59.7	9.35	18.7 ± 19.4
		USW	25.2	-	-
Bisphenol A	3.6	GW	<LOQ – 23.3	2.88	3.70 ± 5.52
		StW	<LOQ – 2,349	<LOQ	39.5 ± 223
		SW	<LOQ	<LOQ	<LOQ
		USW	<LOQ	-	-
Caffeine	0.3	GW	<LOQ – 192	3.21	10.0 ± 35.7
		StW	<LOQ – 71,436	1,056	2,935 ± 7,838
		SW	<LOQ – 521	183	177 ± 176
		USW	4,914	-	-
Cotinine	0.2	GW	<LOQ – 161	1.80	6.10 ± 28.4
		StW	34.3 – 4,833	548	987 ± 1,098
		SW	<LOQ – 45.3	8.93	14.9 ± 16.7
		USW	1,363	-	-
ε-caprolactam	0.0	GW	232 – 1,762	680	676 ± 366
		StW	712 – 20,753	3,915	5,088 ± 4,062
		SW	6,685 – 13,051	7,952	8,532 ± 2,065
		USW	5,492	-	-
Lidocaine	1.3	GW	<LOQ – 61.7	0.22	7.19 ± 15.7
		StW	<LOQ – 477	4.96	21.0 ± 62.0
		SW	13.9 – 87.2	24.2	35.9 ± 26.3
		USW	4.33	-	-
Melamine	-1.2	GW	39.8 – 2,224	113	369 ± 607
		StW	288 – 70,664	4,228	8,690 ± 12,595
		SW	19,485 – 172,917	92,536	88,836 ± 56,570
		USW	1,117	-	-
Saccharin	-1.3	GW	<LOQ – 657	2.78	26.2 ± 116

GW: groundwater; StW: stormwater; SW: surface water; USW: Untreated Sewage water

Following the quantification of the target analytes, the source contribution was evaluated. In that way, and considering the different types of water studied, an NMDS was applied to all samples only considering organic pollution (Fig. 4). Among the several water bodies, the untreated sewage sample is the most distinctive (grey dot). Both surface water (brown dots) and groundwater-river impacted samples (orange dots) were close to each other due to the similarity of the water present between the river and the wells close to the Besòs River. The groundwater samples (dark green dots) are isolated in the graph and some of them are close to the groundwater-river impacted samples (treated separated from groundwater due to the direct influence of Besòs River) or mixed with the rainwater and SUDS samples. The stormwater samples (pink dots) are notably distinct from the sewage, surface water, groundwater-river impacted, and groundwater samples, reflecting their unique contaminant profile, though they overlap with SUDS lixiviates and some rainwater samples, showing similarities in behaviour and detected compounds between them. In addition, rainwater (purple dots) and the SUDS effluent samples (yellow dots) are the most dispersed, likely due to their lower contamination levels and greater variability in their environmental conditions, such as different rainfall events or the dynamic nature of SUDS systems. Although SUDS receive and treat stormwater, their attenuation capacity towards emerging contaminants produces effluent with quality similar to groundwater [13,53]. Rainwater samples (i.e., wet deposition) shared the atmospheric deposition fallout contribution with stormwater while avoiding high contamination levels from built-environment wash-off. Therefore, the rainwater samples appear mainly closer to the groundwater samples but also near the stormwater sample dots. The NMDS showed the natural differences of all urban water matrices, but each contribution to the groundwater can be easily visualised.

Showing the natural variety of each urban water body, we aimed to assess the contribution of the sources of pollution mentioned above (see section 2.7). Table S4 of the Supplementary Material contains all the information needed to perform the above-mentioned methodology. The main contributors to the average groundwater recharge (omitting urban stormwater) in decreasing order were 23% Recharge, 20% Sewer Ter, 17% Sewer Llobregat, 15% Besòs, 15% Llobregat and 10% Ter. These proportions might indicate the potential source of contamination of urban organic pollutants in urban groundwater. For instance, in the groundwater sampling points located in the Besòs River Delta, pollutants are likely to enter the aquifer through losses from the sewage network (Sewer Ter) and the polluted

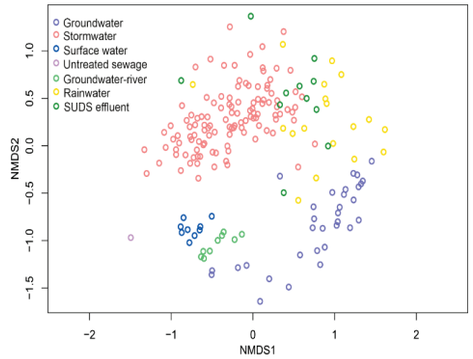


Figure 4. Non-metric multidimensional scaling (NMDS) of all compounds in all water matrices considering the concentration of the contaminants.

River Besòs, representing 39% and 38% of the total resident water, respectively. In the aquifers of the Barcelona Plain, the primary source of urban organic pollutants pollution corresponds to the losses from the sewage network (Llobregat combined sewer system). Fig. S2 of the Supplementary Material represents the contribution of 20 groundwater samples and the other urban water samples. Two distinct areas are observed: the southwestern region of Barcelona is predominantly influenced by contamination from Llobregat river surface water and sewage, alongside rainfall recharge in the non-urban area, whereas the northeastern zone shows a more significant contribution from Ter River water and sewage, with an important additional impact from Besòs river surface water.

3.2.2 Besòs Delta Case Study: Impact of Sources on Urban Pollutants

This subsection focuses on the Besòs Delta as all the urban matrices (groundwater, surface water, untreated sewage and stormwater) are present in the same area. The recharge contribution observed in section 3.2.1 helped to assess the presence of urban organic pollutants in this section. Since direct assessment of stormwater recharge was not feasible, results from previous studies in Barcelona were considered, indicating that stormwater contributes approximately 20% to Besòs Delta groundwater recharge [24,25,54]. Thus, the contribution of three critical sources regarding groundwater organic contamination is further examined. All compounds exhibiting median concentrations higher than 1 ng L^{-1} in Besòs Delta groundwater wells were considered. A total of 30 compounds were included; among them, 16 are classified as highly polar, nine as polar and five as moderately polar pollutants. Indeed, classified by use:

seven are industrial pollutants, 17 are pharmaceuticals, four are sweeteners, one is a personal care product and one is a pesticide. The first conclusion regarding these pollutants is that surface water has the most critical influence on groundwater contamination, closely followed by untreated sewage and the least significant contributor was stormwater, which, due to its more sporadic nature, has a less consistent impact (51.5 %, 43.7 % and 4.8 % average contribution per compound, respectively) (see Table S6 and Equation S1 of the Supplementary Material). Groundwater is under the constant influence of river water, and in greener areas, rainwater, which is relatively clean, tends to infiltrate more predominantly than runoff. This highlights the more stable and continuous contribution of surface water compared to the more episodic nature of rainfall. Regarding the use types (the pesticide methylisothiazolinone and the personal care product paraxanthine were not considered, due to n = 1), different contributions are observed. Stormwater has its maximum

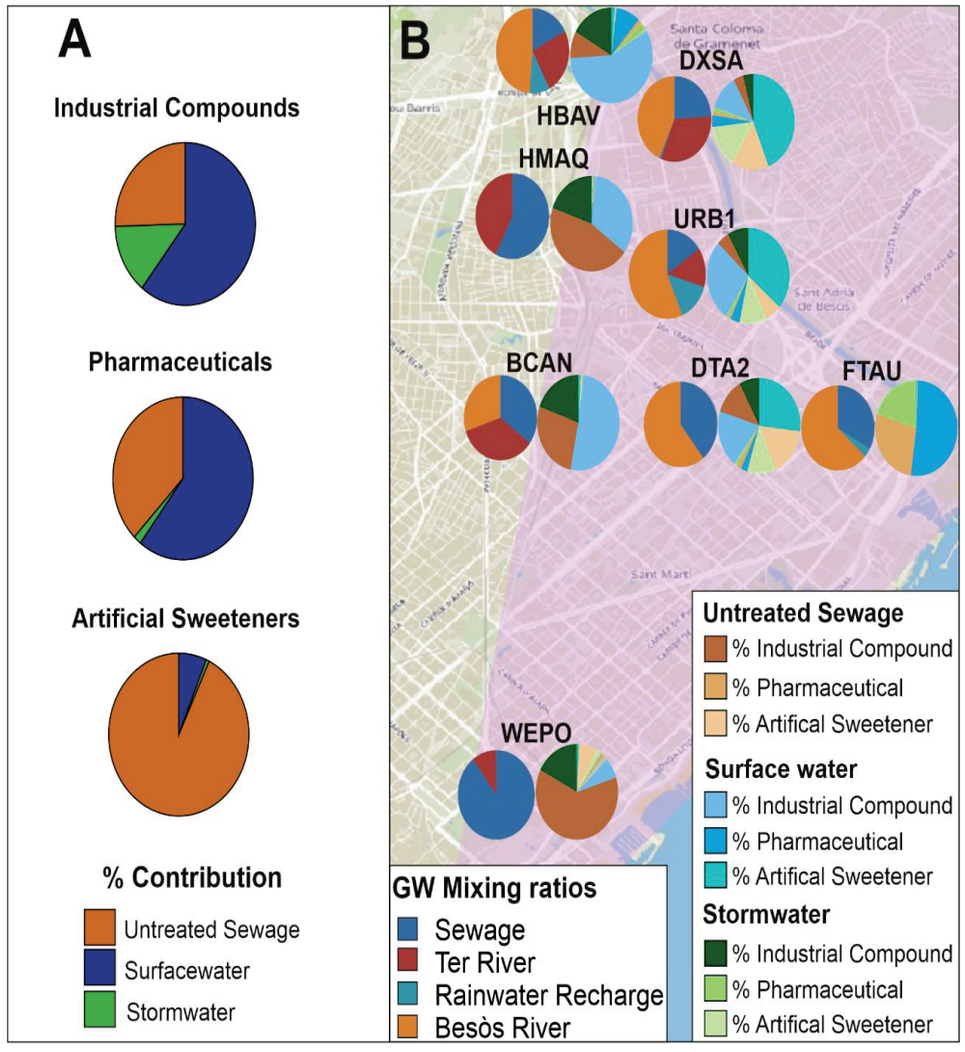


Figure 5. A: Contribution of each source to the groundwater pollution of the Besòs Deltaic area. **B**: Besòs Deltaic area with the sector graphs of eight groundwater samples analyzed. Right graph sectors refer to the groundwater mixing ratios (see section 3.2.1) and; Left graph sectors refer to the contribution of each source's organic pollutants. GW: groundwater.

contribution to industrial pollutants (13.9 %), while a negligible apportion is observed for pharmaceuticals and artificial sweeteners (1.8 % and 0.7 %, respectively). Both industrial pollutants and pharmaceuticals main contributor was surface water (60.6 % and 60.4 %). Taking into consideration the Besòs river samples, collected at the end of the river, it aligns with the known transportation through wastewater treatment plants of both the industrial compounds from factories at the periphery of Barcelona and, the pharmaceuticals accumulation from the wastewater treatment plants and neighbourhood cities of the capital [55]. A minor contribution was observed for the artificial sweeteners (6.4 %) for surface water. Finally, untreated sewage contributed considerably to industrial pollutants (25.5 %) with even a slightly more significant contribution to pharmaceuticals (37.8 %). However, its primary input was regarding artificial sweeteners, with a contribution of 92.8 %, possibly related to the extended use of these pollutants in urbanised zones such as Barcelona. All contribution data is provided in Table S6 of the Supplementary Material (see Equation S1) and visualized in Fig. 5A.

Considering individually all eight wells included in the Besòs Delta, the results of the urban organic pollutants contribution were obtained taking into consideration the recharge apportionment of each groundwater well, considering 20% of stormwater recharge in the eight Besòs Delta groundwater wells. In Fig. 5B, the contribution of both, mixing ratios and urban organic pollutants are shown in the map as sector graphs. It is worth noting the increase in the presence of pharmaceuticals, which goes hand in hand with the flow of the Besòs River, with more of them being present as the mouth of the river approaches. On the other hand, industrial compounds play a major role in wells HBAV, HMAQ, BCAN and WEPO, which could be related to a more urbanized zone, densely constructed, including a higher presence of pedestrian and vehicle traffic. Similarly, the presence of untreated sewage contribution gains importance as wells separate from the Besòs River (e.g., BCAN, HMAQ, and WEPO) and, consequently, these wells have a higher contribution of untreated sewage and its related compounds like ciprofloxacin, hydrochlorothiazide, the artificial sweeteners and paraxanthine, the main caffeine human metabolite. These results could help to a better understanding of the occurrence and fate of polar urban organic contaminants inside a high-dense city for future effective treatment of both groundwater and their main recharge sources.

