



Treball Final de Grau

Study of solubility of mannitol in different organic solvents.

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Las cosas difíciles requieren un largo tiempo, las imposibles un poco más.

André A. Jackson

Primero de todo quería agradecer eternamente a mi tutor Rodrigo Soto, por toda la ayuda, el apoyo y la confianza depositada en mi a lo largo de todo este estudio.

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SUMMARY

Biomass plays a significant role in the renewable energy sector, and sorbitol and mannitol are associated with biomass through their production, use as carbon sources, and modification of biomass-based materials. They can be produced from biomass sources such as corn, wheat, and other plant materials. They can also serve as carbon sources for microorganisms involved in biomass conversion or be used to modify the properties of biomass-based materials.

Both sorbitol and mannitol, as sugar alcohols, have distinct properties and applications. Sorbitol is highly hygroscopic and more soluble in water, while mannitol, a crystalline solid produced by the hydrogenation of fructose, is non-hygroscopic and less soluble.

Through the solubility experiments conducted in this study, the information from the literature has been corroborated, showing that mannitol, despite being an isomer of sorbitol, has lower solubility ranges. It is also demonstrated that mannitol's solubility progressively increases in all solvents as the temperature rises.

The solubility range obtained is 10^{-4} , except for water, which has a range of 10^{-2} . This significant difference in solubility is due to water's ability to form hydrogen bonds with mannitol. As corroborated by the literature, water is the solvent with the Hildebrand parameter closest to that of mannitol.

The range of enthalpies obtained is 28-41 kJ/mol, with a slight deviation from the expected values for MIBK and dioxane.

Regarding the polymorphs of sorbitol, analyzing the commercial sample and all samples from the experiments, it is concluded that mannitol remains in its most stable polymorph, beta.

Overall, the mass ratio solubility decreases at the higher temperature (340K) in order: $H_2O > MeOH > EtOH > TBA > 1-Prop > 2-Prop > ButOH > 2-ButOH > MIBK > Dioxane > Butanone > Acetone$.

Simultaneously, the solubility results have been more favorable for water, followed by polar protic solvents.

RESUM

La biomassa juga un paper significatiu en el sector de l'energia renovable, i el sorbitol i el mannitol estan relacionats amb la biomassa a través de la seva producció, ús com a fonts de carboni i modificació de materials basats en biomassa. Es poden produir a partir de fonts de biomassa com el blat de moro i altres materials vegetals. També poden servir com a fonts de carboni per a microorganismes involucrats en la conversió de biomassa o per a modificar les propietats de materials basats en biomassa.

Tots dos tenen propietats i aplicacions diferents. El sorbitol és altament higroscòpic i més soluble en aigua, mentre que el mannitol, sòlid cristal·lí que es produeix mitjançant hidrogenació de la fructosa, no és higroscòpic i és menys soluble.

Gràcies als experiments realitzats en aquest estudi de solubilitat, s'ha pogut corroborar la informació de la literatura, i que el mannitol, tot i ser isòmer del sorbitol, té uns rangs de solubilitat més baixos. També es demostra que la solubilitat del mannitol augmenta progressivament en tots els dissolvents a mesura que s'incrementa la temperatura.

El rang de solubilitat dels dissolvents és de 10^{-4} , excepte per a l'aigua, que té un rang de 10^{-2} . Aquesta diferència tan abismal en la solubilitat es deu a la capacitat de l'aigua de formar ponts d'hidrogen amb el mannitol. Com s'ha corroborat en la literatura, l'aigua és el dissolvent amb el paràmetre de Hildebrand més proper al del mannitol.

El rang d'entalpies obtingudes és de 28-41 kJ/mol, amb una lleugera desviació respecte als valors esperats per al MIBK i el dioxà.

Pel que fa als polimorfs del sorbitol, analitzant la mostra comercial i totes les mostres de tots els experiments, es conclou que el mannitol segueix sent en el seu polimorf més estable, la beta.

En general, la relació de solubilitat en massa disminueix a temperatures més altes (340K) en l'ordre següent: H₂O > MeOH > EtOH > TBA > 1-Prop > 2-Prop > ButOH > 2-ButOH > MIBK > Dioxà > Butanona > Acetona.

Paral·lelament, els resultats de solubilitat han estat més favorables per a l'aigua en primer lloc, seguit dels dissolvents protònics polars.

1.INTRODUCTION

1.1 THE ROLE OF BIOMASS IN THE NEAR FUTURE

Many entities and organizations around the state predict that the production of energy using biomass plays an important role in the environment nowadays. Numerous countries are promoting the use of biomass for the energy system and pushing the development of knowledge and technology needed. The world biggest economies are concerned of the actual situation, and because of that there is a global agreement fixing that the renewable energies must replace the use of fossil combustible as soon as possible because of the climatical change.

