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Concentrations of bisphenols and phthalate esters in the muscle of Mediterranean striped dolphins (*Stenella coeruleoalba*)

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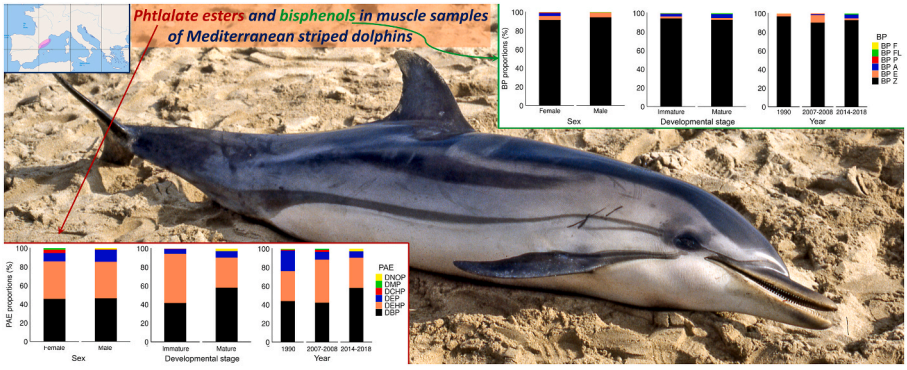
HIGHLIGHTS

- Muscle samples were obtained from 30 stranded Mediterranean striped dolphins.
- Six bisphenols and 6 phtalate esters were detected in the samples.
- BPZ was detected in all the samples, at the highest concentrations.
- Concentrations did not relate with biological traits but varied with time.
- Results confirm dolphin exposure to plasticizers in an already anthropized basin.

GRAPHICAL ABSTRACT



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ABSTRACT

Bisphenols (BPs) and phthalate esters (PAEs) are important compounds for the plastics industry, also called "everywhere chemicals" due to their ubiquity in daily use products. Both chemical groups are well-known environmental contaminants, whose presence has been reported in all environmental compartments, and whose effects, mainly associated to endocrine disruption, are detrimental to living organisms. Cetaceans, due to their long life-span, low reproduction rate and high position in the trophic web, are especially vulnerable to the effects of contaminants. However, little is known about BP and PAE concentrations in cetacean tissues, their potential relation to individual biological variables, or their trends over time. Here, the concentration of 10 BPs and 13 PAEs was assessed in the muscle of 30 striped dolphins (*Stenella coeruleoalba*) stranded along the Spanish Catalan coast (NW Mediterranean) between 1990 and 2018. Six BP and 6 PAE compounds were detected, of which only 4,4′-(cyclohexane-1,1-diyl)diphenol (BPZ) was detected in all the samples, at the highest concentration (mean 16.06 μg g^{-1} lipid weight). Sex or reproductive condition were largely uninfluential on concentrations: only dimethylphthalate (DMP) concentrations were significantly higher in immature individuals than in adults, and the overall PAE concentrations were significantly higher in males than in females. Temporal variations were only detected in bis(4-hydroxyphenyl)ethane (BPE), diethylphthalate (DEP) and dimethylphthalate

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(DMP), whose concentrations were lower, and 9,9-Bis(4-hydroxyphenyl)fluorene (BPFL), which were higher, respectively, in samples taken between 2014 and 2018, probably reflecting shifts in the production and use of these chemicals. These results provide the first assessment of concentrations of several BP and PAE compounds in the muscle of an odontocete cetacean.

1. Introduction

Bisphenols (BPs) and phthalic acid esters (PAEs) have been called "everywhere chemicals" due to their widespread use in the manufacture and processing of plastic and resin products and their ubiquity in human body, wildlife and the environment (Net et al., 2015; Warner and Flaws, 2018; Sangeetha et al., 2021). Indeed, they are important chemical components for the plastics industry, where BPs (and more specifically Bisphenol A (2,2-bis(4-hydroxyphenyl)propane, henceforth BPA), along with its analogues) are used in the manufacture of hard, transparent plastics, such as water bottles, as well as in the production of polycarbonate, polyacrylate, flame retardants, solvents, and other products used for coating, such as epoxy resins, and are present in a large variety of everyday products (Staples et al., 1998; Mustieles et al., 2020; Torres-García et al., 2022). On the other hand, PAEs are used to manufacture soft, flexible and transparent plastics, such as plastic polyvinyl chloride (PVC) products, and a very broad range of products including building materials, toys, personal care products (PCP), food packaging, cosmetics, medical devices (Graham, 1973), and many other daily use products, where their content can be up to 10–60% by weight (Net et al., 2015).

Although plastic materials are chemically inert, the chemical additives used to improve their qualities may be released to the environment during the plastic weathering processes caused by solar radiation, sea corrosion, and chemical and biological degradation (Koelmans et al., 2014; Net et al., 2015). Moreover, BPs and PAEs may also enter the environment during the production process and ultimately be transported at sea through river discharge or atmospheric deposition (Xie et al., 2007). The constant raise of plastic production, and consequent plastic pollution in the worldwide oceans (Jambeck et al., 2015; Geyer et al., 2017; Lambert et al., 2020) is thus expected to increase the concentration of plastic additives such as BPs and PAEs in the marine environment, as a result of their direct deposition and/or their leaching from the large amounts of marine plastic litter that reach the oceans every day.

Indeed, both BPs and PAEs are well-known environmental pollutants, which have been detected in every natural compartment, including air, soil, sediments, fresh and marine waters (Xie et al., 2007; Zeng et al., 2009; Ben Sghaier et al., 2017; Paluselli et al., 2018; Moustafa et al., 2022; Torres-García et al., 2022; Xing et al., 2022), as well as in the tissues of several animal species (Kang et al., 2007; Koelmans et al., 2014; Nehring et al., 2017; Routti et al., 2021). Both *in vivo* and *in vitro* studies have proven their toxic effects to living organisms. *In vitro* studies with laboratory animals and epidemiological studies in humans showed that BPA, several of its analogues, and most PAEs, cause severe endocrine effects (Basak et al., 2020), as well as potential neurological and carcinogenic effects (*e.g.*, Benjamin et al., 2017; Li et al., 2018; Pelch et al., 2019; Han et al., 2021). Although most BPs and PAEs are subject to efficient metabolic degradation and elimination (Kang et al., 2006; Net et al., 2015), the increased levels of environmental and dietary exposure to which living organisms are subject may maintain their tissue concentrations at chronic or sub-chronic levels, and trigger detrimental effects (Silva et al., 2018; Warner and Flaws, 2018).

Cetaceans are particularly vulnerable to the effects of lipophilic contaminants. Being mammals with a long life-span, low reproduction rate, and high position in the trophic web, they are subject to both the bioaccumulation and biomagnification of pollutants (Loganathan, 2012). Despite the proven toxic effects of BPs and PAEs to mammals, and their potentially high concentrations in the marine environment, their concentrations in the tissues of marine mammals have been determined only by a handful of studies so far. Most of the published research focuses on the assessment of PAEs and their metabolites in the tissues of two main species: the bottlenose dolphin (*Tursiops truncatus*, *i.e.*, Dziobak et al., 2021, 2022; Hart et al., 2018, 2020) and the fin whale (*Balaenoptaera physalus*, *i.e.*, Baini et al., 2017; Fossi et al., 2012, 2014, 2016; Garcia-Garin et al., 2022); while other marine mammal species have been scarcely studied (*e.g.*, Rian et al., 2020; Routti et al., 2021), and the concentrations of BPs in these organisms have been barely investigated (*i.e.*, Montoro-Martínez et al., 2021; Page-Karjian et al., 2020). Little is known regarding the concentrations of these contaminants, and especially of BPs and PAEs other than the more commonly studied BPA and di-(2-ethylhexyl) phthalate (DEHP), in marine mammals, their potential relation with biological variables, or their trends over time.