3.3. Environmental risk assessment

An environmental risk assessment was conducted to identify compounds posing potential environmental threats based on their concentrations observed in the urban water bodies studied. In Table S7 of the Supplementary Material, all ecotoxicological risk values are reported. Several organic pollutants exceeded the ERQ threshold of 0.01, indicating adverse ecological effects. Three pharmaceuticals, atorvastatin, ciprofloxacin, and iopamidol, pose a high environmental risk, presenting ERQ_{95} between 1.2 and 60.2. Atorvastatin highly affects surface water and untreated sewage; ciprofloxacin poses a high risk in groundwater and sewage, while iopamidol poses a high risk only in groundwater. When considering the ERQ_{Max}, the same three compounds plus benzoylecgonine (a metabolite of cocaine) and β-estradiol (a hormone) stand out with ERQ_{Max} from 1.4 to 2307. In Fig. 6, all the compounds posing an environmental risk (ERQ_{95} > 0.01) are represented (Fig. S4 of the Supplementary Material shows a similar figure using the ERQ_{Max}). Fig. 6 shows how the compounds are more toxic when polarity increases (log D_{ow} decreases). As aforementioned, ciprofloxacin (log D_{ow} = -2.2), atorvastatin (log D_{ow} = 1.3), and iopamidol (log D_{ow} = -2.3) exhibited high environmental risk quotients as previous studies reported [56,57]. Ciprofloxacin is an antibiotic belonging to the fluoroquinolone class in charge of treating several infections in different human compartments, such as the respiratory, urinary, skin, gastrointestinal, and many others, with an approximate production of hundreds of tons per year [58]. Atorvastatin, another pharmaceutical, is mainly used to reduce cholesterol levels and the risk of cardiovascular diseases, with an expected production similar to ciprofloxacin due to the extended use of this medicine [59]. Iopamidol, in contrast, is a widely used contrast agent mainly used in diagnostic imaging, and its production is considered moderate, lower than the other two pharmaceuticals, demonstrating the high concentration found of this compound in groundwater [60]. Regarding groundwater, aside from ciprofloxacin and iopamidol, only two other molecules presented ERQ higher than the minimum threshold; those are the pesticide fipronil (ERQ_{95} = 0.01, ERQ_{Max} = 0.02) and one of their metabolites, fipronil sulfide (ERQ_{95} = ERQ_{Max} = 0.02). Zhang et al. examined numerous stormwater studies and reported that those two compounds present a high environmental risk to urban stormwater [22]. Herein, fipronil presented a low ERQ_{95} of 0.09 and intermediate ERQ_{Max} of 0.13, while fipronil sulfide showed a low impact only in the maximum concentration found (ERQ_{Max} = 0.02). Additionally, β-estradiol (log D_{ow} = 3.6) showed high environmental risk in maximum concentrations in stormwater (ERQ_{Max} = 84.2). At the

same time, their review concluded with insignificant adverse effects for this hormone (ERQ < 0.01) [22]. Additionally, benzoylecgonine ERQ_{Max} = 1.4, the primary metabolite of cocaine, was present at high concentrations in stormwater. Focusing on the surface water, four compounds exhibited intermediate environmental risk: the BP4, the most polar UV filter studied (log D_{ow} = -3.5); the widely used industrial compound melamine (log D_{ow} = -1.2); and two contrast agents, iohexol and iopamidol (log D_{ow} = -3.2 and -2.3, respectively).

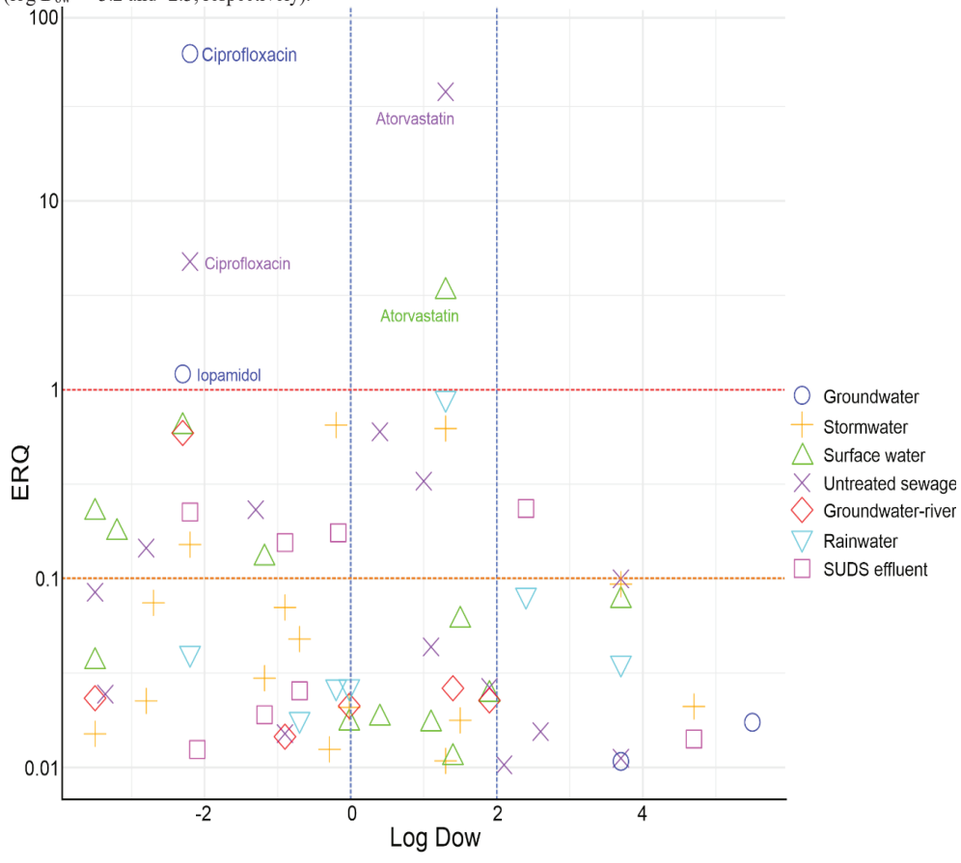


Figure 6. Environmental risk quotient (ERQ_{95}) of all compounds showing risk (ERQ > 0.01) in the seven urban water matrices studies compared to their mobility. Low environmental risk: compounds below the orange dotted line; Moderate environmental risk: compounds between the orange and the red dotted lines and; High environmental risk: compounds above the red dotted line. Blue dotted lines serve to identify highly polar, polar and moderately polar compounds.

4. Conclusions

Urban waters are home to hundreds of organic chemicals that pose significant risks to groundwater. This study highlights the presence of urban organic pollutants across six urban water matrices: groundwater, stormwater, surface water, untreated sewage, rainwater, and SUDS lixiviated effluent. Notably, findings reveal a higher prevalence of highly polar pollutants within these matrices, emphasizing the urgent need to develop targeted mitigation strategies to protect high-quality water sources like urban groundwater.

Source apportionment studies are critical for understanding the true extent and dynamics of urban diffuse contamination. In this research, the Besòs Deltaic zone was extensively examined, offering detailed insights into the sources and mechanisms of groundwater contamination. The study faced certain limitations, including reliance on a single sewer sample, which may not reflect temporal fluctuations and could impact both

risk assessments and model accuracy. Nevertheless, hazardous untreated sewage is generally considered temporally stable and is notoriously difficult to sample through municipalities, justifying its inclusion. Furthermore, major ions were not analyzed in stormwater samples, limiting the direct assessment of this source contribution (MIX performance) to groundwater contamination. Despite this, sampling stormwater during the first flush provides a conservative estimate that, while potentially overestimating concentrations, ensures a cautious evaluation of potential impacts.

Surface water and untreated sewage have emerged as major contributors to urban aquifer degradation, whereas stormwater plays a less prominent but still non-negligible role. Additionally, the analysis of deep water provided crucial data on the persistence and polarity of urban organic pollutants, such as acetaminophen, cocaine, and sulfadiazine. These pollutants merit further investigation due to their potential to pose serious risks to water resources. Up to three compounds, including iopamidol and ciprofloxacin, were identified as posing high environmental risks in groundwater. However, a substantial number of urban contaminants were found to pose low to moderate risks, highlighting the importance of continued monitoring to preserve the quality of urban groundwater.

The study offers several practical applications: i) promoting further research on polar organic pollutants in urban waters, a field currently lacking comprehensive data; ii) identifying and prioritizing sources of groundwater contamination to prevent further degradation; iii) updating urban water quality databases; and iv) guiding the development of management strategies for high-density urban areas to safeguard the future availability of high-quality freshwater resources.

CRediT authorship contribution statement

Francesc Labad: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Anna Jurado:** Methodology, Writing – review & editing, Conceptualization. **Laura Scheiber:** Methodology. **Marc Teixidó:** Methodology, Writing – review & editing. **Enric Vázquez-Suñé:** Funding acquisition, Writing – review & editing. **Sandra Pérez:** Funding acquisition, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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PUBLICACIÓ CIENTÍFICA #7

SUPPLEMENTARY INFORMATION

Identifying sources and environmental risks of mobile organic pollutants in urban groundwater

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Identifying sources and environmental risks of mobile organic pollutants in urban groundwater

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Table S1. Compound name, CAS, molecular formula, molecular weight, and log D_{ow} (pH 7.4) of the 133 target organic pollutants.

Compound name	CAS	Molecular formula	Molecular weight (g mol^{-1})	Log D_{ow} (pH 7.4)
17-α-ethinylestradiol	57-63-6	C20H24O2	296.4	3.7
1-cyanoguanidine	461-58-5	C2H4N4	84.1	-1.1
1H-Benzotriazole	95-14-7	C6H5N3	119.1	1.5
4-Hydroxidiclofenac	69002-84-2	C14H11Cl2NO3	312.1	3.7
4-nitrosulfamethoxazole	29699-89-6	C10H9N3O5S	283.3	1.4
5-Desamino-oxo-lamotrigine	252186-78-0	C9H6Cl2N4O	257.1	1.3
5-methylbenzotriazole	136-85-6	C7H7N3	133.2	1.7
6α-Methylprednisolone	83-43-2	C22H30O5	374.5	2.0
6-methyl-1,3,5-triazine-2,4-diamine	542-02-9	C4H7N5	125.1	-0.2
Acephate	30560-19-1	C4H10NO3PS	183.2	-0.5
Acesulfame	33665-90-6	C4H5NO4S	163.2	-2.8
Acetaminophen	103-90-2	C8H9NO2	151.2	0.4
Acridone	578-95-0	C13H9NO	195.2	3.7
Acrylamide	79-06-1	C3H5NO	71.1	-0.7
Acyclovir	59277-89-3	C8H11N5O3	225.2	-1.5
Alprazolam	28981-97-7	C17H13ClN4	308.8	2.6
Amantadine	768-94-5	C10H17N	151.3	-0.4
Atenolol	29122-68-7	C14H22N2O3	266.3	-1.9
Atorvastatin	134523-00-5	C33H35FN2O5	558.6	1.3
Azithromycin	83905-01-5	C38H72N2O12	749.0	1.4
Benzoylecgonine	519-09-5	C16H19NO4	289.3	-0.2
β-Estradiol	50-28-2	C18H24O2	272.4	3.6
Bezafibrate	41859-67-0	C19H20ClNO4	361.8	-0.1
Bisphenol-A	80-05-7	C15H16O2	228.3	3.6
BP1	131-56-6	C13H10O3	214.2	3.2
BP2	131-55-5	C13H10O5	246.2	1.4

BP4	4065-45-6	C14H12O6S	308.3	-3.5
Bromazepam	1812-30-2	C14H10BrN3O	316.2	2.1
Caffeine	58-08-2	C8H10N4O2	194.2	0.3
Carazolol	57775-29-8	C18H22N2O2	298.4	1.1
Carbamazepine	298-46-4	C15H12N2O	236.3	2.3
Carbamazepine epoxide	36507-30-9	C15H12N2O2	252.3	1.3
Carisoprodol	78-44-4	C12H24N2O4	260.3	1.9
Chloramphenicol	56-75-7	C11H12Cl2N2O5	323.1	1.0
Ciprofloxacin	85721-33-1	C17H18FN3O3	331.3	-2.2
Citalopram	59729-33-8	C20H21FN2O	324.4	1.3
Clarithromycin	81103-11-9	C38H69NO13	748.0	2.4
Climbazole	38083-17-9	C15H17ClN2O2	292.8	3.3
Clofibric acid	882-09-7	C10H11ClO3	214.6	-0.9
Clothianidin	210880-92-5	C6H8ClN5O2S	249.7	0.0
Cocaethylene	529-38-4	C18H23NO4	317.4	1.5
Cocaine	50-36-2	C17H21NO4	303.4	1.2
Cotinine	486-56-6	C10H12N2O	176.2	0.2
Crotamiton	483-63-6	C13H17NO	203.3	2.4
Cyclamate	100-88-9	C6H13NO3S	179.2	-3.5
Diazepam	439-14-5	C16H13ClN2O	284.7	2.9
Diclofenac	15307-86-5	C14H11Cl2NO2	296.1	1.4
Diltiazem	42399-41-7	C22H26N204S	414.5	2.1
ε-caprolactam	105-60-2	C6H11NO	113.2	0.0
Enrofloxacin	93106-60-6	C19H22FN3O3	359.4	-0.9
Erythromycin	114-07-8	C37H67NO13	733.9	1.7
Estriol	50-27-1	C18H24O3	288.4	2.7
Estrone	53-16-7	C18H22O2	270.4	3.4
Ezetimibe	163222-33-1	C24H21F2NO3	409.4	3.7
Fipronil	120068-37-3	C12H4Cl2F6N4OS	437.2	3.7