Biomass pretreatment processes are crucial for separating the major components of lignocellulosic biomass [1], allowing for their efficient utilization and value addition. Cellulose, the most abundant biopolymer, has received significant attention for producing biofuels, particularly through the production of 5-(hydroxymethyl)furfural (HMF) from sugars and polymeric carbohydrates under acid catalysis. Various biomass sources can be used, and acid catalysts are commonly employed, although challenges such as the formation of humin and the purification of HMF exist. Alternative reaction media and solvent systems have been explored, but further optimization is needed. Additionally, furfural (FF) and levulinic acid (LA) can be produced from pentose sugars and furfuryl alcohol (FAL), respectively. The synthesis of LA directly from cellulose without isolating HMF is advantageous.

However, the production of LA from aqueous reaction mixtures for fuel purposes is energy intensive.

Biomass covers a whole heterogeneous set of organic materials, both by their origin. In the energy context, the term of biomass is used to describe renewable energy source based on the use of organic matter formed by biological pathway in the immediate past or products derived from it. [2]

There are 3 different types of biomasses, described below:

- Solid biomass: It has a thermal and electrical use of organic matter of animal and vegetable origin, such as energy crops (those in which cultivated species have as a specific use the energy production) residues generated in pruning of vineyards and fruit trees generally, and crop residues in winter.
- Biogas: Obtained by an anaerobic fermentation process of the organic matter produced by bacteria in oxygen free environments. Such degassing of waste can be so landfills or induces in biodigesters.
- Organic fraction of urban solid waste: For this type of waste emphasis is placed on management in the energy production process that is given in four stages:
 - i. -Prevention or reduction of waste production.
 - ii. -Recovery waste through recycling, reuse and collection or any other process that allows the extraction of secondary raw materials.
 - iii. -Use of waste as an energy source.

- iv. -Dumping of waste. The used of solid waste in energy production prevents the generation of gases by substituting fossil fuels and bypassing much methane emissions in landfills.

Mannitol can be related to biomass in several ways. Biomass refers to organic matter derived from living or recently living organisms, and it is a promising source of renewable energy and bioproducts. Sorbitol and mannitol can be related to biomass by the following ways:

- 1) Production from biomass: Sorbitol and mannitol can be produced from various types of biomasses, including corn, wheat, and other plant materials. The process typically involves the enzymatic or chemical conversion of sugars or starches into sorbitol or mannitol.[3]
- 2) Use as carbon sources: Sorbitol and mannitol can be used as carbon sources for the growth of microorganisms that can convert biomass into useful products, such as biofuels or bioplastics. Some microorganisms can metabolize sorbitol or mannitol more efficiently than other sugars, which makes them attractive carbon sources for bioprocessing.[3]
- 3) Modification of biomass properties: Sorbitol and mannitol can be used to modify the properties of biomass-based materials. For example, they can be used as plasticizers to improve the flexibility and durability of bioplastics made from biomass-derived polymers.[4] They can also be used to enhance the solubility or stability of certain types of biomass-based materials.

Mannitol and sorbitol are also products that serve as crucial precursors for the production of various compounds [5], including liquid fuels, bioplastic monomers, and fragrances. They play a vital role in the synthesis and

development of these important substances, contributing to advancements in the fields of energy, sustainable materials, and aromatic compounds.

1.2 SORBITOL AND MANNITOL

Sorbitol is a crystalline substance with a white color, and its molecular formula is $C_6H_{14}O_6$. Its production typically involves using dextrose (glucose) as the starting material, which can be obtained from various raw sources. However, the most used source is dextrose derived from starch, which is a relatively inexpensive and efficient process. Enzyme technologies are utilized in conventional starch processing to yield a high-dextrose content syrup, containing typically 94-96% dextrose on a dry basis. The dextrose is then crystallized out as a monohydrate to increase its purity. Next, it is redissolved in water, and hydrogenated to produce sorbitol. Among the polyols, sorbitol is the most soluble. Although it can crystallize at high concentrations and low temperatures, the resulting crystals are small and not easily recovered from the mother liquor [6].

Mannitol is a crystalline, white compound with the same chemical formula as sorbitol. The production of mannitol can be achieved through various methods, with the most common one involving the hydrogenation of fructose. Fructose can be derived from either starch or sugar, depending on its cost. When an aldo-sugar is hydrogenated, only one product is formed. For example, dextrose is converted into sorbitol, and maltose is converted into maltitol. However, when a keto-sugar, such as fructose, is hydrogenated, two products are formed due to the two possible orientations of the hydroxyl groups on C2 in fructose during hydrogenation reactions [7]. This results in the conversion of $C=O$ to either $H-C-OH$ or $HO-C-H$,

which produces equal amounts of both products by adjusting the pH during hydrogenation under normal reaction conditions. Sorbitol and mannitol differ only in the position of the hydroxyl group on carbon 2 in the molecule and are therefore isomers.

Sorbitol and mannitol are six-carbon, straight-chain polyhydric alcohols, meaning they have more than one hydroxyl group. Both sorbitol and mannitol have six hydroxyl groups and the same molecular formula, $C_6H_{14}O_6$ [8]. They are isomers of one another and have different molecular configurations. The difference between sorbitol and mannitol occurs in the planar orientation of the hydroxyl group on the second carbon atom (Fig. 1). This dissimilarity has a powerful influence and results in an individual set of properties for each isomer.