With the aim of contributing to fill such information gap, here we analysed 10 BPs and 13 PAEs in the muscle of 30 striped dolphins (*Stenella coeruleoalba*) stranded along the Mediterranean coast of Spain between 1990 and 2018. Our results are discussed taking into account the potential influence of biological variables, such as sex and maturation stage of the individuals, and of the year of death, which might reflect the increasing levels of plastic pollution in the Mediterranean Sea and the regulation of some of the analysed compounds, like BPA and DEHP. Although the Mediterranean striped dolphin is currently not in a concerning conservation status, cetaceans are often subject to a variety of human impacts that, combined, may compromise the healthy survival of their populations (Hart et al., 2020, Dziobak et al., 2021). The pathways and levels of exposure to these increasingly widespread pollutants of potentially vulnerable marine fauna such as cetaceans deserve in-depth investigation.

2. Materials and methods

2.1. Study area and sampling

Muscle samples were collected from 30 striped dolphins found stranded along the Spanish Catalan coast, in the NW Mediterranean Sea (Fig. 1), during three separate periods between 1990 and 2018 (*i.e.*, 1990, 2007–08, and 2014–18), and preserved in the biological tissue bank of the University of Barcelona (BMA Tissue Bank). Since muscle represents approximately 50% of dolphins weight and its average lipid content is 6%, this tissue was considered representative enough to assess the levels of BPs and PAEs in the dolphins. The cause of death for most dolphins was related with the morbillivirus epizootics occurred in the Mediterranean Sea during 1990 and 2006–07 periods. As age information was only available from 7 out of the 30 dolphins, individuals were classified according to their sexual maturation stage, defined based on their body length. Individuals whose body was shorter than 1.3 m were classified as immature, and individuals whose body was longer than 1.8 m were classified as adult (Table 1). Overall, sampled individuals included 24 adults (12 males and 12 females), and 6 immature individuals (2 males and 4 females, Table 1). Muscle samples, stored at −20 °C, were subsampled using stainless steel material to obtain individual subsamples of 25–30 g, which were placed in glass bottles and preserved frozen until analysis. To avoid contamination, no plastic material was used during this procedure.

2.2. Sample preparation

After 48 h lyophilization, a subsample of 4 g (dry weight, dw), was taken from the central portion (to avoid possible contamination) of each muscle sample and homogenised. Each subsample was then transferred in 50 mL centrifuge tubes and diluted in a mixture of 10 mL acetonitrile, 10 mL Milli-Q water, 100 μL internal standard (d_4-DIBP), and extraction salts (composed by 1 g NaCl, 4 g $MgSO_4$, 1 g $C_6H_5Na_3O_7{\cdot}2H_2O$ and 0.5 g $C_6H_6Na_2O_7{\cdot}1.5H_2O$). After stirring in a vortex mixer with ceramic homogenizers and centrifugating for 5 min at 5000 rpm, 8 mL of each extract were transferred to centrifuge tubes containing the dispersive solid phase extraction clean-up salts (400 mg PSA, 400 mg GCB, 1200 mg MgSO4 and 400 mg C18EC). The mixture was then vortexed and centrifuged again at 5000 rpm for 5 min. Five (5) mL of the supernatant were transferred to a vial, and the extraction was repeated a second time using 10 mL ethyl acetate. The two resulting extracts were then combined and reduced under a gentle nitrogen stream to 200 μL and 50 μL for PAEs and BPs, respectively. Prior to PAE GC-MS/MS analyses, extracts were stored frozen in glass tubes. For BPs, each extract was derivatized with 50 μL of BSTFA containing 1% TMCS and heated at 65 °C during 2 h. After derivatization, samples were kept at room temperature during 15 min prior to GC-MS analysis (Sghaier et al., 2017).

Due to the lipophilic nature of PAEs and BPs, it is generally recommended to report their concentrations on a lipidic weight (lw) basis to prevent any bias related to the individual, specific, or tissue-related differences in lipid concentrations (Krahn et al., 2003). Thus, following Garcia-Garin et al. (2020), 1 g dw of each sample was used to determine the lw gravimetrically by a 15 min sonication in a 15 mL solution of hexane:acetone (1:1). Two extractions were performed and the resulting extracts were mixed. After the solvent evaporation under nitrogen stream, the remaining lipids were dried at 90 °C until they reached a constant weight.

2.3. Instrumental analysis, standards and reagents

Ten BP and thirteen PAE compounds were analysed, namely: BPA, 4,4′-(1-Phenylethylidene)bisphenol (BPAP), 1,1-Bis(4-hydroxyphenyl)-1,1-diphenylmethane (BPBP), 2,2-Bis(4-hydroxy-3-methylphenyl)propane (BPC), bis(4-hydroxyphenyl)ethane (BPE), (bis(4-hydroxypheny) methane (BPF), 9,9-Bis(4-hydroxyphenyl)fluorene (BPFL), 4,4′-(1,3-Phenylenediisopropylidene)bisphenol (BPM), 4,4′-(1,4-Phenylenediisopropylidene)bisphenol (BPP), 4,4′-(cyclohexane-1,1-diyl) diphenol (BPZ), dimethylphthalate (DMP), diethylphthalate (DEP), di-*n*-butylphthalate (DBP), bis(2-methoxyethyl) phthalate (DMEP), dipentylphthalate (DPP), bis(2-ethoxyethyl) phthalate (DEEP), benzyl butyl phthalate (BBP), phthalic acid dicyclohexyl ester (DCHP), bis(4-methyl-2-pentyl) phthalate (BMPP), di-*n*-hexyl phthalate (DHP), bis(2-*n*-butoxyethyl) phthalate (DBEP), bis(2-ethylhexyl) phthalate (DEHP) and di-*n*-octyl phthalate (DNOP). Analytical standards of BPs and PAEs were purchased from TCI Europe (Zwijndrecht, Belgium) and Restek (Lisses, France), respectively. Deuterated BPA (BPA d16) and labelled phthalic acid diisobutyl ester (d_4-DIBP) were obtained from Sigma-Aldrich (St. Louis, MO, USA); acetonitrile and ethyl acetate (for HPLC isocratic grade) for trace analysis were provided by VWR; the extraction salts were provided by Merck Acetone (SupraSolv®) and Agilent Technologies; and the BSTFA + TMCS (99:1) solution was provided by Supelco.

An Agilent 7890 GC coupled to an Agilent 7000C Triple Quadrupole GC/MS system (Agilent Technologies, France) were used for analyses. An Agilent DB-17ms, 30 m × 0.25 mm, 0.25 μm column, with a constant flow of 1.2 mL helium (99.999% purity) min^{-1}, was used to produce analyte separation. The solvent vent injection mode was used through an ultra-inert inlet liner, with a glass wool frit from Agilent, to inject samples in a multimode inlet. The injector operated with an injection

Fig. 1. Map of the Western Mediterranean Sea highlighting (in pink) the area of the Spanish Catalan coast, where the striped dolphins sampled in this study were found stranded.

volume of 3 μL and a temperature cycle of: 0.8 min at 50 °C (solvent evaporation), raise to 300 °C at 720 °C min^{-1}; 5 min hold; cooling down to 280 °C; 10 min hold. The quenching and collision gas were helium (99.999% purity; flow rate of 2.25 mL min^{-1}) and nitrogen (99.999% purity; flow rate of 1.5 mL min^{-1}), respectively. The temperature cycle of the oven included: 2 min at 40 °C, a first raise to 220 °C at 30 °C min^{-1}, a second raise to 260 °C at 5 °C min^{-1} and a last raise to 280 °C at 20 °C min^{-1}, 7 min hold; for a total run time of 24 min. Electron impact ionisation (EI) at 70 eV ionising energy, and the MRM mode were set to operate the triple quadrupole mass spectrometer, at temperatures of 280 °C for the transfer line, 230 °C for the ion source and 150 °C for quadrupoles 1 and 2.