Fipronil desulfynil	205650-65-3	C12H4Cl2F6N4	389.1	4.6
Fipronil Sulfide	120067-83-6	C12H4Cl2F6N4S	421.2	5.5
Fipronil sulfone	120068-36-2	C12H4Cl2F6N4O2S	453.2	4.7
Florfenicol	73231-34-2	C12H14Cl2FNO4S	358.2	0.4
Fluconazole	86386-73-4	C13H12F2N6O	306.3	0.7
Flumequine	42835-25-6	C14H12FNO3	261.2	-0.7
Fluticasone	80474-14-2	C22H27F3O4S	444.5	2.6
Furazolidone	67-45-8	C8H7N3O5	225.2	0.4
Furosemide	54-31-9	C12H11ClN2O5S	330.7	0.8
Gabapentin	60142-96-3	C9H17NO2	171.2	-1.4
Gemfibrozil	25812-30-0	C15H22O3	250.3	1.6
Hydrochlorothiazide	58-93-5	C7H8ClN3O4S2	297.7	0.0
Hydroxychloroquine	118-42-3	C18H26ClN3O	335.9	2.0
Hyoscine	149-64-4	C21H30BrNO4	440.4	0.3
Irbesartan	138402-11-6	C25H28N6O	428.5	1.2
Imidacloprid	138261-41-3	C9H10ClN5O2S	255.7	-0.3
Indomethacin	53-86-1	C19H16ClNO4	357.8	0.8
Iodixanol	92339-11-2	C35H44I6N6O15	1550.2	-3.7
Iohexol	66108-95-0	C19H26I3N3O9	821.1	-3.2
Iopamidol	60166-93-0	C17H22I3N3O8	777.1	-2.3
Ketoprofen	22071-15-4	C16H14O3	254.3	0.1
Lamotrigine	84057-84-1	C9H7Cl2N5	256.1	1.7
Lamotrogine-N2-oxide	136565-76-9	C9H7Cl2N5O	272.1	1.4
Levofloxacin	100986-85-4	C18H20FN3O4	361.4	-2.1
Lidocaine	137-58-6	C14H22N2O	234.3	1.3
Lincomycin	154-21-2	C18H34N2O6S	406.5	-0.4
Lorazepam	846-49-1	C15H10Cl2N2O2	321.2	1.9
Mefenamic acid	61-68-7	C15H15NO2	241.3	2.0
Melamine	108-78-1	C3H6N6	126.1	-1.2

Metformin	657-24-9	C4H11N5	129.2	-3.4
Methadone	76-99-3	C21H27NO	309.4	2.8
Methylisothiazolinone	2682-20-4	C4H5NOS	115.2	-0.2
Metoprolol	37350-58-6	C15H25NO3	267.4	-0.3
Metronidazole	443-48-1	C6H9N3O3	171.2	0.1
Midazolam	59467-70-8	C18H13ClFN3	325.8	3.4
N-3-dimethylaminopropylacrylamide	5205-93-6	C9H18N2O	170.3	-1.2
N-acetylsulfamethoxazole	21312-10-7	C12H13N3O4S	295.3	-0.3
Nalidixic acid	389-08-2	C12H12N2O3	232.2	-0.3
Naphtalene-1-sulfonic acid	85-47-2	C10H8O3S	208.2	-2.7
Naproxen	22204-53-1	C14H14O3	230.3	0.5
Neotame	165450-17-9	C20H30N2O5	378.5	0.6
Nitrodiclofenac	174316-61-1	C14H10Cl2N2O3	325.2	1.5
O-desmethylvenlafaxine	93413-62-8	C16H25NO2	263.4	2.6
Oseltamivir	196618-13-0	C16H28N2O4	312.4	0.6
Oseltamivir carboxylate	187227-45-8	C14H24N2O4	284.4	-1.9
Oxazepam	604-75-1	C15H11ClN2O2	286.7	1.5
Paraxanthine	611-59-6	C7H8N4O2	180.2	-0.2
Paroxetine	61869-08-7	C19H20FNO3	329.4	1.5
Pentobarbital	76-74-4	C11H18N2O3	226.3	1.9
Phenytoin	57-41-0	C15H12N2O2	252.3	-1.0
Pipemidic acid	51940-44-4	C14H17N5O3	303.3	-3.6
Pregabalin	148553-50-8	C8H17NO2	159.2	-1.3
Primidone	125-33-7	C12H14N2O2	218.3	-0.7
Propranolol	525-66-6	C16H21NO2	259.3	1.2
Propyphenazone	479-92-5	C14H18N2O	230.3	2.1
Rosuvastatin	287714-41-4	C22H28FN3O6S	481.5	1.0
Saccharin	81-07-2	C7H5NO3S	183.2	-1.3
Sitagliptin	486460-32-6	C16H15F6N5O	407.3	1.1

Sotalol	3930-20-9	C12H20N2O3S	272.4	-1.6
Stevioside	57817-89-7	C38H60O18	804.9	0.4
Sucralose	56038-13-2	C12H19Cl3O8	397.6	-0.2
Sulfadiazine	68-35-9	C10H10N4O2S	250.3	-0.8
Sulfamethazine	57-68-1	C12H14N4O2S	278.3	0.2
Sulfamethizole	144-82-1	C9H10N4O2S2	270.3	-1.1
Sulfamethoxazole	723-46-6	C10H11N3O3S	253.3	-0.6
Sulfapyridine	144-83-2	C11H11N3O2S	249.3	0.4
Sulfathiazole	72-14-0	C9H9N3O2S2	255.3	0.0
Thiamethoxam	153719-23-4	C8H10ClN5O3S	291.7	-0.3
Thiourea	2062-56-6	CH4N2S	76.1	-2.8
Tramadol	3715-90-0	C16H25NO2	263.4	0.5
Triethylenediamine	280-57-9	C6H12N2	112.2	-1.3
Trifluoromethanesulfonic acid	1493-13-6	CHF3O3S	150.1	-3.9
Trimethoprim	738-70-5	C14H18N4O3	290.3	-1.2
Valsartan	137862-53-4	C24H29N5O3	435.5	-0.9
Valsartan acid	164265-78-5	C14H10N4O2	266.3	2.3
Venlafaxine	93413-69-5	C17H27NO2	277.4	1.4
Verapamil	52-53-9	C27H38N2O4	454.6	2.4
Warfarin	81-81-2	C19H16O4	308.3	0.3

Table S2. Coordinates of all samples used in this study.

Sample name	Type	Latitude	Longitude
BCAN	Groundwater	41.42089933	2.197608991
BOP	Groundwater	41.43877969	2.205830926
BURG	Groundwater	41.37274416	2.133537204
CALP	Groundwater	41.37540150	2.160921378
CANM	Groundwater	41.35982130	2.144779296
CANS	Groundwater	41.42533523	2.132687885
CNGV	Groundwater	41.35047161	2.118600170
CPF2	Groundwater	41.43071313	2.155329560
DDDO	Groundwater	41.38129736	2.129013731
DEIN	Groundwater	41.38688858	2.148704165
DFI2	Groundwater	41.35519046	2.137740364
DFIR2	Groundwater	41.35519046	2.137740364
DTA2	Groundwater	41.42092226	2.216132225
DXSA	Groundwater	41.44558850	2.202611382
DZUN	Groundwater	41.38342478	2.118905154
FENG	Groundwater	41.41773540	2.132165846
FTAU	Groundwater	41.41963968	2.227031858
FVIL	Groundwater	41.43628229	2.167167563
HBAV	Groundwater	41.45036842	2.199823258
HJOM	Groundwater	41.37674980	2.148729141
HMAQ	Groundwater	41.43734956	2.196726696
HTLL	Groundwater	41.42799675	2.175459850
HURG	Groundwater	41.41963968	2.227031858
MSAN	Groundwater	41.37567776	2.125912862
ORDU	Groundwater	41.43375107	2.172798068
TAHI	Groundwater	41.3932665	2.168872408
TRME	Groundwater	41.41397539	2.186596678
URB1	Groundwater	41.43283058	2.203660174
VITP	Groundwater	41.36800062	2.161996279
WEPO	Groundwater	41.39059129	2.188373211
SAP2b	Groundwater-river	41.42999000	2.215175000
Bon Pastor Sostre	Rainwater	41.43759771	2.205427289
Ca n'Alier Sostre	Rainwater	41.40908641	2.205093392
Calabria66 Sostre	Rainwater	41.37750051	2.157909617
Alfarràs	Stormwater	41.43750329	2.204911995
Ardèvol	Stormwater	41.43726464	2.205494293
Ardèvol bar	Stormwater	41.43759771	2.205427289
Biosca	Stormwater	41.43778099	2.206552346
CGG	Stormwater	41.43838703	2.205034869
Madriguera	Stormwater	41.43742389	2.203103546
Sas	Stormwater	41.4374614	2.204275433
St Adrià	Stormwater	41.43583311	2.201557187
Ca n'Alier calle	Stormwater	41.40881453	2.204873233
Ca n'Alier plaza	Stormwater	41.40908641	2.205093392
Fluvià	Stormwater	41.40837112	2.205133539
Provençals	Stormwater	41.40885041	2.206745313
Selva de mar	Stormwater	41.40984821	2.207694545
Treball	Stormwater	41.41119395	2.208142790
Borrell nord	Stormwater	41.38006410	2.159097477
Borrell sud	Stormwater	41.37992157	2.159273161
Calabria	Stormwater	41.37750051	2.157909617
Casanova	Stormwater	41.38348972	2.161282019
Viladomat	Stormwater	41.38261882	2.160178697
Villaroel	Stormwater	41.38261882	2.160178697
Clavaguera	Untreated sewage	41.43230321	2.218886493
Besòs Riu	Surface water	41.42970700	2.214793000

Table S3. Standard deviations applied to end-members and observation points.

Species	Standard deviation	
	Recharge sources	Observation points
CE	0.20	0.07
Cl^-	0.20	0.07
Na^+	0.50	0.10
SO_4^{2-}	0.50	0.20
HCO_3^-	0.50	0.25
Mg^{2+}	0.50	0.25
Ca^{2+}	0.50	0.20
NO_3^-	1.00	10.00

CE: Electrical Conductivity

Table S4. Mean concentration, relative standard deviation (RSD), median concentration, frequency of detection (FD), and the FD counts of all compounds in all samples (n = 197).

Compound	Average (ng L^{-1})	RSD (%)	Median (ng L^{-1})	FD (%)	FD (counts)
17-α-Ethynilestradiol	553	690	553	1.02	2
1-cyanoguanidine	599	715	364	78.2	154
1H-Benzotriazole	115	161	61.9	98.0	193
4-Hydroxidiclofenac	30.3	7.89	27.7	1.52	3
4-nitrosulfamethoxazole	75.5	176	0.07	6.09	12
5-Desamino-oxo-lamotrigine	28.1	22.8	27.4	20.3	40
5-methylbenzotriazole	325	871	76.3	100	197
6α-Methylprednisolone	111	173	41.5	28.4	56
6-methyl-1,3,5-triazine-2,4-diamine	13.6	61.4	6.36	76.7	151
Acephate	6.35	-	6.35	0.51	1
Acesulfame	8585	37309	682	99.5	196
Acetaminophen	2619	27375	39.0	82.2	162
Acridone	2.20	2.96	1.03	62.4	123
Acrylamide	4773	5893	2175	80.7	159
Acyclovir	63.2	63.4	45.5	8.12	16
Alprazolam	6.11	5.49	5.05	55.3	109
Amantadine	210	1797	15.6	74.6	147
Atenolol	99.2	604	20.2	82.7	163
Atorvastatin	3441	11491	23.5	8.63	17
Azithromycin	10.6	12.14	5.21	10.2	20
Benzoylecgonine	3313	8695	430	98.5	194
β-Estradiol	226257	597937	342	5.08	10
Bezafibrate	11.2	20.5	3.80	14.7	29
Bisphenol-A	90.9	298	15.5	99.5	196
BP1	17.5	19.1	11.0	71.1	140
BP2	28.0	25.6	23.1	19.3	38
BP4	216	880	25.6	41.6	82
Bromazepam	35.3	11.8	33.9	2.54	5
Caffeine	2255	6894	498	100	197
Carazolol	13.0	11.9	8.90	32.5	64
Carbamazepine	6.53	13.2	1.40	73.1	144
Carbamazepine epoxide	3.52	3.09	4.50	22.8	45
Carisoprodol	7.36	-	7.36	0.51	1
Chloramphenicol	13.1	-	13.1	0.51	1
Ciprofloxacin	4142	35865	33.8	69.0	136
Citalopram	24.8	46.6	5.44	34.5	68
Clarithromycin	5.55	4.09	5.53	12.7	25
Climbazole	2.84	5.82	0.50	60.9	120
Clofibric acid	30.5	21.9	41.1	9.64	19
Clothianidin	13.6	28.6	2.76	10.2	20
Cocaine	28.6	77.9	6.59	25.9	51
Coc-ethylene	127	271	33.7	59.4	117
Cotinine	706	1019	314	100	197
Crotamiton	0.73	0.57	0.65	22.8	45

Cyclamate	1770	6373	196	87.3	172
Diazepam	10.5	17.2	5.11	60.9	120
Diclofenac	83.9	63.0	62.2	15.2	30
Diltiazem	14.0	22.8	6.97	11.7	23
ε-caprolactam	4502	4564	3035	100	197
Enrofloxacin	41.9	118	6.97	53.8	106
Erythromycin	8.80	9.48	3.88	12.2	24
Estriol	493	353	378	9.1	18
Estrone	28.0	-	28.0	0.51	1
Ezetimibe	n.d.	n.d.	n.d.	0.51	1
Fipronil	4.28	2.57	3.40	33.0	65
Fipronil desulfynil	3.04	3.64	1.86	14.7	29
Fipronil Sulfide	1.79	1.94	0.67	9.14	18
Fipronil sulfone	3.70	2.04	2.80	39.6	78
Florfenicol	36.9	68.6	5.34	7.61	15
Fluconazole	18.2	13.4	19.4	25.9	51
Flumequine	3.62	5.42	2.12	31.5	62
Fluticasone	7463	-	7463	0.51	1
Furazolidone	n.d.	n.d.	n.d.	0	0
Furosemide	105	157	33.2	14.7	29
Gabapentin	523	2738	50.2	75.1	148
Gemfibrozil	132	201	89.5	42.1	83
Hydrochlorothiazide	104	379	13.6	99.0	195
Hydroxychloroquine	75.5	91.5	45.7	37.6	74
Hyoscine	56.3	78.3	18	7.11	14
Irbesartan	148	246	27	10.7	21
Imidacloprid	517	1012	146	51.8	102
Indomethacin	0.79	-	0.79	0.51	1
Iodixanol	n.d.	n.d.	n.d.	1.52	3
Iohexol	190	323	21.8	41.6	82
Iopamidol	886	762	759	13.7	27
Ketoprofen	3361	12241	66.9	25.4	50
Lamotrigine	90.2	146	14.1	33.0	65
Lamotrogine-N2-oxide	7.42	16.2	1.84	6.60	13
Levofloxacin	103	663.	7.44	66.0	130
Lidocaine	20.0	52.6	5.23	99.5	196
Lincomycin	24.1	36.9	13.2	15.7	31
Lorazepam	34.5	23.2	41.8	3.05	6
Mefenamic acid	156	163	86.9	14.2	28
Melamine	10026	23488	2764	100	197
Metformin	3728	12100	720	99.5	196
Methadone	6.30	16.7	2.81	30.0	59
Methylisothiazolinone	57.7	107	16.5	74.6	147
Metoprolol	159	333	37.5	40.1	79
Metronidazole	234	915	23.2	23.9	47
Midazolam	0.88	0.38	0.87	5.58	11
N-3-dimethylaminopropylacrylamide	524	532	488	86.3	170
N-acetylsulfamethoxazole	287	650	25.2	8.12	16

Nalidixic acid	2.30	4.13	0.80	26.9	53
Naphtalene-1-sulfonic acid	1567	5248	239	90.4	178
Naproxen	290	45.8	285	3.05	6
Neotame	174	173	177	2.54	5
Nitrodiclofenac	39.2	48.4	25.0	7.11	14
O-desmethylvenlafaxine	96.7	236	29.9	48.7	96
Oseltamivir	n.d.	n.d.	n.d.	0	0
Oseltamivir carboxylate	64.0	-	64.0	1.02	2
Oxazepam	1.06	0.59	1.05	1.52	3
Paraxanthine	285	845	95.8	62.9	124
Paroxetine	3.42	0.61	3.39	2.54	5
Pentobarbital	67.4	197	4.27	9.14	18
Phenytoin	5.44	7.78	1.69	17.8	35
Pipemidic acid	164	242	83.4	18.3	36
Pregabalin	3126	19892	52.8	43.7	86
Primidone	114	231	29.2	12.2	24
Propranolol	8.57	21.0	2.34	15.7	31
Propyphenazone	1.80	3.76	0.58	40.1	79
Rosuvastatin	141	-	141	0.51	1
Saccharin	2868	8872	353	100	197
Sitagliptin	182	241	60.9	12.2	24
Sotalol	5.13	3.50	5.03	16.2	32
Stevioside	467	205	467	1.02	2
Sucralose	13498	155229	255	81.7	161
Sulfadiazine	4.33	4.47	3.07	17.3	34
Sulfamethazine	5.41	5.80	4.54	11.2	22
Sulfamethizole	6.01	10.1	0.59	7.6	15
Sulfamethoxazole	38.3	83.6	8.71	19.3	38
Sulfapyridine	5.12	5.37	3.84	14.2	28
Sulfathiazole	151	303	42.9	4.06	8
Thiamethoxam	n.d.	n.d.	n.d.	0	0
Thiourea	n.d.	n.d.	n.d.	0	0
Tramadol	28.5	149	2.88	100	197
Triethylenediamine	1100	2061	427	100	197
Trifluoromethanesulfonic acid	98.0	328	22.2	100	197
Trimethoprim	97.1	602	2.45	73.6	145
Valsartan	143	180	45.2	21.3	42
Valsartan acid	371	917	175	14.7	29
Venlafaxine	11.4	46.2	0.92	78.7	155
Verapamil	101	153	35.7	34.0	67
Warfarin	16.2	15.7	13.8	31.5	62

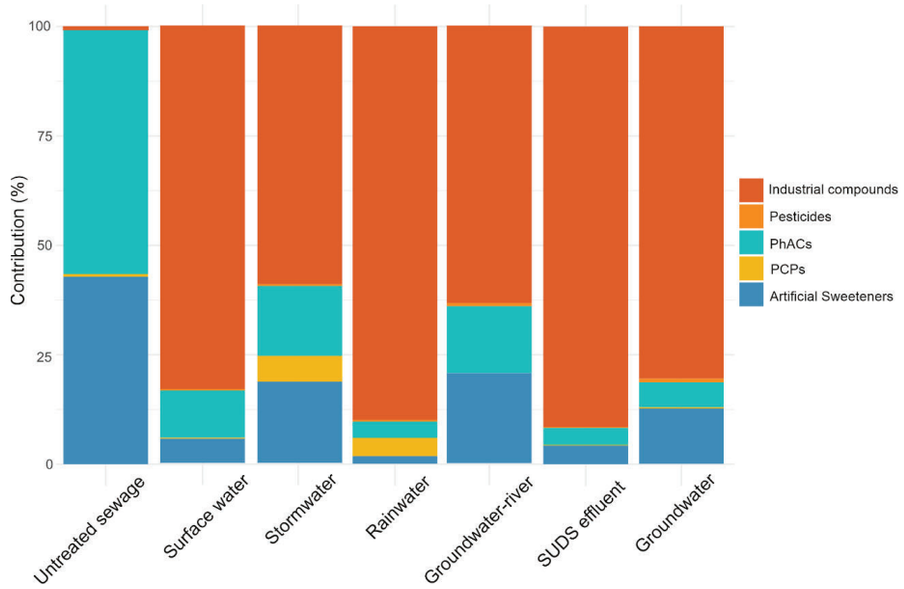


Figure S1. Concentration contribution of target compounds in each sample type based on their uses. PhACs: Pharmaceuticals, PCPs: Personal Care products.

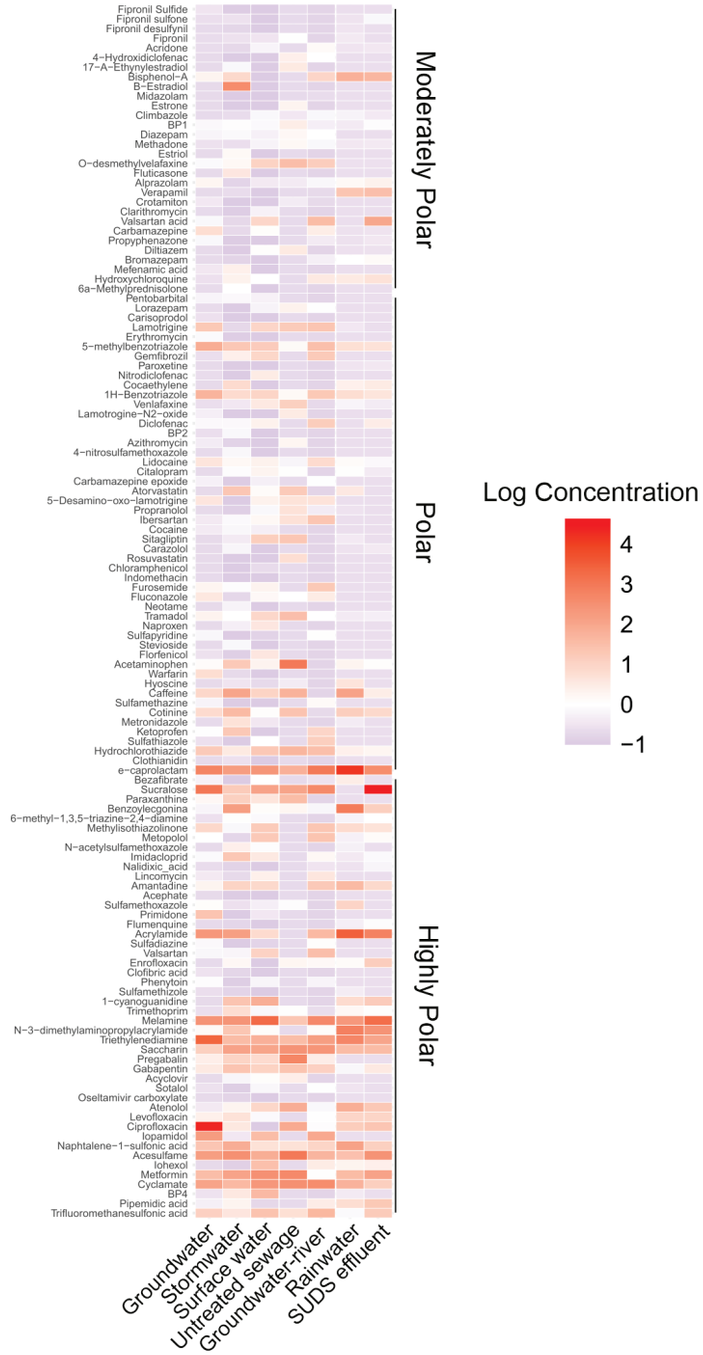


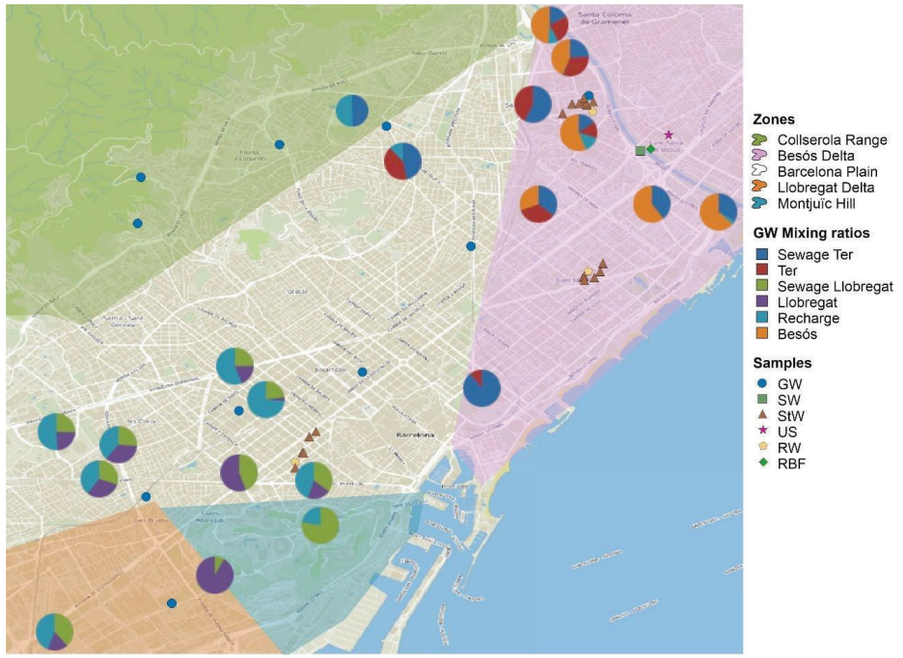
Figure S2. Heatmap of the normalised concentrations (log10) of the compounds sorted by polarity in each water sample type. Only compounds detected at least once above the limit of quantification were considered.