2.4. Quality assurance

To prevent sample contamination, all procedures were performed in clean laboratory conditions: samples and standards preparation, extraction, clean-up and the pre-concentration step were carried out in a laminar flow cabinet. Glassware was washed with detergent (Decon), rinsed with ultra-pure water (Milli-Q water), washed with acid solution (HCl) and again rinsed with Milli-Q water follow by acetone, and was dried at 120 °C prior to use. Analytical blanks were included every 10 samples to minimize the error of quantification. Targeted compounds in blanks should be lower than limit of quantification (LOQ) value: if they were higher than LOQ in the samples, the concentration detected in the blank was subtracted from the corresponding batch of samples (Net et al., 2015). BPs and PAEs were lower than LOQ in the procedural blanks. Limit of detection (LOD) and LOQ for each compound were estimated as 3-times and 10-times the baseline of blank chromatograms, respectively, and were confirmed by experimental analysis. LOQs for BPs and PAEs were in the range of 0.73–4.36 and 0.012–0.062 ng g^{-1} dw, respectively. The recovery rate of each BP and PAE was calculated by spiking the targeted compounds into a real matrix of interest. The mean BP recovery was estimated at 99.7% with a rate of 108, 102, 110, 106, 94 and 97% for BPA, BPE, BPF, BPFL, BPP, and BPZ, respectively. The mean PAE recovery was estimated at 92% with a rate of 104, 81, 86, 98, 76 and 106% for DMP, DEP, DBP, DEHP, DCHP and DNOP, respectively. Samples were not replicated but the analytical procedure was repeated to check its replicability: Standard deviations obtained were <5% when the concentration of the compound was higher than 0.1 ng g^{-1} and ~12% when the concentration of the compound was close to the LOQs. Calibration curves were obtained in the range of 0.1–5000 μg L^{-1} with the correlation coefficients of ≥0.994.

The University of Lille LASIRE laboratory (UMR CNRS 8516) provided the infrastructure and support to perform all above analyses.

2.5. Statistical analysis

The distribution of each BP and PAE concentration was tested for normality and heteroscedasticity through a Shapiro Wilk and Levene tests, respectively. As concentrations were not normally distributed, data were analysed using non-parametric tests, considering both each BP and PAE compound individually, as well as the sum of all BP and of all PAE compounds. To exclude potential biases, results obtained from mature individuals (n = 24) were used to assess the relative influence of sex and year of death, split in three groups (*i.e.*, 1990, 2007–2008 and 2014–2018), through a Kruskal Wallis and a Spearman's rho correlation test, respectively. Results obtained from the 2014–2018 samples (n = 15) were used to assess the potential effect of the maturation stage through a Kruskal Wallis test. The level of significance was set at $p < 0.05$. Analyses were performed in R (R Core Team, 2021).

3. Results

The overall concentrations of BPs and PAEs detected in each sample are shown in Table 1. Minimum, maximum and mean concentrations of each BP and PAE, as well as their frequency of occurrence, are summarized in Table 2. Out of the 10 BPs and 13 PAEs analysed, 6 BPs and 6 PAEs were detected, respectively. The concentrations of the majority of selected BPs and PAEs were below the LOQ, meaning that these

Table 1
Sex, body length (in m), maturation stage and age (when determined) of the sampled striped dolphins, along with the lipid content and overall phthalate esters and bisphenol compounds concentrations found in their muscle (expressed in ug g^{-1} lipid weight (lw)).

Sample	Year	Sex	Length	Maturation stage	Age	Lipid content (%)	∑PAE	∑BP
2007_1	2007	M	2.1	MATURE	NA	1.24	72.499	1.277
2007_3	2007	F	1.8	MATURE	NA	1.21	9.564	17.251
2007_4	2007	F	1.95	MATURE	NA	0.69	30.430	32.939
2007_6	2007	M	1.85	MATURE	NA	1.10	23.231	17.249
2008_1	2008	F	2.1	MATURE	NA	15.46	3.568	0.369
2008_6	2008	F	1.89	MATURE	NA	1.08	46.250	26.104
2008_7	2008	M	1.85	MATURE	NA	1.04	7.923	42.594
9033	1990	M	1.93	MATURE	16	1.87	26.645	2.714
9034	1990	F	1.96	MATURE	14	1.64	3.542	8.971
9040	1990	M	1.81	MATURE	7	1.77	14.713	13.499
9042	1990	M	1.87	MATURE	10	1.67	4.463	50.728
9043	1990	F	1.8	MATURE	9	1.85	1.547	4.665
9046	1990	F	1.82	MATURE	30	1.58	5.192	9.069
9054	1990	F	2	MATURE	23	1.77	5.020	17.188
9067	1990	M	1.91	MATURE	NA	1.86	36.006	28.954
N_1_18	2018	F	2	MATURE	NA	1.04	2.089	1.905
N_168_17	2017	M	1.93	MATURE	NA	1.30	18.476	5.756
N_21_18	2018	M	1.82	MATURE	NA	1.40	15.992	0.924
N_286_15	2015	F	1	IMMATURE	NA	2.88	13.259	10.305
N_291_14	2014	F	1.04	IMMATURE	NA	16.78	1.832	0.154
N_352_14	2014	M	1.3	IMMATURE	NA	1.39	0.006	15.661
N_355_14	2014	F	1.07	IMMATURE	NA	3.10	9.681	33.913
N_370_14	2014	M	2.04	MATURE	NA	1.42	4.522	2.240
N_407_15	2015	M	2.1	MATURE	NA	1.22	6.141	20.854
N_45_17	2017	F	1.23	IMMATURE	NA	3.02	80.258	13.801
N_488_17	2017	M	1.98	MATURE	NA	1.38	16.826	24.986
N_49_15	2015	F	1.9	MATURE	NA	2.06	11.118	5.772
N_497_17	2017	F	1.9	MATURE	NA	8.77	1.806	3.242
N_523_17	2017	M	1.03	IMMATURE	NA	2.70	8.303	96.396
N_77_17	2017	F	1.81	MATURE	NA	1.41	1.372	4.375

Table 2
Mean concentrations and ranges of individual and overall BP and PAE compound concentrations expressed on a lipid weight (lw) basis, and frequency of occurrence (FO) in the muscle of stranded striped dolphins. Values below LOQ are expressed as 0.

	Mean lw (μg g^{-1})	Range (μg g^{-1} lw)	FO (%)
BPA	0.29	0–4.93	10
BPE	0.67	0–6.17	90
BPF	0.01	0–0.07	67
BPFL	0.05	0–0.44	47
BPP	0.03	0–0.94	7
BPZ	16.06	0.12–94.9	100
ΣBP	17.13	0.15–96.4	
DBP	7.24	0–26.59	73
DCHP	0.19	0–3.03	13
DEHP	6.85	0–48.9	63
DEP	1.62	0–8.04	80
DMP	0.08	0–1.38	38
DNOP	0.09	0–2.1	7
ΣPAE	16.08	0.01–80.29	

compounds were not detected in all the sampled dolphins. Indeed, BPZ was the only compound detected in all samples, at higher concentrations than any other compound (Table 2). DEP, DBP and DEHP were the only other compounds whose mean concentrations were higher than 1 μg g^{-1} lw, and were detected in 80%, 73% and 63% of samples, respectively (Table 2, Fig. 2).

Results of the comparison of BP and PAE concentrations between sexes, mature and immature individuals, and sampling periods are shown in Table 3. No significant difference was detected between sexes for individual BPs or PAEs. However, the overall concentration of PAEs was significantly higher ($p = 0.024$, Kruskal-Wallis test) in samples from males than in those from females. No significant difference was detected between the concentrations of BPs or PAEs in mature and immature dolphins, with the exception of DMP, whose concentrations were significantly higher ($p = 0.023$, Kruskal-Wallis test) in immature individuals than in adults. Finally, a significant positive correlation between the concentration of BPFL and the period of sampling ($\rho = 0.46$, $p = 0.024$), and significant negative correlations between the concentrations of BPE, DEP, and DMP and the period of sampling were detected ($\rho = -0.49$, $p = 0.016$, $\rho = -0.494$, $p = 0.014$; $\rho = -0.708$, $p < 0.001$, respectively) (Spearman's rho test, Table 3, Fig. 3).