40 **Table S4**. Occurrence and types of samples where each compound was detected.

Compound	Occurrence
17-A-Ethynilestradiol	Present in two to six water sample type
1-cyanoguanidine	Present in two to six water sample type
1H-Benzotriazole	Present in all samples
4-Hydroxidiclofenac	Present in only one sample (Untreated sewage)
4-nitrosulfamethoxazole	Present in two to six water sample type
5-Desamino-oxo-lamotrigine	Present in two to six water sample type
5-methylbenzotriazole	Present in all samples
6α-Methylprednisolone	Present in two to six water sample type
6-methyl-1,3,5-triazine-2,4-diamine	Present in two to six water sample type
Acephate	Present in only one sample (Stormwater)
Acesulfame	Present in all samples
Acetaminophen	Present in two to six water sample type
Acridone	Present in two to six water sample type
Acrylamide	Present in two to six water sample type
Acyclovir	Present in two to six water sample type
Alprazolam	Present in all samples
Amantadine	Present in two to six water sample type
Atenolol	Present in all samples
Atorvastatin	Present in two to six water sample type
Azithromycin	Present in two to six water sample type
Benzoylecgonine	Present in all samples
β-Estradiol	Present in only one sample (Stormwater)
Bezafibrate	Present in two to six water sample type
Bisphenol-A	Present in two to six water sample type
BP1	Present in all samples
BP2	Present in two to six water sample type
BP4	Present in two to six water sample type
Bromazepam	Present in only one sample (Stormwater)
Caffeine	Present in all samples
Carazolol	Present in two to six water sample type
Carbamazepine	Present in two to six water sample type
Carbamazepine epoxide	Present in two to six water sample type
Carisoprodol	Present in only one sample (Groundwater)
Chloramphenicol	Present in only one sample (Surface water)
Ciprofloxacin	Present in two to six water sample type
Citalopram	Present in two to six water sample type
Clarithromycin	Present in two to six water sample type
Climbazole	Present in all samples
Clofibric acid	Present in two to six water sample type
Clothianidin	Present in only one sample (Stormwater)
Coca-ethylene	Present in only one sample (Stormwater)
Cocaine	Present in two to six water sample type
Cotinine	Present in all samples
Crotamiton	Present in two to six water sample type
Cyclamate	Present in all samples
Diazepam	Present in two to six water sample type
Diclofenac	Present in two to six water sample type
Diltiazem	Present in two to six water sample type
ε-caprolactam	Present in all samples
Enrofloxacin	Present in all samples
Erythromycin	Present in two to six water sample type
Estriol	Present in two to six water sample type
Estrone	Present in only one sample (Untreated sewage)
Ezetimibe	Present in only one sample (Surface water)
Fipronil	Present in two to six water sample type
Fipronil desulfynil	Present in two to six water sample type
Fipronil Sulfide	Present in two to six water sample type
Fipronil sulfone	Present in two to six water sample type
Florfenicol	Present in two to six water sample type
Fluconazole	Present in two to six water sample type
Flumenquine	Present in two to six water sample type
Fluticasone	Present in only one sample (Stormwater)
Furosemide	Present in two to six water sample type
Gabapentin	Present in all samples
Gemfibrozil	Present in two to six water sample type
Hydrochlorothiazide	Present in all samples
Hydroxychloroquine	Present in two to six water sample type
Hyoscine	Present in two to six water sample type
Irbesartan	Present in two to six water sample type
Imidacloprid	Present in two to six water sample type
Indomethacin	Present in only one sample (Groundwater)
Iodixanol	Present in only one sample (Surface water)
Iohexol	Present in two to six water sample type
Iopamidol	Present in two to six water sample type
Ketoprofen	Present in two to six water sample type
Lamotrigine	Present in two to six water sample type
Lamotrogine-N2-oxide	Present in two to six water sample type
Levofloxacin	Present in two to six water sample type
Lidocaine	Present in all samples
Lincomycin	Present in two to six water sample type
Lorazepam	Present in two to six water sample type
Mefenamic acid	Present in two to six water sample type
Melamine	Present in all samples
Metformin	Present in all samples
Methadone	Present in all samples
Methylisothiazolinone	Present in two to six water sample type
Metoprolol	Present in two to six water sample type
Metronidazole	Present in two to six water sample type
Midazolam	Present in two to six water sample type
N-3-dimethylaminopropylacrylamide	Present in all samples
N-acetylsulfamethoxazole	Present in two to six water sample type
Nalidixic acid	Present in two to six water sample type

Naphtalene-1-sulfonic acid	Present in all samples
Naproxen	Present in two to six water sample type
Neotame	Present in only one sample (Stormwater)
Nitrodiclofenac	Present in two to six water sample type
O-desmethylvenlafaxine	Present in all samples
Oseltamivir carboxylate	Present in only one sample (Stormwater)
Oxazepam	Present in only one sample (Groundwater)
Paraxanthine	Present in two to six water sample type
Paroxetine	Present in only one sample (Stormwater)
Pentobarbital	Present in two to six water sample type
Phenytoin	Present in two to six water sample type
Pipemidic acid	Present in two to six water sample type
Pregabalin	Present in two to six water sample type
Primidone	Present in two to six water sample type
Propranolol	Present in two to six water sample type
Propyphenazone	Present in two to six water sample type
Rosuvastatin	Present in only one sample (Untreated sewage)
Saccharin	Present in all samples
Sitagliptin	Present in two to six water sample type
Sotalol	Present in two to six water sample type
Stevioside	Present in only one sample (Stormwater)
Sucralose	Present in two to six water sample type
Sulfadiazine	Present in two to six water sample type
Sulfamethazine	Present in two to six water sample type
Sulfamethizole	Present in two to six water sample type
Sulfamethoxazole	Present in two to six water sample type
Sulfapyridine	Present in two to six water sample type
Sulfathiazole	Present in two to six water sample type
Tramadol	Present in all samples
Triethylenediamine	Present in all samples
Trifluoromethanesulfonic acid	Present in all samples
Trimethoprim	Present in all samples
Valsartan	Present in two to six water sample type
Valsartan acid	Present in two to six water sample type
Venlafaxine	Present in all samples
Verapamil	Present in only one sample (Stormwater)
Warfarin	Present in two to six water sample type

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43 **Figure S3**. Map of the sources contribution to groundwater samples. GW: groundwater; SW:
44 surface water; StW: stormwater; US: untreated sewage; RW: rainwater; RBF: Groundwater-
45 river.

Table S5. Physico-chemical properties and major inorganic ions of groundwater samples. Depth refers to the sampling depth in meters from the surface where the water was collected at the time of sampling.

Samples	Ca^{2+} (mg L^{-1})	Mg^{2+} (mg L^{-1})	Na^{+} (mg L^{-1})	K^{+} (mg L^{-1})	Cl^{-} (mg L^{-1})	HCO_3^{-} (mg L^{-1})	NO_3^{-} (mg L^{-1})	SO_4^{2-} (mg L^{-1})	pH	EC (µS cm^{-1})	Depth (m)
BCAN	116	25.2	103	12.2	121	469	75.8	176	6.78	1430	10
BOP	57.2	23.1	107	13.8	133	-	24.5	130	5.52	580	-
BURG	143	55.0	107	1.56	231	-	65.9	220	4.20	600	20
CALP	148	52.4	120	1.62	225	500	69.4	208	6.30	1175	8.0
CANM	181	40.6	167	13.0	361	281	66.3	153	6.20	1.82	10
CANS	104	38.9	70.3	1.29	203	406	18.4	134	6.18	1272	150
CNGV	155	61.5	105	4.13	242	531	45.1	246	6.32	1730	6.3
CPF2	167	42.5	58.7	2.34	134	-	77.5	207	-	-	100
DDDO	162	69.4	115	1.50	242	313	62.6	219	5.68	2.05	30
DEIN	152	66.0	109	1.86	222	-	62.8	209	-	-	18
DFI2	-	-	-	-	-	-	-	-	5.33	1082	-
DFIR2	257	79.5	193	25.7	309	-	0.00	486	-	-	4.0
DRAV	164	65.0	184	7.38	385	-	70.3	189	5.17	1780	-
DRAV2	-	-	-	-	-	-	-	-	-	-	-
DTA2	151	40.2	148	11.6	179	500	11.4	260	6.83	1730	-
DXSA	116	23.4	113	16.4	130	531	18.4	137	6.90	1270	5.5
DZUN	140	57.6	91.2	1.48	216	438	43.6	202	6.66	1738	60
FENG	82.4	25.4	63.7	1.32	93.7	500	21.6	87.8	6.95	933	120
FTAU	142	34.7	131	10.5	181	500	11.8	247	6.62	1699	1.50
FVIL	162	57.9	59.9	1.78	96.9	625	111	193	7.10	-	70
HBAV	123	24.9	104	11.6	140	438	13.3	139	6.68	1163	5.8
HJOM	396	159	465	3.98	1092	313	204	280	6.25	5.51	15
HMAQ	148	36.0	89.2	1.24	86.8	563	80.0	201	7.10	1404	-
HTLL	139	31.1	66.5	2.53	92.2	375	111	173	6.70	-	30
HURG	122	58.5	88.2	1.34	196	375	80.7	208	6.30	1577	1.6
MSAN	143	60.1	113	1.54	249	438	57.7	223	6.57	490	25
ORDU	64.6	10.0	29.7	5.42	35.8	313	7.71	47.5	6.28	538	50
TAHI	129	58.1	70.0	2.06	136	500	103	133	6.95	1462	20
TRME	79.5	19.7	22.5	11.2	18.8	-	1.77	70.6	7.30	673	15
URB1	144	31.4	115	7.28	150	375	26.4	137	6.72	1422	-
VITP	241	35.8	172	8.00	293	719	49.7	386	6.40	1500	5.5
WEPO	163	57.2	250	28.4	433	438	23.6	236	6.60	2360	2.4

Table S6. Compounds detected in Besòs Delta groundwater above 1 ng L^{-1} sorted by use classification and the contribution of the three main groundwater sources, untreated sewage, surface water, and stormwater.

Compound	Polarity	Classification	% Contribution Untreated Sewage	% Contribution Surface water	% Contribution Stormwater
1H-Benzotriazole	Polar	Industrial Compound	7.6	78.8	13.6
5-Methyl-1H-Benzotriazole	Polar	Industrial Compound	4.6	80.5	14.9
Bisphenol A	Moderately-Polar	Industrial Compound	33.3	33.3	33.3
ε-Caprolactam	Highly-Polar	Industrial Compound	33.2	48.0	18.8
Melamine	Highly-Polar	Industrial Compound	1.1	95.2	3.7
Triethylenediamine	Highly-Polar	Industrial Compound	52.5	42.0	5.5
Trifluoromethanesulfonic acid	Highly-Polar	Industrial Compound	46.2	46.6	7.2
Methylisothiazolinone	Highly-Polar	Pesticide	0	99.4	0.6
5-Desamino-oxo-Lamotrigine	Polar	Pharmaceutical	74.9	25.1	0
Alprazolam	Moderately-Polar	Pharmaceutical	31.7	68.3	0
Amantadine	Highly-Polar	Pharmaceutical	0	97.4	2.6
Carbamazepine	Moderately-Polar	Pharmaceutical	0	99.1	0.9
Ciprofloxacin	Highly-Polar	Pharmaceutical	100	0	0
Diazepam	Moderately-Polar	Pharmaceutical	74.9	18.8	6.3
Fluconazole	Polar	Pharmaceutical	27.5	72.5	0
Hydrochlorothiazide	Polar	Pharmaceutical	89.1	10.6	0.2
Lamotrigine	Polar	Pharmaceutical	80.5	19.5	0
Levofloxacin	Highly-Polar	Pharmaceutical	0	100	0
Lidocaine	Polar	Pharmaceutical	13.2	73.8	13.0
Metoprolol	Highly-Polar	Pharmaceutical	0	100	0
Pentobarbital	Polar	Pharmaceutical	0	0	0
Phenytoin	Highly-Polar	Pharmaceutical	0	0	0
Propyphenazone	Moderately-Polar	Pharmaceutical	0	100	0
Sulfadiazine	Highly-Polar	Pharmaceutical	0	0	0
Sulfamethazine	Polar	Pharmaceutical	0	0	0
Paraxanthine	Highly-Polar	Personal Care Product	95.3	2.8	1.9
Acesulfame	Highly-Polar	Artificial Sweetener	98.9	0.5	0.6
Cyclamate	Highly-Polar	Artificial Sweetener	99.3	0.5	0.2
Saccharin	Highly-Polar	Artificial Sweetener	96.6	2.3	1.2
Sucralose	Highly-Polar	Artificial Sweetener	76.6	22.4	0.9

The calculations of the contribution for each compound were performed by dividing the median concentration of the compound in the source studied by the sum of the median concentrations of the same compound in the other three recharge sources, and multiplying by 100, as shown in Equation S1:

$$\%\ Cx = \left(\frac{Cx}{(Csw+Cstw+Cus)}\right) * 100 \qquad \text{Equation S1}$$

Where Cx represents the median concentration of a compound in either surface water, stormwater, or untreated sewage.
sw: surface water; stw: stormwater and; us: untreated sewage.

57 **Table S7**. Ecotoxicological parameters of all target analytes including EC_{50}, AF and PNEC.

Compound	EC_{50} (mg L^{-1}) Fathead Minnow	EC_{50} (mg L^{-1}) Daphnia Magna	EC_{50} (mg L^{-1}) Tetrahymena Pyriform	AF	PNEC (mg L^{-1})
17-α-Ethynilestradiol	1.01	N/A	1.79	50	0.020
1-cyanoguanidine	N/A	132	N/A	100	1.32
1H-Benzotriazole	N/A	N/A	N/A	N/A	N/A
4-Hydroxidiclofenac	0.350	2.64	1.66	100	0.0035
4-nitrosulfamethoxazole	N/A	N/A	N/A	N/A	N/A
5-Desamino-oxo-lamotrigine	N/A	45.3	N/A	100	0.450
5-methylbenzotriazole	N/A	N/A	N/A	N/A	N/A
6α-Methylprednisolone	10.9	23.4	N/A	100	0.110
6-methyl-1,3,5-triazine-2,4-diamine	813	22.4	1446	50	0.450
Acephate	N/A	3.85	N/A	100	0.039
Acesulfame	231	751	N/A	100	2.31
Acetaminophen	89.7	27.1	274	50	0.543
Acridone	4.83	4.97	21.6	50	0.097
Acrylamide	43.8	17.3	747	50	0.346
Acyclovir	N/A	867	N/A	100	8.67
Alprazolam	0.640	2.78	N/A	100	0.0064
Amantadine	43.2	13.2	N/A	100	0.132
Atenolol	57.2	45.3	89.4	50	0.905
Atorvastatin	0.001	0.620	N/A	100	0.000020
Azithromycin	N/A	94.1	N/A	100	0.941
Benzoylecgonine	2.39	36.6	44.6	50	0.0478
β-Estradiol	0.940	3.15	2.79	50	0.0188
Bezafibrate	0.78	16.0	4.07	50	0.0156
Bisphenol-A	3.24	1.58	5.30	50	0.0316
BP1	6.99	5.66	15.9	50	0.113
BP2	2.41	1.51	11.9	50	0.0302
BP4	2.18	N/A	N/A	100	0.0218
Bromazepam	0.840	2.87	N/A	100	0.0084
Caffeine	502	182	N/A	100	1.82
Carazolol	2.78	2.88	9.26	50	0.0556
Carbamazepine	N/A	3.56	N/A	100	0.0356
Carbamazepine epoxide	0.310	1.69	N/A	100	0.0031
Carisoprodol	5.58	0.30	N/A	100	0.0030
Chloramphenicol	1.61	59.3	32.8	50	0.0322
Ciprofloxacin	0.190	2.84	N/A	100	0.0019
Citalopram	1.20	0.340	7.99	50	0.0068
Clarithromycin	N/A	83.7	N/A	100	0.837
Climbazole	4.84	3.43	13.4	50	0.0686
Clofibric acid	33.0	33.8	62.4	50	0.659
Clothianidin	N/A	N/A	N/A	N/A	N/A
Cocaine	1.24	9.33	11.9	50	0.0248
Coc-ethylene	1.49	8.86	28.8	50	0.0298
Cotinine	200	42.0	413	50	0.839

Crotamiton	11.4	4.03	24.4	50	0.0806
Cyclamate	75.7	N/A	N/A	100	0.757
Diazepam	1.12	4.15	N/A	100	0.011
Diclofenac	0.400	3.50	1.98	50	0.0080
Diltiazem	0.310	2.27	4.44	50	0.0062
ε-caprolactam	227	70.4	N/A	100	0.704
Enrofloxacin	0.160	2.31	N/A	100	0.0016
Erythromycin	N/A	161	N/A	100	1.61
Estriol	1.69	6.08	5.71	50	0.0338
Estrone	1.07	3.60	1.95	50	0.0214
Fipronil	0.010	0.240	N/A	100	0.000086
Fipronil desulfynil	0.130	0.600	N/A	100	0.0013
Fipronil sulfide	0.020	0.100	N/A	100	0.00024
Fipronil sulfone	0.040	0.340	N/A	100	0.00036
Florfenicol	1.01	62.6	N/A	100	0.0101
Fluconazole	187	96.7	N/A	100	0.967
Flumequine	0.510	7.21	8.56	50	0.0102
Fluticasone	N/A	N/A	N/A	N/A	N/A
Furosemide	N/A	N/A	N/A	N/A	N/A
Gabapentin	122	36.3	135	50	0.725
Gemfibrozil	3.89	5.13	5.01	50	0.0778
Hydrochlorothiazide	N/A	N/A	N/A	N/A	N/A
Hydroxychloroquine	2.11	12.0	2.87	50	0.0422
Hyoscine	0.540	8.18	N/A	100	0.0054
Imidacloprid	N/A	17.4	N/A	100	0.174
Indomethacin	0.370	5.91	4.92	50	0.0074
Iohexol	0.600	N/A	N/A	100	0.0060
Iopamidol	0.210	N/A	N/A	100	0.0021
Irbesartan	N/A	N/A	N/A	N/A	N/A
Ketoprofen	2.86	9.40	22.6	50	0.0572
Lamotrigine	7.58	17.8	N/A	100	0.0758
Lamotrogine-N2-oxide	N/A	N/A	N/A	N/A	N/A
Levofloxacin	1.24	17.0	N/A	100	0.0124
Lidocaine	7.14	14.7	49.2	50	0.143
Lincomycin	10.8	772	N/A	100	0.108
Lorazepam	0.130	4.48	N/A	100	0.0013
Mefenamic acid	4.27	17.6	20.4	50	0.0854
Melamine	3154	62.8	3095	50	1.26
Metformin	N/A	413	N/A	100	4.13
Methadone	3.93	4.53	3.70	50	0.074
Methylisothiazolinone	168	49.2	N/A	100	0.492
Metoprolol	33.5	51.6	28.6	50	0.572
Metronidazole	424	39.1	270	50	0.783
Midazolam	0.130	0.930	N/A	100	0.0013
N-3-dimethylaminopropylacrylamide	160	16.1	603	50	0.322
N-acetylsulfamethoxazole	N/A	N/A	N/A	N/A	N/A
Nalidixic acid	11.9	64.5	30.8	50	0.237
Naphtalene-1-sulfonic acid	18.6	N/A	N/A	100	0.186

Naproxen	4.52	12.9	25.0	50	0.0904
Neotame	3.45	23.5	10.4	50	0.0690
Nitrodiclofenac	0.200	5.22	N/A	100	0.0020
O-desmethylvenlafaxine	7.54	6.58	14.0	50	0.132
Oseltamivir carboxylate	37.1	57.9	97.9	50	0.742
Oxazepam	0.650	9.78	N/A	100	0.0065
Paraxanthine	1852	417	N/A	100	4.17
Paroxetine	0.230	1.13	6.60	50	0.0046
Pentobarbital	N/A	196	N/A	100	1.96
Phenytoin	45.0	10.7	N/A	100	0.107
Pipemidic acid	11.2	46.6	50.2	50	0.223
Pregabalin	84.1	31.9	27	50	0.637
Primidone	181	115	123	50	2.30
Propranolol	9.70	20.1	10.3	50	0.194
Propyphenazone	5.21	3.19	N/A	100	0.0319
Rosuvastatin	0.040	38.3	N/A	100	0.00043
Saccharin	N/A	N/A	N/A	N/A	N/A
Sitagliptin	2.45	6.25	N/A	100	0.0245
Sotalol	16.7	87.5	N/A	100	0.167
Stevioside	N/A	358	N/A	100	3.58
Sucralose	551	1008	N/A	100	5.51
Sulfadiazine	N/A	N/A	N/A	N/A	N/A
Sulfamethazine	N/A	N/A	N/A	N/A	N/A
Sulfamethizole	N/A	N/A	N/A	N/A	N/A
Sulfamethoxazole	N/A	N/A	N/A	N/A	N/A
Sulfapyridine	N/A	N/A	N/A	N/A	N/A
Sulfathiazole	N/A	N/A	N/A	N/A	N/A
Tramadol	N/A	N/A	N/A	N/A	N/A
Triethylenediamine	2255	111	726	50	2.22
Trifluoromethanesulfonic acid	51.04	N/A	N/A	100	0.510
Trimethoprim	10.7	15.2	102	50	0.214
Valsartan	N/A	N/A	N/A	N/A	N/A
Valsartan acid	N/A	N/A	N/A	N/A	N/A
Venlafaxine	6.31	8.18	8.98	50	0.126
Verapamil	0.100	0.130	0.68	50	0.0019
Warfarin	5.30	11.6	27.4	50	0.106

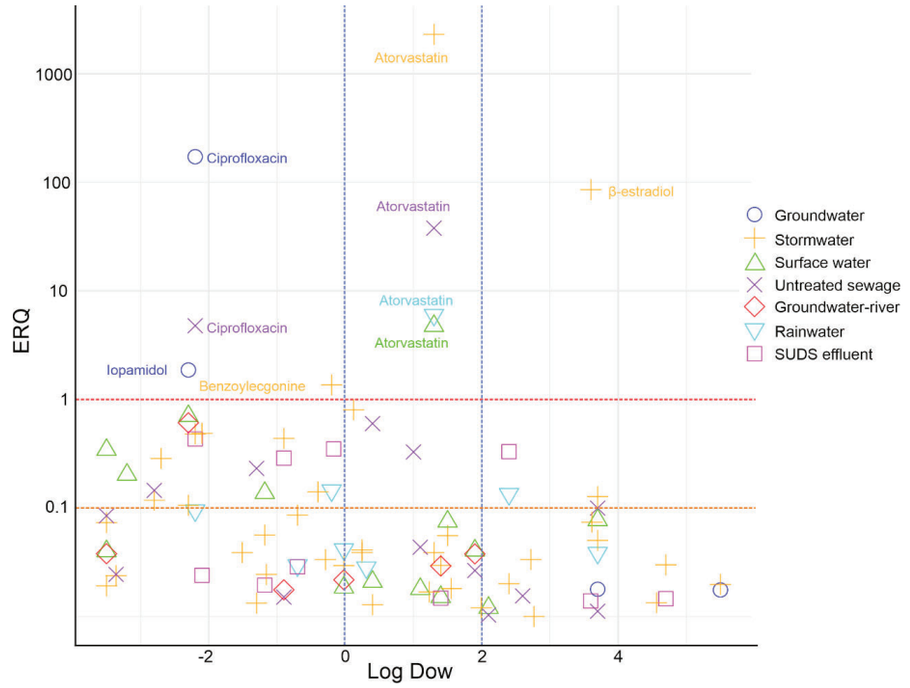


Figure S4. Maximum environmental risk quotient (ERQ_{Max}) of all compounds showing risk (ERQ > 0.01) in the seven urban water matrices studies compared to their mobility (using log D_{ow} as a polarity surrogate). Low environmental risk: compounds below the orange dotted line; Moderate environmental risk: compounds between the orange and the red dotted lines and; High environmental risk: compounds above the red dotted line. Blue dotted lines serve to identify highly polar, polar and moderately polar compounds.

5.4 Discussió

Aquest capítol tracta de la presència de TrOCs, principalment en aigua subterrània, i les possibles fonts de la seva recàrrega, l'aigua superficial, aigua d'escorrentia, aigua de pluja, aigua de clavegueram, així com dels sistemes de tractament de l'aigua d'escorrentia dels SUDS, de la ciutat de Barcelona. Les dues publicacions tenen en comú l'ús de models matemàtics basats en les concentracions de, o bé compostos inorgànics, o bé de TrOCs, per identificar la contribució de recàrrega de cada font d'aigua. La publicació #6 es va centrar en aigües subterrànies (tot i que s'inclouen mostres d'aigües superficials del riu Besòs) de l'àmbit de Sant Adrià del Besòs, molt properes al riu Besòs, mentre que a la publicació #7 es va tenir en compte totes les mostres de Barcelona (Figura 5.1). Encara que els resultats i les discussions s'exposen detalladament a cada article, en aquesta secció es presenta una anàlisi global que integra els resultats de les dues publicacions.