4. Discussion

In this study, we assess the occurrence and concentration of BPs and PAEs in striped dolphins that stranded in the Western Mediterranean Sea across the 30-year period between 1990 and 2018, and provide the first record, to our knowledge, of the presence of a number of these compounds in the muscular tissue of cetaceans. We discuss our results in light of the scarce literature available on the concentration of these contaminants in the marine environment, and specifically in marine mammals. In the published literature, summarized in Table 4, these pollutants are assessed in cetaceans or marine mammals through a variety of tissues, including muscle, liver, blubber, skin, plasma and urine, which only allows a speculative discussion of the different values observed by other studies. Taking the limitations implied by the relatively low number of samples analysed into account, we also consider the potential influence of factors liable of influencing the detected concentrations, such as the individual sex, maturation stage, and year of death. As information regarding the cause of death was not available for all individuals, and most of the sampled dolphins were killed by the morbillivirus epizootic, results could not be related to any potential toxic or detrimental effect to the health status of dolphins.

4.1. BP concentrations

Since its commercialization in the 1950s, BPA has been the most widely used BP during decades (Staples et al., 1998). However, after several studies alerted about its adverse effects on reproduction, development, and neural networks, as well as on the cardiovascular, metabolic, and immune systems of living organisms, its use was discontinued for most applications in the European Union (EC, 2011/8/EU), as well as in Canada, United States, Japan, Brazil, China and Malaysia (Akhbarizadeh et al., 2020). Industry soon after began to develop alternative compounds to replace it, and in 2016, 16 BP analogues were industrially applied, of which BPF, BPS and BPAF were the most widely used (Chen et al., 2016). Due to their increased production and use, several of these compounds were soon detected in foodstuff, household dust, and PCPs, and high concentrations were detected in both the environment and human tissues (Pelch et al., 2019; Park et al., 2020).

In this study, we detected 6 of the 10 BPs analysed, which, in decreasing order of frequency, were: BPZ, BPE, BPF, BPFL, BPA, BPP, and, in decreasing order of concentration: BPZ, BPE, BPA, BPFL, BPP, BPF. Diet is the main intake route for marine mammals, which can ingest BPs either indirectly through contaminated prey (*i.e.*, fish or molluscs) and water, or directly from accidently ingested pieces of plastics, microplastics, or other materials that may release BPs during their degradation (Nehring et al., 2017). In smaller proportions, marine mammals may also be exposed to these contaminants through the

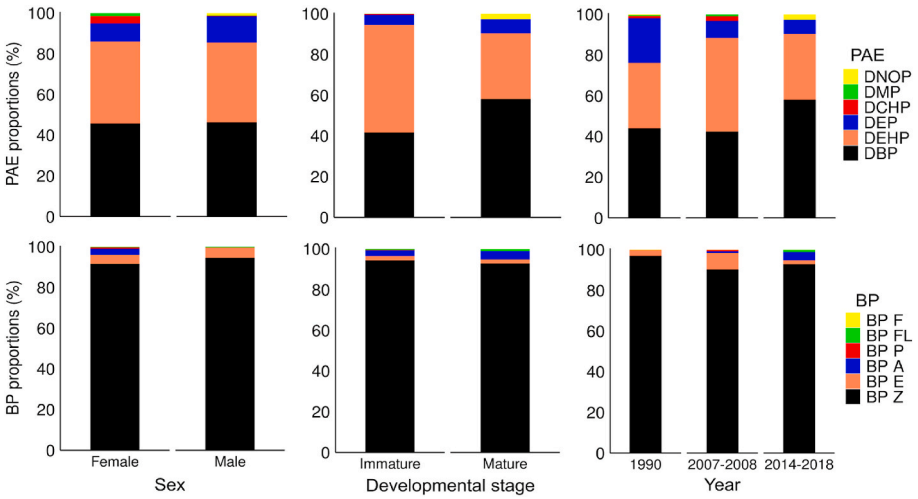

Fig. 2. Relative contribution of the detected BP and PAE compounds split by sex, maturation stage, and sampling period.

Table 3
Results of the statistic tests performed to compare the concentrations of BPs and PAEs between males and females, mature and immature individuals, and the three sampling periods. The number of samples considered for each test is indicated in brackets. K–W refers to Kruskall-Wallis test. Significant results ($p < 0.05$) are marked with an asterisk (*).

	Sex (24 samples)		Maturation Stage (15 samples)		Sampling period (24 samples)		
	K–W chi-squared	*p*-value	K–W chi-squared	*p*-value	Spearmans' S	Spearmans' rho	*p*-value
BPA	2.087	0.1486	0.15873	0.6903	1910.3	0.169422	0.4287
BPE	0.27047	0.603	3.5619	0.05912	3422.3	−0.487936	0.01557*
BPF	0.65906	0.4169	3.0247	0.08201	3022	−0.3139107	0.1352
BPFL	0.15862	0.6904	1.2763	0.2586	1245.2	0.4585894	0.0242*
BPP	1	0.3173	1.5	0.2207	2336.8	−0.01599233	0.9409
BPZ	0.65333	0.4189	2	0.1573	3056	−0.328701	0.1168
ΣBP	0.40333	0.5254	2	0.1573	3007.2	−0.3074647	0.1439
DBP	1.0967	0.295	0.057613	0.8103	2395.2	−0.04140386	0.8477
DCHP	0.4943	0.482	1.5	0.2207	2671.3	−0.1614263	0.4511
DEHP	2.3774	0.1231	0.12963	0.7188	2376.3	−0.03319363	0.8776
DEP	3.4433	0.06351	0.031818	0.8584	3435.8	−0.4938182	0.01419*
DMP	0.14256	0.7057	5.1734	0.02294*	3928.4	−0.7079887	0.0001086*
DNOP	2.087	0.1486	0.66667	0.4142	2292.3	0.003369187	0.9875
ΣPAE	5.07	0.02434*	0	1	2489	−0.08217524	0.7027

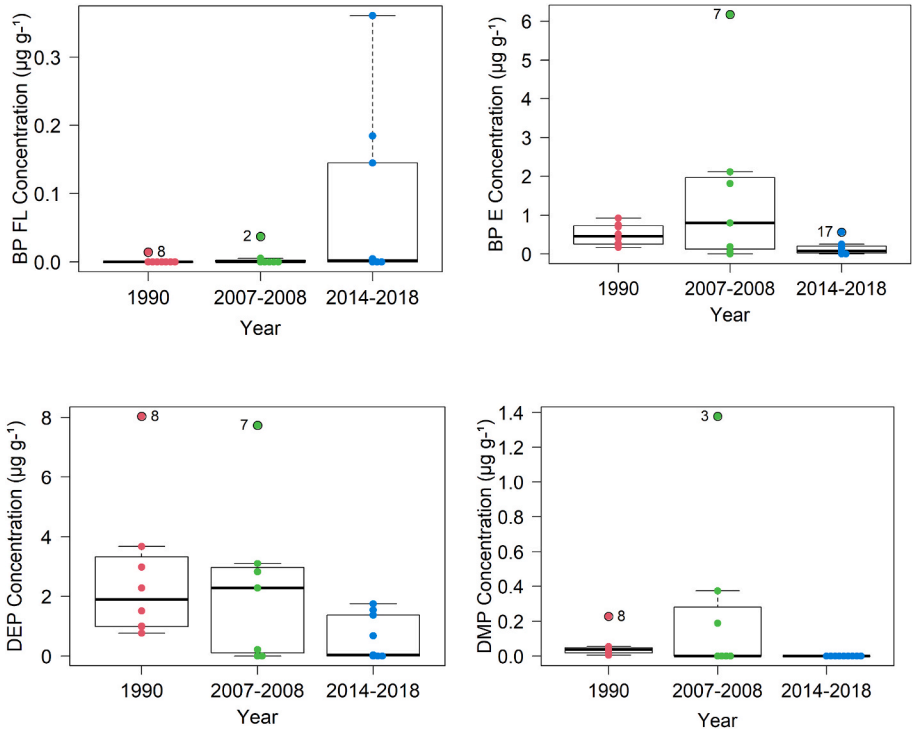

Fig. 3. Boxplots showing the significant correlations between the BPs (BPFL and BPE, top graphs) and PAEs (DEP and DMP, bottom graphs) concentrations detected in samples from adult individuals and the period of sampling. Boxes show the first and the third quartiles, horizontal lines represent the median, and whiskers cover extreme values within the 1.5 IQR value. Outliers are marked as dots.

inhalation of polluted air (Nehring et al., 2017).

According to our results, BPZ was the most common and most concentrated compound (mean 16.06, range 0.12–94.9 µg g^{-1} lw), followed by BPE (mean 0.67, range 0–6.17 µg g^{-1} lw), which was detected in 90% of the samples, at slightly higher concentrations than the other four BP compounds detected. Unfortunately, very little is known about the environmental concentration of both compounds. BPZ is a component widely used in European countries for the manufacture of epoxy resins and polycarbonate plastics, and has been detected in PCP (0.71–0.74 ng g^{-1}), foodstuff (0.03–0.08 µg g^{-1}), soft drinks (0.09 µg L^{-1}) and human biomonitoring samples (0.06 µg L^{-1}), as well as in indoor dust and sludge (at 0.001–0.5, and up to 1.8 ng g^{-1}, respectively, Chen et al., 2016), which may explain its higher concentration in all the analysed samples. On the other hand, BPE is used for polycarbonate and cyanate and epoxy resins, and recent studies have shown that it is commonly detected in source and drinking water (0.83 ng L^{-1}, Zheng et al., 2019), as well as in municipal sewage sludge (0.980 µg g^{-1}, Šauer et al., 2021). Moreover, according to Danzl et al. (2009), BPE in seawater is slightly more resistant to biodegradation than other compounds such as BPA, BPF or BPP, which may justify its presence in 90% of the samples analysed.

The other four BPs were not detected in all the samples, as their lowest concentrations were below the LOQ. Mean and maximum concentrations were below 1 µg g^{-1} lw for all these compounds, except for BPA, which was only detected in three individuals, but whose maximum concentration was one order of magnitude higher than BPP, BPFL and two orders of magnitude higher than BPF. Indeed, although in Europe the use of BPA has been banned from several products, this compound is

Table 4
Concentrations of BP and PAE compounds assessed in the tissues of marine mammal species. All concentrations are expressed in ng g^{-1}, with the exception of those in urine samples, which are expressed in ng mL^{-1}. The matrix in which the compounds analysed, along with the number of samples and the specification on the basis on which concentrations are calculated (dw: dry weight, ww: wet weight, lw: lipid weight) are indicated in the first column; the geographic area of each study, along with the corresponding reference are indicated in the last column.

Species	#samples, matrix	BBP	DBP	DCHP	DEHP	MEHP	DEP	MEP	DMP	DNOP	BPA	BPF	BPS	Area, reference
Fin whale (*Balaenoptera physalus*)	5, Blubber (ww/lw)					58/177								Italy[a,b]
	30/10, skin + blubber biopsies (ww)					55; 40								Mediterranean Sea/Sea of Cortez[c]
	3, skin (dw)				7051	nd								Mediterranean Sea[d]
	6, Blubber (ww)	<10		<10	42		<37			<10				Svalbard[e]
	31, Muscle (dw)		303	<0.1	10		303		8					Iceland[f]
Blue whale (*Balaenoptera musculus*)	7, Blubber (ww)	<10		<10	20		<37			<10				Svalbard[e]
Bowhead whale (*Balaena mysticetus*)	5, Blubber (ww)	<10		<10	n.a		<37			<10				Svalbard[e]
Minke whale (*Balaenoptera acutorostrata*)	2, Liver (ww)	29.7	10.7		86.2		15.1		2.5	6.7				Greenland[g]
Striped dolphin (*Stenella coeruleoalba*)	2, Skin (dw)				21,460	1720								Mediterranean Sea[d]
	5, Muscle		419		514		52				304	101	174	Canaries[h]
	30, Muscle (lw)		7240	190	6850		1620		80	90	290	10		This study
Stenella spp.	5, Blubber (dw)						70				<10			USA[i]
Risso's dolphin (*Grampus griseus*)	1, Skin (dw)				1130	464								Mediterranean Sea[d]
	2, Muscle		552		381		42				163	89	37	Canaries[h]
Bottlenose dolphin (*Tursiops truncatus*)	1, Skin (dw)				26,068	1770								Mediterranean Sea[d]
	2, Muscle		413		783		0				201	110	10	Canaries[h]
	46, Blubber (dw)						4800				50,400			U·S.[i]
	17/51/50,					1.9		5.4						U·S.,[j]
	Urine (ng mL^{-1})					4.57		4.51						U·S.[k, l]
						0.17–76.6								U·S.[m]
Pilot whale (*Globicephala melas*)	3, Liver (ww)	28	15.1		103.6		23.2		2.50	5.6				Faroe[f]
Short-finned pilot whale (*Globicephala macrorhynchus*)	1, Muscle		969		335		0				732	81	12	Canaries[h]
Harbour porpoise (*Phocoena*)	100, Liver (ww)							5.99						Norway[n]
Pygmy sperm whale (Kogia breviceps)	1, Muscle		664		102		0				181	47	213	Canaries[h]
Kogia spp	22, Blubber (dw)						170				1650			U·S.[i]
Fraser's dolphin (*Lagenodelphis hosei*)	1, Muscle		552		330		98				72	67	28	Canaries[h]
White-beaked dolphin (*Lagenorhynchus albirostris*	1, Blubber (dw)						13,800				397,400			U·S.[i]
Melon-headed whale (*Peponocephala electra*)	3, Blubber (dw)						500				<10			U·S.[i]
Polar bear (*Ursus maritimus*)	12, Fat tissue (ww)	<10		<10	n.a.		<37.5			<10				Svalbard[e]
	13, Plasma (ww)					<0.8		<0.8						Svalbard[e]
	2, Liver (ww)	31	12.8		142.6		22.7		51.4	22				Greenland[f]
Ringed seal (*Phoca hispida*)	4, Liver (ww)	128.6	7.3		117.2		21		3.7	7.6				Greenland[f]

[a] Fossi et al (2012).

[b] Fossi et al (2014).
[c] Fossi et al (2016).
[d] Baini et al (2017)(also analysed MBzP, MBP, BBzP, DIOIP).
[e] Routti et al (2021)(also assessed DMPP, DHxP, and DnNP, DnBP, DiBP, DiNP and DiDP in blubber of cetaceans and adipose tissue of polar bear; and MMP, MEOHP, MiBP, MnBP, MBzB, MEHHP in the blood plasma of polar bear).
[f] Garcia-Garin et al (2022).
[g] Vorkamp et al (2004).
[h] Montoto-Martinez et al. (2021)
[i] Page-Karjian et al (2020)(they also analysed muscle samples from Mesoplodon spp, G. griseus and Z. cavirostris for BPA and DEP, which were not detected).
[j] Hart et al (2018)(also analysed MEOHP and MBP).
[k] Hart et al, 2020 (also assessed MBP).
[l] Dziobak et al (2021)(also assessed MBP, MBzP, MiBP, MEOHP, MEHHP, MMP).
[m] Dziobak et al. (2022)
[n] Rian et al (2020)(also assessed mIBP, mBP, PA, mMP, mHxP, mEHHP, mNP, mOP, mEOHP, mHpP, mBzP, mDP).

still widely produced and has been found in surface waters (0.25 μg L^{-1}, Zheng et al., 2019), sewage sludge (0.12–6.50 μg g^{-1}, Šauer et al., 2021), bivalves, holothurians and fish from the Balearic Island, in the Western Mediterranean Sea (0.29; 0.45 and 0.32 μg g^{-1} ww, respectively, Rios-Fuster et al., 2022), samples of herring gull feathers, Baltic grey seal fur, and human hair (0.1, 0.07 and 0.34 μg g^{-1}, respectively, Nehring et al., 2017), as well as in the few cetacean species analysed so far (Page-Karjian et al., 2020, Montoto-Martínez et al., 2021), which also included 5 striped dolphins (Table 4). Ozhan and Kocaman (2019) detected BPA levels in the highly anthropized waters of the Black Sea, Bosphorus, and Sea of Marmara in a range of 8.85–14.76 μg L^{-1}. However, BPA is rapidly degraded in seawater (Staples et al., 1998), where it can last only up to 30 days (Kang et al., 2007) and, similarly to other BPs, its excretion rate in mammals is high (Kang et al., 2006), which possibly explains its low presence in the dolphins analysed (*i.e.*, 3 out of 30).