Impacte del riu Besòs en l'aigua subterrània

El primer que es pot extreure d'aquests resultats és la gran diferència de concentracions trobades en el conjunt de les mostres i les trobades en les mostres d'aigua subterrània influenciades directament per la recàrrega des del riu Besòs respecte a la resta. Degut a que la majoria de compostos estudiats presenta distribucions no-normals (test Shapiro-Whilks, p-value < 0.05), els futurs tests estadístics seran no paramètrics. Com era d'esperar, les aigües subterrànies properes al riu Besòs contenen unes concentracions molt més altes que la resta d'aqüífers, tal i com indica el test Mann-Whitney (p-value $3.6*10^{-6}$). A la Figura 5.2 es representa gràficament les diferències evidents entre els dos grups d'aigües subterrànies, on les aigües subterrànies amb major influència del riu Besòs contenen concentracions totals de TrOCs més altes que les mostres d'aigua subterrànies amb menys influència del riu (més allunyades del riu). Aquest fet posa de manifest dos aspectes principals: d'una banda, la influència directa de la infiltració d'aigua superficial del riu en els aqüífers propers, i de l'altra, l'atenuació natural exercida pel sòl sobre els TrOCs que el riu introdueix (Tubau et al., 2014).

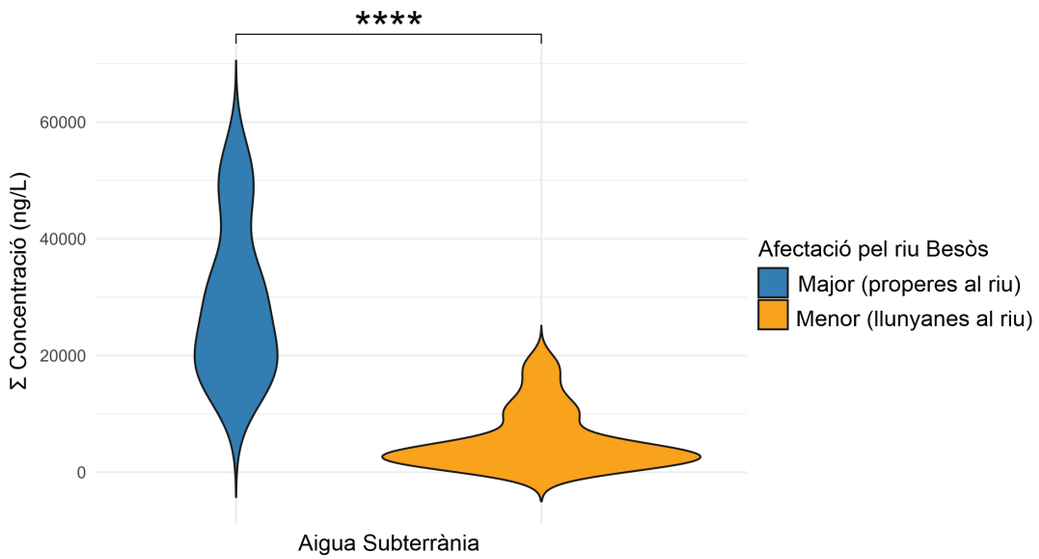


Figura 5.2. Diagrama de violí de la suma de concentracions de tots els TrOCs en les aigües subterrànies afectades pel riu Besòs: Blau: Properes al riu; Taronja: Llunyanes al riu. Els * representen diferències significatives.

Relació entre la profunditat dels pous i la presència de TrOCs

S'ha evidenciat que la distància d'un aqüífer respecte una font de recàrrega, com l'aigua superficial provinent del riu, afecta de forma clara amb una major presència i concentracions. D'altra banda, es interessant conèixer el comportament dels TrOCs, basant-se amb la seva presència, respecte la profunditat dels pous estudiats (Jurado et al., 2014, 2013). És lògic pensar que quan l'aigua subterrània es poc profunda (< 30 m), el temps de residència tendeix a ser menor i, aleshores, tant la presència com la concentració total pot ser major (Fan et al., 2013). D'altra banda, per pous amb aigües profundes (> 30 m), els TrOCs presents hauran de tenir propietats més resilients i persistir en el medi aquàtic durant períodes més llargs sense degradar-se o transformar-se (Fan et al., 2013). En aquesta tesi, la profunditat de l'aigua subterrània ha estat determinada per a un total de 25 pous, dels quals 17 contenien aigües a profunditats menors de 30 metres i 8 superiors a aquesta distància. Per veure adequadament la distribució dels compostos en aquest dos tipus d'aigua subterrània, s'ha emprat las medianes dels compostos enlloc de la mitjana, degut a la variabilitat de les dades. Per tant, dels 133 compostos

analitzats, 99 han estat detectats almenys un cop en aigua subterrània, però d'aquests, 29 complien tenir medianes superiors a 0 o <LOQ en almenys un dels dos tipus d'aigua subterrània. Per facilitar la identificació de tendències a la Figura 5.3, els 29 compostos seleccionats es van classificar segons la seva polaritat (log D_{ow}) en tres categories: mitjanament polars (log D_{ow} > 2), polars (2 ≥ log D_{ow} ≥ 0) i molt polars (log D_{ow} < 0). No obstant això, cal destacar que, segons la comunitat científica i, concretament, la normativa REACH, responsable de la classificació de PMTs i vPvM, els compostos polars solen definir-se com aquells amb un log D_{ow} ≤ 3 (Neumann et al., 2019).

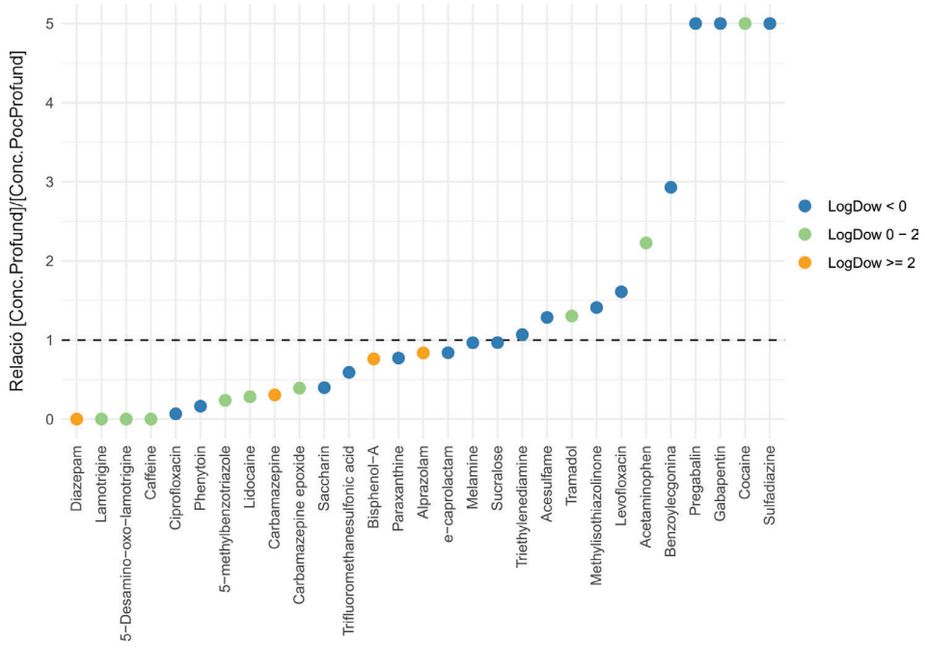


Figura 5.3. Gràfic de dispersió de la relació entre la mediana de les concentracions dels TrOCs estudiats en aigües subterrànies poc profundes i profundes. La línia discontinua negre indica que els compostos superiors a aquest llindar estan més concentrats en aigües subterrànies profundes.

A la Figura 5.3 18 TrOCs presenten una tendència a concentrar-se més en aigües subterrànies poc profundes, mentre que 11 TrOCs mostren el comportament oposat, amb una major concentració en aigües profundes. Tots els compostos per sobre del llindar d'1 s'han classificat com a polars, concretament 8 d'ells són molt polars. Com a curiositat, tant la lamotrigina (log D_{ow} = 1.7) i el 5-desamino-oxo-lamotrigine (log D_{ow} = 1.3), com la carbamazepina (log D_{ow} = 2.3) i la carbamazepina epòxid

(log D_{ow} = 1.3), presenten comportaments similars en base a la relació de concentracions trobada (Figura 5.3). Per contra, la cafeïna (log D_{ow} = 0.3) i un dels seus principals metabòlits humans, la paraxantina (log D_{ow} = - 0.2) presenten comportaments diferents (Figura 5.3). Mentre que la cafeïna s'ha detectat únicament a les aigües subterrànies poc profundes, la paraxantina, tot i tenir lleugerament més presència en aigües poc profundes, la relació és propera a 1 (0.77) suggerint que compostos que es degraden o metabolitzen a TrOCs més polars tenen la capacitat de tenir destins diferents i, sovint, toxicitats desconegudes (Zahn et al., 2024).

Per aprofundir en aquest tema, és important no només centrar l'atenció en la polaritat/mobilitat dels compostos estudiats, si no que la persistència dels mateixos en el medi aquós es també imprescindible per a que es puguin trobar en aigües profundes sense degradar-se o transformar-se. Segons la normativa REACH, un TrOC es considera persistent quan la seva vida mitjana de degradació en aigua dolça (aplicable a l'aigua subterrània) supera els 40 dies, i es classifica com a molt persistent quan aquest temps excedeix els 60 dies. Fent servir el software EPISuite™, que utilitza prediccions *in silico*, s'ha determinat la persistència dels 29 TrOCs analitzats prèviament emprant el model de fugacitat de nivell III, basat en el mètode *EQC*. Aquest model estima la distribució d'un compost entre aire, aigua, sòl i sediment, tenint en compte les emissions, les semivides de degradació i les propietats fisicoquímiques del compost (Bautista et al., 2024). A la Taula 5.1 els valors estimats de persistència (en dies) i el log K_{oc}, també calculats amb EPISuite™ usant el mètode K_{ow}, que estima el log Koc a partir de la correlació empírica entre el log K_{ow} i la capacitat d'adsorció al sòl del compost objectiu.

Taula 5.1. Mobilitat i Persistència dels 29 compostos objectiu. Persist.: Persistència

Compost	log D_{ow} (pH 7.4)	log K_{oc} *in silico*	Mobilitat (REACH)	Persist. (dies)	Persist. (REACH)
5-desamino-oxo-lamotrigina	1.30	2.39	vM	106	vP
5-metilbenzotriazola	1.70	1.94	vM	22	Non-P
Acesulfam	-2.80	0.35	vM	21	Non-P
Acetaminofèn	0.40	1.32	vM	25	Non-P
Alprazolam	2.60	2.17	vM	62	vP
Benzoylecgonina	-0.20	-0.71	vM	24	Non-P
Bisphenol A	3.60	3.10	M	76	vP
Cafeïna	0.30	0.98	vM	24	Non-P
Carbamazepina	2.30	2.23	vM	66	vP
Carbamazepina epòxid	1.30	1.31	vM	44	P
Ciprofloxacina	-2.20	0.00	vM	50	P
Cocaïna	1.20	2.00	vM	65	vP
Diazepam	2.90	2.44	vM	71	vP
ε-caprolactam	-0.02	1.27	vM	21	Non-P
Fenitoína	-0.98	2.26	vM	65	vP
Gabapentina	-1.40	-0.48	vM	24	Non-P
Lamotrigina	1.70	2.18	vM	100	vP
Levofloxacina	-2.10	0.00	vM	63	vP
Lidocaïna	1.30	2.18	vM	96	vP
Melamina	-1.18	0.00	vM	41	P
Metilisotiazolinona	-0.23	0.44	vM	18	Non-P
Paraxantina	-0.20	0.92	vM	24	Non-P
Pregabalina	-1.30	-0.85	vM	24	Non-P
Sacarina	-1.29	1.36	vM	25	Non-P
Sucralosa	-0.17	-0.72	vM	41	P
Sulfadiazina	-0.79	1.39	vM	40	P
Tramadol	0.50	2.24	vM	69	vP
Trietilendiamina	-1.28	0.52	vM	40	P
Àcid trifluorometansulfònic	-3.88	0.65	vM	36	Non-P

Queda clar que la mobilitat, seguint els criteris de la REACH, té una correlació directe (tant emprant els valors de log D_{ow} com els log K_{oc} estimats) amb la distribució dels compostos tant horitzontal com verticalment, fent que TrOCs mòbils tinguin la capacitat de viatjar en ambdós direccions amb més facilitat. Respecte a la persistència, i tenint en compte que els valors utilitzats per classificar cada compost com a no persistent, persistent o molt persistent han estat estimats mitjançant prediccions in silico, no s'ha pogut identificar una tendència clara que la relacioni amb les deteccions observades a les diferents mostres d'aigua subterrània. Dels 29 compostos analitzats, 11 es classifiquen com a

molt persistents (vP), 6 com a persistents (P) i 12 com a no persistents (Non-P) (Taula 5.1). No obstant això, les emissions d'aquests compostos també exerceixen un paper clau en la seva presència a grans profunditats i la seva distribució a través de tota la ciutat.