BPFL was detected in almost half of the samples, at lower concentrations than all the previously mentioned compounds. This compound is a novel BPA substitute used in the plastics industry as an organic (fluorinate) synthesis intermediate (Zhang et al., 2021), and extensively applied to synthesize polyesters, epoxy resins, polycarbonates, and in consumer products that are labelled BPA-free (Özkan-Kotiloğlu et al., 2022). Aside from its detection in animal feeds (0.24 ng g^{-1} dw, Wang et al., 2021) and in environmental samples of water bodies and sediments (0.056–0.069 ng L^{-1}, Jin and Zhu, 2016), the information regarding this compound is very limited. However, its increasing use may be the reason of its presence in almost half of the sampled dolphins.

Finally, mean BPP and BPF concentrations were similarly low, but while BPP was detected only in 2 samples (7%), BPF was detected in almost 70% of them. Indeed, BPF is widely applied for the manufacture of lacquers, varnishes, liners, adhesives plastics, and water pipes, as well as in dental sealants, oral prosthetic devices, tissue substitutes and coatings for food packaging (Chen et al., 2016). Both compounds have been detected in foodstuff (*e.g.*, 0.24 μg g^{-1} BPP, and 1.13 μg g^{-1} BPF, respectively, in samples from mustard and ginger, Liao and Kannan, 2013), household dust (up to 2 ng g^{-1} BPP, and up to 1 μg g^{-1} BPF, respectively, Chen et al., 2016), and PCPs (0.79–0.99 ng g^{-1} BPP, and 0.820.99 μg g^{-1} BPF, respectively, Chen et al., 2016), and BPF has also been detected in sewage sludge (0–3.1 μg g^{-1}, Šauer et al., 2021), surface water (0.2 μg L^{-1}, Chen et al., 2016, 0.002 μg L^{-1}, Zheng et al., 2019; 0–0.075 μg L^{-1}, Šauer et al., 2021), marine fish (0.005 μg g^{-1} ww, 0.001 μg g^{-1} dw, Akhbarizadeh et al., 2020), in bivalves, holothurians and fish in the Cabrera archipelago, not far from our sampling area (0.29, 0.1 and 0.1 μg g^{-1} ww, respectively, Rios-Fuster et al., 2022) and in the cetacean species analysed by Montoto-Martínez et al. (2021, Table 4). According to Danzl et al. (2009), BPF in seawater is more biodegradable than BPP, which may explain its lower concentrations, while its higher frequency of detection may be justified by its wider use and applications. On the other hand, BPP is one of the few BP analogues with a log K_{ow} value higher than 5 (Chen et al., 2016), which indicates a tendency to accumulate in tissues, and thus be a liable factor contributing to the relatively higher concentration found in the two samples where it was detected.

The scarcity of literature regarding environmental concentrations of BP compounds, especially in the Mediterranean waters, as well as the almost totally lacking data on their concentration in marine wildlife, and particularly cetaceans, prevents any comparison or further speculation on the environmental factors determining the concentrations detected. Furthermore, the variety of tissues analysed within the available studies on marine mammals, only allows a qualitative comparison between the concentrations detected in the different cetacean species or geographical regions. However, even at low concentrations, the presence of several BP compounds in often a large proportion of the individuals analysed indicates that Mediterranean dolphins are somehow exposed to these contaminants. Some of the BPs detected in the muscle of striped dolphins were also detected in the Mediterranean waters, and bivalve, holothurians, and fish (Errico et al., 2017; Ozhan and Kocaman, 2019; Rios-Fuster et al., 2022) from the NW Mediterranean Sea. Interestingly, the concentrations found by these authors were generally higher than those found here. The scattered nature of these data and the different measurement methods applied prevent from assessing the potential occurrence of bioconentration or biomagnification of these pollutants. However, despite tissue levels of pollutants may vary depending on their chemical properties and the species/individual metabolism, the presence of BPs in the dolphin tissues can only be attributed to the pollution of the Mediterranean seawater, either from plastic waste, industrial and domestic effluents, landfill wastes, and/or atmospheric deposition.

4.2. PAE concentrations

DEHP was the first PAE to be synthesized, in the 1930s, for its application as a plasticizer for the newly developed hard PVC (Graham, 1973). Since then, the industry of PAEs grew and diversified along with their applications, which range from home furnishings to transportation, construction, apparel, food, PCP, and the medical industry (Graham, 1973). However, research demonstrated that also PAEs can leach from plastics to the environment and that the exposure to these chemicals can produce toxic effects (Warner and Flaws, 2018). Several PAE compounds, such as DEHP, DBP and DIBP, have been included as hazardous for the environment in the European REACH regulation to protect human health from chemical risks (EU, 1907/2006), and their use has been banned in the EU from a number of applications (Net et al., 2015). They have also been included, along with a few others, in the list of priority hazardous pollutants in China and the USA (CPSC, 2018), and are already subject to some restrictions in the USA. Although the use of PAE has declined, they still make up over 55% of world plasticizers, which are consumed at a growing rate of 3.5% per year (IHSMarkit, 2021) and are thus expected to end up in large quantities in the marine environment.

The analysis of PAEs is challenging, because the sample manipulation and the use of organic solvent may lead to possible contamination of the samples and/or of the laboratory environment (Panio et al., 2020). In this study, we detected 6 of the 13 PAEs analysed, which, in decreasing order of frequency, were: DEP, DBP, DEHP, DMP, DCHP,

DNOP, and, in decreasing order of concentration: DBP, DEHP, DEP, DCHP, DNOP, DMP. Marine mammals are exposed to PAEs mainly through the ingestion of materials that may release these compounds once they are made bioavailable by digestive surfactants (Teuten et al., 2007), or through contaminated food, water and air. However, as PAEs are rapidly degraded in the environment (Xie et al., 2007) and metabolized by living organisms (Mackintosh et al., 2004), and they do not appear to biomagnify in aquatic food webs (Mackintosh et al., 2004; Routti et al., 2021), exposure through prey ingestion is expected to be limited (Hart et al., 2020).

In the NW Mediterranean Sea, PAE concentrations have been found to range from 100 to 527 ng L^{-1} in seawater, from 12 to 610 ng g^{-1} dw in sediment, and from 0.9 to 47 μg g^{-1} dw in zooplankton (Schmidt et al., 2021). Consistently with Garcia-Garin et al. (2022) and Montoto-Martínez et al. (2021), the only two studies assessing PAEs in cetacean muscle, our results showed a high variability of the overall individual PAE concentrations, and identified DEHP, DEP and DBP as the most common and most concentrated compounds. Indeed, these compounds are among the most frequently detected PAEs in surface waters (Net et al., 2015; Hart et al., 2020).