Aquests resultats evidencien la falta d'estudis experimentals que avaluïn els paràmetres de mobilitat (log K_{oc}) i els de persistència (vida mitjana en medis aquosos), per poder discernir sobre aquells TrOCs que realment poden ser una amenaça per a la qualitat de la potencial aigua potable o d'ús per al consum humà. Conèixer els TrOCs presents i les seves concentracions en una ciutat com Barcelona és essencial per idear estratègies que en redueixin la presència als llocs d'origen i per implementar futures directives enfocades especialment als TrOCs mòbils amb altes freqüències de detecció i concentracions en les aigües urbanes. Aquestes accions són especialment importants per a les aigües subterrànies, que tenen un gran potencial per ser utilitzades en el consum humà.

TrOCs específics com a traçadors potencials de fonts d'aigua

A la secció anterior s'ha discutit la presència dels TrOCs en relació a la distància d'una font de contaminació o profunditat de l'aigua subterrània. Conèixer la presència de TrOCs específics de cada matriu és interessant per esbrinar tendències, orígens i saber el per què de la presència d'alguns compostos en les aigües subterrànies urbanes. Els anàlisis mostren 12 compostos únics diferents de cada matriu, tot i que aquí només s'aprofundirà en 5, ja que les freqüències de detecció són superiors al 10 %. Per tant, només dos matrius presenten TrOCs exclusius, es tracta l'aigua superficial del riu i l'aigua residual, que són les fonts que contribueixen més a la recàrrega dels aqüífers, sent la tercera l'aigua d'escorrentia (publicació #7). Els TrOCs detectats únicament a l'aigua superficial son tres fàrmacs: el cloramfenicol, l'ezetimibe i el iodixanol. D'altra banda, a l'aigua residual urbana es troba el fàrmac rosuvastatina i l'hormona estrona. Tot i que aquests TrOCs no arriben a l'aigua subterrània, poden ajudar a discernir patrons en el tipus de compostos que cada matriu conté.

Presència de TrOCs en totes les matrius aquoses urbanes

L'última secció d'aquest capítol posarà en evidència els compostos detectats en totes les matrius aquoses urbanes i que presentin un 100 % de freqüència de detecció. A la secció 5.2 d'aquest capítol s'especifiquen les mostres analitzades en aquesta tesi, obtenint un total de 7 tipus d'aigua urbana. Dels 133 compostos analitzats en aquest estudi, 9 compostos es van detectar amb un 100% de freqüència en totes les 7 matrius analitzades. Aquests compostos, que abasten una varietat de categories, inclouen:

Compostos industrials (5 compostos):

- **5-Methyl-1H-benzotriazol**: Emprat com a antioxidant en la indústria del plàstic.
- **ε-Caprolactam**: TrOC intermediari en la producció del plàstic niló.
- **Melamina**: Utilitzada en la producció de resines i plàstics, així com en la fabricació de taulers de fibra de fusta.
- **Triethylenediamina**: S'utilitza com a agent enduridor en la fabricació de plàstics i com a estabilitzador en diversos processos industrials.
- **Àcid trifluorometansulfònic**: Utilitzat en la síntesi de productes farmacèutics i altres aplicacions industrials.

Productes de cura personal (2 compostos):

- Cafeïna: Estimulant àmpliament consumit, present en diferent begudes i aliments.
- Cotinina: El metabòlit principal de la nicotina.

Edulcorants artificials (1 compost):

- Sacarina: Edulcorant artificial utilitzat com a substitut del sucre en una varietat de productes alimentaris i begudes.

Fàrmacs (1 compost):

- Tramadol: Analgèsic sintètic utilitzat en el tractament del dolor moderat a sever. També pot tenir un ús recreatiu.

Aquests compostos mostren un caràcter omnipresent en l'entorn urbà, fet que afecta la qualitat de l'aigua urbana i també representen una amenaça per als ecosistemes aquàtics urbans com per exemple zones humides al entorn del rius Besòs, incloent-hi la flora i la fauna. La seva presència generalitzada en les diverses fonts d'aigua subratlla la seva capacitat de persistir i acumular-se en l'entorn.

A més, remarcar que tots els 9 TrOCs destacats compleixen els requeriments per ser considerats vM, amb valors de log D_{ow} que oscil·len entre 1.7 i -3.9, tornant a recalcar la importància d'aquesta propietat físico-química en matrius aquoses.

Finalment, aquests compostos podrien ser utilitzats com a traçadors en l'estudi de les aigües subterrànies i els seus contaminants, així com per a la creació de models matemàtics que permetin predir el comportament dels contaminants en l'aigua subterrània, la qual cosa podria ser útil per a la gestió dels recursos hídrics i el control de la contaminació en entorns urbans.

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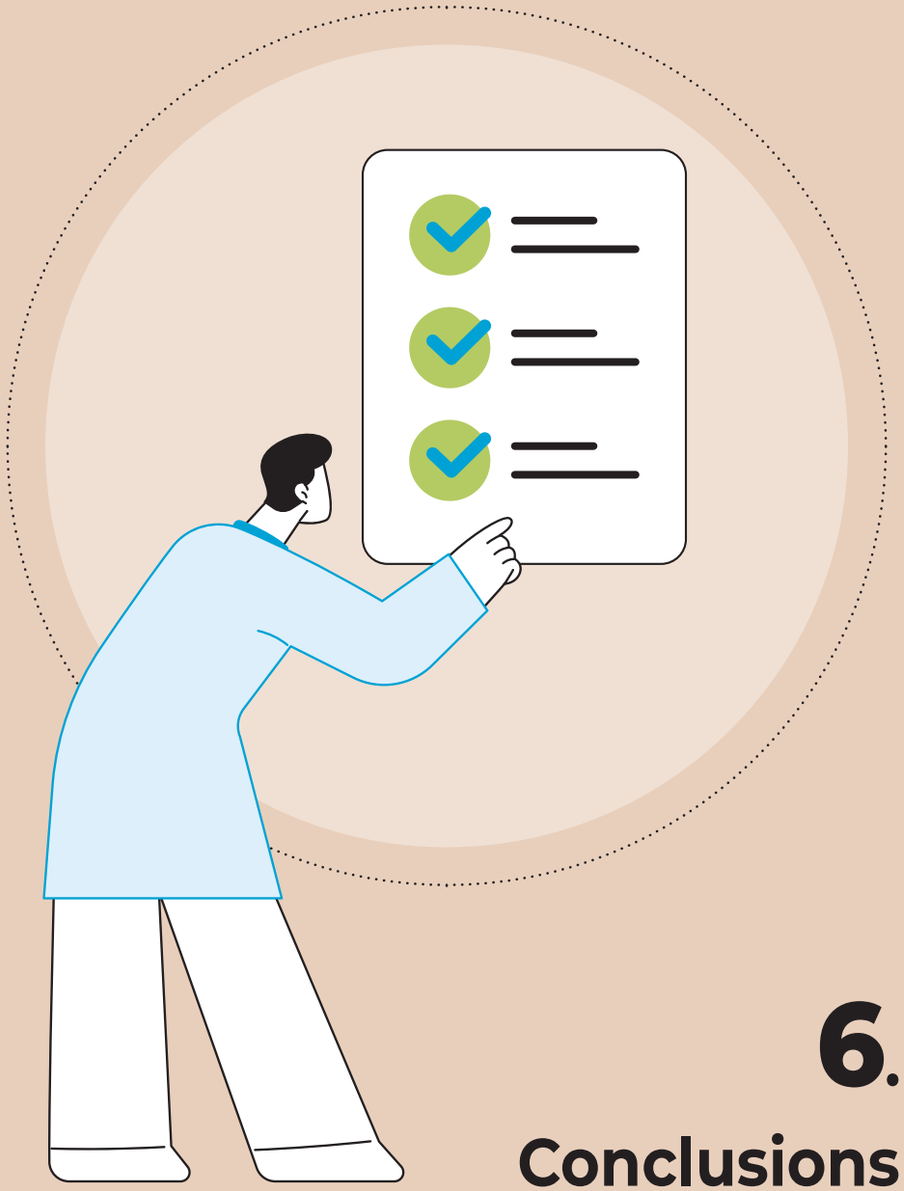
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Capítol



6.
Conclusions

CONCLUSIONS

6.1 Conclusions generals

Through this thesis, analytical methods have been developed for the analysis of environmental contaminants from different families and with varying physicochemical properties in water, with special attention to polar and highly polar TrOCs. Furthermore, their presence has been assessed in various types of urban waters, including groundwater, surface water, rainwater, runoff, sewage, and SUDS effluents, allowing for an evaluation of the contamination sources recharging Barcelona's groundwater. The conclusions drawn from the results presented in the previous chapters are as follows:

1. Several analytical methodologies have been developed for the analysis of TrOCs with a wide range of polarities, showing that VAE enrichment provides adequate recoveries for most polar and highly polar compounds, such as metformin (RR = 93.5%) or 5-fluorouracil (RR = 99.9%). Meanwhile, msSPE extraction has proven to be more suitable for moderately polar compounds, such as carba-

mazepine (RR = 97.3%) or diclofenac (RR = 91.0%). Therefore, it is concluded that the combination of VAE and msSPE extraction is suitable for the determination of TrOCs with a broad range of polarities.

2. Different chromatographic columns have been evaluated to identify those that offer the best performance in terms of retention and peak shape for TrOCs with a wide range of polarities. For highly polar compounds, normal-phase liquid chromatography (HILIC) provides ideal conditions to efficiently retain these TrOCs, such as zanamivir (RT = 13.1 min) or metformin (RT = 9.32 min). Conversely, reversed-phase chromatography, with a wide variety of modified columns available on the market today, stands out for its versatility in separating compounds ranging from low polarities, such as fipronil (RT = 16.0 min) or diazepam (RT = 15.1 min), to even some highly polar ones like cyclamate. Therefore, for comprehensive analyses, it is essential to combine both chromatographic modalities to achieve optimal and complete separation.

3. Despite using both liquid chromatography modalities, some compounds, often the highly polar ones, cannot be sufficiently retained even with the HILIC column. Here, IM spectroscopy has been shown to play a key role in the analysis of these TrOCs, which are and will remain in the spotlight of scientists and organizations to ensure good water quality. Since IM does not depend on the polarity of the compounds, it has proven useful for analysing these TrOCs, adding a new dimension to small-molecule separation based on CCS. This study includes specific CCS results for 33 highly polar compounds, providing key information for future monitoring of these substances using IM.

4. The first study focused on highly polar compounds (log Dow < 0) in urban rainwater and first-flush runoff has been conducted in this thesis. In fact, for the first time, 12 TrOCs have been identified and reported in urban water, demonstrating that the analysis of polar TrOCs must be a priority to ensure high water quality and minimize potential environmental and human health impacts. Some of these compounds include 1-naphthalenesulfonic acid, acrylamide,

cyanoguanidine, and trifluoromethanesulfonic acid.

5. This thesis has also provided evidence of contamination sources in urban groundwater. It has been determined, in a global assessment, that groundwater is contaminated by organic pollutants with contributions of 51.5% from surface water (Besòs River), 43.7% from untreated wastewater, and 4.8% from runoff. Understanding how and where contamination of this precious freshwater resource, groundwater, originates is crucial to preventing future pollution by focusing on the contamination of recharge sources.

6. TrOCs have been identified as potential organic tracers to detect inputs of wastewater, surface water, rainwater, or other sources into groundwater, such as the pharmaceutical carbamazepine. Additionally, they can help describe flow dynamics and physicochemical conditions both locally and regionally within aquatic environments like groundwater. Using TrOCs as tracers can enhance the characterization of their behaviour in the subsurface, thereby improving the understanding of TrOC attenuation processes and the mixing between recharge water and deeper groundwater.

7. The calculation of ERQ in different urban waters, including runoff, surface water, and groundwater, has helped identify TrOCs that pose environmental risks. Two compounds have been found to seriously threaten surface water quality, both contrast agents, iopamidol and iohexol. Additionally, other compounds present risks to surface water and runoff quality, such as the industrial compound melamine, the pesticide fipronil, or benzoylecgonine, the primary human metabolite of cocaine. Identifying TrOCs with environmental risks is essential for continuous monitoring and, consequently, for protecting urban water sources.

8. Similarly, the HRQ assessment highlights compounds that pose risks to human health. The results indicate that both valsartan, a drug used to treat hypertension, and its primary metabolite, valsartan acid, present a moderate risk to adults but a high risk to children. Likewise, the pharmaceuticals irbesartan and lamotrigine pose health hazards for children. Although the analyzed waters are

not intended for direct consumption, depending on the concentration, constant exposure to these types of water through drinking water sources could pose significant health risks. This thesis underscores the need for proper monitoring of urban groundwater and, if necessary, the application of ad-hoc treatments based on the intended use of the water to remove the present TrOCs.

Overall, this study concludes that TrOCs, particularly those with high polarity, are present in all types of urban water at significant concentrations. Moreover, many of them meet mobility and persistence criteria, making them difficult to capture, analyse, and ultimately remove from the water cycle. To preserve urban groundwater as a resilient freshwater source amid climate change, special attention should be given to these compounds by identifying their sources of contamination and using the methodologies developed in this thesis. This will help mitigate environmental and even human health risks in urban environments.