DEHP has been detected in the Mediterranean waters of the Gulf of Marseille at concentrations ranging from 15.8 to 923.8 ng L^{-1} (Paluselli et al., 2018), and was the more abundant PAE compound observed in the surface sediments across the Gulf of Lion (Alkan et al., 2021). It was detected in the gonads of sea urchins from Sardinia (17 ng g^{-1}, Raguso et al., 2022), in bivalves, holothurians and fish from the Balearic Islands (mean 2.58, 1.48 and 0.88 μg g^{-1} ww, respectively, Rios-Fuster et al., 2022) and in biopsies taken from cetaceans (including two striped dolphins) in the Pelagos Sanctuary (Baini et al., 2017), where high concentrations of this compound and its metabolites were also detected in marine neuston and plankton samples (Fossi et al., 2012; Baini et al., 2017). DEHP was also detected in the cetacean samples analysed by Vorkamp et al. (2004), Routti et al. (2021), and Montoto-Martínez et al. (2021) in the North Atlantic Ocean (Table 4). As this compound is the most widely used to increase flexibility of plastics (especially PVC), and in 2015 it represented over 35% of the global plasticizer market (Routti et al., 2021), it is also the most studied, along with its metabolites. Given that DEHP has low solubility in water and preferentially partitions to suspended particles and sediments, it is prone to bioaccumulate in lipid-rich tissues and to biomagnify along marine food webs, and the main exposure for marine mammals happens through the food (Dziobak et al., 2021; Routti et al., 2021). These combined factors may explain why this compound was detected at the highest concentrations in our samples.

On the other hand, studies on low molecular weight PAEs, such as DBP and DEP, in the tissues of aquatic organisms are scarcer. Indeed, these compounds have been reported to accumulate at low level in aquatic species (Net et al., 2015), and their half-life is short both in the marine environment (*i.e.*, over 90% degradation within a week, Staples et al., 1997) and in fish tissues (Net et al., 2015). DEP was detected in the waters of Marseille Bay at concentrations ranging from 3.3 to 50 ng L^{-1} (Paluselli et al., 2018), in a small proportion of sediment samples from the Gulf of Lion (Alkan et al., 2021), in bivalves, holothurians and fish from the Balearic Islands (0.54, 0.49 and 0.17 μg g^{-1} ww, respectively, Rios-Fuster et al., 2022), in 40% of the samples of cetacean muscle analysed by Montoto-Martínez et al. (2021), as well as in the tissues of the dolphins analysed by Page-Karjian et al. (2020) and in the muscle of the fin whales analysed by Garcia-Garin et al. (2022). DBP was detected in the gonads of sea urchins from Sardinia (10 ng g^{-1}, Raguso et al., 2022), in bivalves, holothurians and fish from the Balearic Islands (0.78, 1.24, 0.72 μg g^{-1} ww, respectively, Rios-Fuster et al., 2022), and in the samples of cetacean muscle analysed by Montoto-Martínez et al. (2021) and Garcia-Garin et al. (2022) (Table 4). The concentrations found in these studies were of comparable order of magnitude as those we detected, despite not all the cited studies analysed the same tissues, which prevents a rigorous comparison of concentrations, and the frequency of detection varied among studies and species, probably indicating that, while the metabolism of this compound is similar among cetacean species, its level of exposure varies between geographical areas. Its metabolite, MEP, was also detected in the samples of dolphin urine analysed by Hart et al. (2018, 2020) and in the liver of harbour porpoises (Rian et al., 2020, Table 4).

DMP is also a low molecular weight PAE, which is used, along with DBP and DEP, as a component of industrial solvents, adhesives, waxes, inks, insecticides, PCPs and pharmaceutical products (Net et al., 2015). This compound was detected in the waters of the Marseille Bay at concentrations ranging between 0.8 and 11.9 ng L^{-1} (Paluselli et al., 2018) and in the sediments of the Gulf of Lion (Alkan et al., 2021). We detected this compound in half of our samples, at very low concentrations, similar to those detected in the liver of ringed seals and polar bears by Vorkamp et al. (2004), and in the muscle of fin whales by Garcia-Garin et al. (2022), who observed it in a higher proportion of samples (Table 4). Rian et al. (2020) also detected the presence of its metabolite, mMP, in the liver of 69% of the 100 harbour porpoises they analysed. The apparent lower prevalence of this compound in our and other Mediterranean samples, as compared to those from other areas, is likely related to different rates of DMP deposition in the Mediterranean Sea than in the Atlantic Ocean, which could be the result of lower rates of production and use in the countries bordering the Mediterranean Sea.

Paluselli et al. (2018) highlighted that the origin and aging of plastic materials may affect the concentration of PAEs in both the seawater and the guts of marine organisms. Moreover, while compounds like DEHP are denser than seawater and thus subject to sinking, phthalates can also leach from positively buoyant polymers such as polyethylene (PE), polypropylene (PP), and polystyrene (PS) (Paluselli et al., 2019). Thus, the highly variable concentrations detected, and the variability found among studies may not only derive from different environmental deposition rates among compounds, but also from different feeding habits of the cetacean species or of the individuals analysed (*i.e.*, pelagic vs benthic), along with the intrinsic differences related to the assessment of these pollutants in different tissues.

Finally, DCHP and DNOP were only detected in 4 and 2 dolphins, respectively, at lower concentrations than most other compounds. To our knowledge, the only study reporting these compounds in a cetacean tissue is that from Garcia-Garin et al. (2022), which detected DCHP in one of the fin whale muscle samples analysed, while this compound was below the limit of quantifications in the marine mammal samples analysed by Routti et al. (2021) (Table 4). This result might indicate that the exposure to these contaminants in the marine environment is relatively low, but the scarce literature available prevents from relating the levels found to the local uses and production rates.

4.3. *Influence of biological traits*

4.3.1. *Sex*

None of the single BP or PAE compounds analysed was detected at significantly different concentrations in samples from adult males and females. This result is consistent with the few publications analysing these compounds in mammals of different sex, including marine mammals and clinical studies in humans. Published research is consistent in stating that these compounds do not bioaccumulate in tissues; on the contrary, they are largely excreted through the urine, faeces, bile, hair or fur (Kang et al., 2006; Chen et al., 2016; Nehring et al., 2017). Dziobak et al. (2021) and Rian et al. (2020) also showed that the concentrations of phthalate metabolites in the urine and liver of odontocete species do not differ between sexes. However, the metabolism of each compound may vary according to its chemical characteristics, as well as to individual variables and habits like the diet (Akhbarizadeh et al., 2020). In humans, diet, lifestyle, and other individual habits, were proven to be the main factors determining different metabolite concentrations in males and females (*e.g.*, Hartmann et al., 2015; Huang et al., 2015; Silva et al., 2004). Moreover, the metabolism of female mammals often differs

from that of males as a consequence of their hormone cycle, pregnancy, and lactation, which can affect the concentration of contaminants in their tissues (Aguilar et al., 1999). Indeed, laboratory studies show that female rats metabolize BPA faster than males, and different BPA concentrations have been found in the human serum, as a consequence of differences in the androgen-related metabolism (Kang et al., 2007). These factors may also explain why, although the concentration of none of the compounds was significantly different between sexes, the summation of all PAE compound concentrations was overall higher in samples from males than in those from female dolphins. However, given the limited number of samples used to perform this analysis, this result is to be interpreted with caution.

4.3.2. *Maturation stage*

In contrast with certain organic compounds such as PCBs and chlorinated pesticides that show age-related accumulation in cetaceans (*e.g.*, Tanabe et al., 1987), neither BPs nor PAEs tend to bioaccumulate in animal tissues. Indeed, most of the few studies that assessed potential variations of these compounds with the size or age of marine mammals did not detect any specific trend (*e.g.*, Garcia-Garin et al., 2022, Montoto-Martínez et al., 2021). Our results showed no significant difference between sexually mature and immature dolphins, with the exception of DMP, whose concentrations were higher in samples from immature individuals. Indeed, out of the 15 samples analysed from the 2014–2018 period, this compound was only detected in three immature females, while its concentration was below the LOQ in all the remaining samples from this period. Although the statistical significance of the test is likely weak due to the limited number of samples, other authors have shown that adult mammals tend to have a more efficient metabolism of some contaminants than immature specimens. Indeed, Rian et al. (2020) found that the concentration of a common metabolite of PAE, the phthalic acid (PA), decreased with body length in dolphins, and Hart et al. (2020) found that mean concentrations of the overall PAE analysed and of MEHP were higher in calves than in adult dolphins, possibly reflecting a more efficient biotransformation process of these compounds in adult individuals. Maternal transfer during pregnancy and through lactation may also increase pollutant concentrations in newborn or calf mammals (*e.g.*, Borrell et al., 1995; Addison and Brodie, 1977; Borrell and Aguilar, 2005; Frouin et al., 2012; Barbosa et al., 2018); however, this phenomenon has only been reported for human milk and the more lipophilic phthalate diesters and metabolites, such as DEHP/MEHP, while information on this regard for marine mammals is absent. As both BPs and PAEs are rapidly metabolized and do not bioaccumulate in tissues, we believe unlikely that this process is relevant to explain our results. Rather, the exposure to chemicals between adult and immature dolphins may be influenced by dissimilarities in their diet, physiology and/or activity levels, as suggested by Hart et al. (2018) and Rian et al. (2020).

4.4. *Influence of year of death*

The increased demand of plastic, and plastic-related materials, has led the production of plastic additives such as BP and PAEs to raise exponentially during the past decades (Net et al., 2015). Indeed, PAEs production reached 8 million tons in 2011, and in 2020 PAEs made up 55% of the world consumption of plasticizers (IHSMarkit, 2021). Given such a wider production, a higher amount of these compounds is expected to reach the seas, either directly from spills during the production process, or in the form of leachates dispersed from the large quantities of plastic or plastic-related items that increasingly pollute the seas (Jambeck et al., 2015). However, the high liability of these compounds limits their environmental persistence, and, indeed, according to several authors, atmospheric PAE concentration in the North Atlantic did not change substantially from the 1970s (Giam et al., 1978; Atlas and Giam, 1981; Bohlin-Nizzetto et al., 2018). Consistently, Garcia-Garin et al. (2022) did not detect any significant temporal trend between 1986 and 2015 in the concentration of PAE compounds in samples of fin whale muscle.

Although our temporal analyses were based only on 24 samples and thus the observed trends must be interpreted with caution, in line with the above findings, the concentrations of most compounds did not vary significantly during the three periods (1990, 2007–2008 and 2014–2018), with the exception of two BP and two PAE compounds. Interestingly, the concentration of three (BPE, DEP, DMP) compounds showed a significant decreasing temporal trend, while concentrations of BPFL showed a significant increase in the most recent samples. The concentrations of BPFL were higher than the LOQ only in one sample from the 90s, and in two samples from the 2007–2008 period, while they were above the limit in most of samples from the 2014–2018 period. This result might be explained by the relative novelty of this compound, which only began to be produced and used massively as a replacement of BPA in the so-called "BPA-free" products (Özkan-Kotiloğlu et al., 2022), once the use of BPA as additive was banned in numerous products in several countries and in the EU in the early 2010s.

BPE, in turn, was detected in 90% of samples, independently of the period, but its concentrations showed a slightly decreasing trend, with the lowest concentrations occurring in the most recent samples and the peak of concentrations detected in two samples from the 2007–2008 period. The slightly higher persistence of this compound (Danzl et al., 2009) likely justifies its detection in most samples, however, as little is known on its trends of production and use, we may only assume that this compound, commonly used in cyanate resins (Zheng et al., 2019), has been recently replaced by other analogues and is reaching the Mediterranean waters in reducing quantities.

Similarly, DMP was detected, although at very low concentrations, in all samples from the 1990s, at slightly higher concentrations in only three samples from the 2007–2008 period, and again at very low concentrations in only three samples from immature individuals from the 2014–2018 period. Finally, DEP was detected in a consistent proportion of the individuals analysed from the three periods, but its concentrations were substantially and significantly lower in the samples from the 2014–2018 period than in those from the two earlier periods. Both compounds have been included in the lists of priority pollutants in USA, EU and China (Net et al., 2015), which may imply that the rates at which they are produced and used are every time more restricted. Indeed, while the market of high molecular weight PAEs has kept generally steady in Europe, that of low molecular weight PAEs such as DMP and DEP has been decreasing since the beginning of the 2000s: in 2017, low molecular weight PAEs still represented 40% of the global plasticizers market, but only 11% of the European one (IHSMarkit, 2021). The limited number of samples hampers a proper interpretation of results also in this case. However, given the low persistence of these compounds in the marine environment, in contrast to the behaviour of persistent organic pollutants that exhibit very slow decline in concentrations in cetacean tissues (Loganathan et al., 1990), the lower frequency and concentrations observed in the most recent samples might reflect a recent shift in the commercial production of these PAEs.

Indeed, our sampling period spans almost three decades, during which there have been significant changes in the production and use of these chemicals. However, the observed temporal variability may also be the result of the degradation of certain compounds (biodegradation or photodegradation), while the non-detection of certain other compounds could be related to the presence of possible unknown metabolites.

4.5. *Implications for the mediterranean striped dolphin population*

The Mediterranean striped dolphin is currently classified by the IUCN red list under the "least concern" category (IUCN, 2019). However, this population has experimented a series of mortality events, during 1990–1992, and 2006–2007, related with morbillivirus epizootics (Aguilar and Raga, 1993; Domingo et al., 1990, 1995; Keck et al.,

2010), and its individuals are known to carry in their tissues extremely high levels of pollutants (Aguilar and Borrell, 1994; Aguilar, 2000). While, in principle, there should be no direct correlation between contaminant burden and morbillivirus, it might be possible that individuals suffering from heavy contamination have a weaker immune system and thus are more susceptible to contract a virus. Unfortunately, this possibility could not be addressed here; however, the concentrations we detected were relatively low and most probably did not have any health effect on the dolphins. Despite the tissue concentration of organochlorine pollutants and mercury in striped dolphins have shown decreasing trends (Aguilar and Borrell, 2005; Borrell et al., 2014), and the concentration of plastics ingested by Mediterranean striped dolphins is generally low (Novillo et al., 2020), the main threat for this species in the Mediterranean is still associated with marine pollution (IUCN, 2019). The extreme anthropization of the basin causes these animals to be constantly and increasingly exposed to a mixture of pollutants and subject to a variety of stress factors (Marsili et al., 2018; Aznar-Alemany et al., 2021). Although the detected concentrations do not appear to be concerningly high, and neither BPs nor PAEs seem to bioaccumulate in the tissues of dolphins, the long-term exposure to these chemicals, combined with other multiple stressors, may potentially produce adverse effects to long living animals such as cetaceans (Hart et al., 2020, Dziobak et al., 2021).

5. Conclusions

Our results provide the first assessment of a number of BP analogues and PAE compounds in the muscle of an odontocete cetacean, and indicate that Mediterranean dolphins are exposed to these pollutants. While no significant relation was detected between the concentration of these compounds and the dolphins' biological traits (sex and sexual maturation), some temporal trends emerged. The limited number of samples available (n = 30) allows only a partial interpretation of results, however, the observed trends might reflect a shift in the commercial production and use of some BP and PAE compounds, and the detected values contribute to enlarge the limited knowledge base on their levels in the marine fauna. Given the increasing rate of production and use of these compounds, and the scarce information regarding their presence in the marine environment, it is of utterly importance to continue investigating their levels in sensitive marine fauna like cetaceans, along with their sources, intake routes, metabolism, and potential long-term effects.

Credit author statement

Morgana Vighi: Conceptualization, Investigation, Writing - Original Draft, Visualization, Supervision; Asunción Borrell: Conceptualization, Methodology, Resources, Writing - Review & Editing, Supervision; Wissam Sahyoun: Methodology, Formal analysis; Sopheak Net: Methodology, Resources, Writing - Review & Editing, Supervision; Alex Aguilar: Conceptualization, Resources, Writing - Review & Editing, Supervision; Baghdad Ouddane: Methodology, Resources; Odei Garcia-Garin: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - Review & Editing, Visualization, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interestsOdei Garcia-Garin reports financial support was provided by European Social Fund.

Data availability

Data will be made available on request.

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