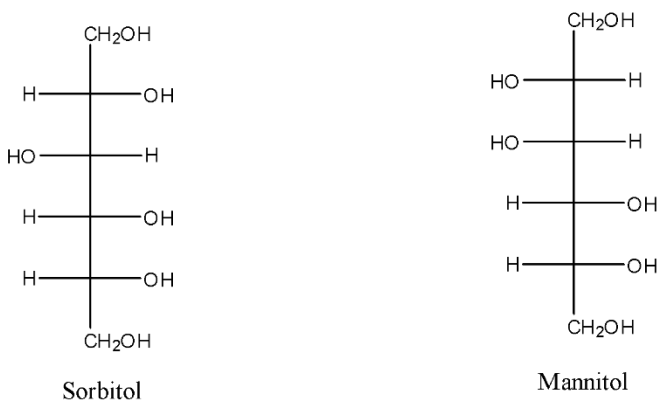


Figure 1. Sorbitol and mannitol structure. [9]

Sorbitol and mannitol are both sugar alcohols that can exist in different polymeric forms, meaning they can have slightly different molecular structures that affect their properties. Mannitol has four different polymorphs (alpha, beta, gamma and delta) and most stable form is the beta form, while sorbitol can exist as well in four

different forms (alpha, beta, gamma, and delta) [8], as well as a glass transition form (E). Each of these forms has different properties, including solubility, melting range, and stability. From the different forms of sorbitol, the gamma form is the most stable [6]. Modern manufacturing techniques predominantly produce sorbitol powder in this form to avoid changes in the food or pharmaceutical product in which the powder is included. During processing and storage, the unstable forms of sorbitol can change to the stable gamma form, which can lead to changes in the final product [10]. While these changes occur slowly, high temperatures can accelerate the process, and all the polymorphs will eventually assume the more stable gamma form.

Despite their structural similarity, sorbitol and mannitol have different properties that lead to specific applications for each product. One of the most significant differences between them is their hygroscopic tendencies. Hygroscopicity refers to the ability of a substance to absorb moisture from the environment. Mannitol is considered non-hygroscopic, while sorbitol is considered highly hygroscopic. Mannitol is the least hygroscopic of the polyols (mannitol and sorbitol), and it does not begin to absorb moisture until the relative humidity is over 90%. In contrast, sorbitol has a greater affinity for water and reaches about 65% humidity [6]. This difference can cause problems during food production and storage, as well as in the storage of the ingredient itself. When sorbitol is used in foods, the absorbed moisture can affect the proper running of presses during tableting. In Europe, where the typical relative humidity is about 65-75%, humidity control is essential in factories that handle sorbitol. Finished products must also be well packed to prevent softening due to moisture absorption.

Another difference between sorbitol and mannitol is their solubility. Solubility is defined as the amount of a solute that can be dissolved in a solvent at a given temperature before becoming saturated. Typically, as the temperature of the solution increases, more solids can be dissolved. If the solution is then cooled, forming a so-called supersaturated solution, the solute will crystallize out. Mannitol is the least soluble polyol (mannitol and sorbitol), with only 22g dissolvable in 100 g of water at 25°C. In contrast, for sorbitol, this figure is 235 g/100 g of water [8].

Being isomers, both mannitol and sorbitol have a six-membered ring structure with hydroxyl groups (-OH) in different positions. This means that both compounds have the ability to form hydrogen bonds with water molecules.

In terms of solubility in water, sorbitol is generally considered more soluble than mannitol. The difference in solubility is due to the greater number of hydroxyl groups in sorbitol and their spatial arrangement, which increases the capacity for hydrogen bond formation with water molecules [8]. This increased capacity for hydrogen bonding in sorbitol facilitates its dissolution and dispersion in water compared to mannitol.

Hydrogen bonds are attractive forces that occur between a hydrogen atom bonded to an electronegative atom (such as oxygen, nitrogen, or fluorine) and another electronegative atom in a different molecule or within the same molecule. In the case of mannitol and sorbitol, the hydroxyl groups (-OH) act as hydrogen bond donors [11], while the oxygen atoms in water molecules act as hydrogen bond acceptors.

When a hydroxyl group of mannitol or sorbitol approaches a water molecule, the positively charged hydrogen atom of the hydroxyl group is attracted to the partially

negative oxygen atom of the water molecule. This electrostatic interaction results in the formation of a hydrogen bond between the hydroxyl group of the sugar alcohol and the water molecule.

The formation of hydrogen bonds allows for strong intermolecular attractions between the sugar alcohols and water, promoting their solubility [12]. In the case of sorbitol, the presence of multiple hydroxyl groups in different positions provides more opportunities for hydrogen bond formation, leading to its higher solubility in water compared to mannitol.

Overall, the ability of mannitol and sorbitol to form hydrogen bonds with water plays a crucial role in their solubility behavior and their interactions with water molecules.

1.3 CHEMICAL PRODUCTION OF MANNITOL

Mannitol is industrially produced by a high-pressure hydrogenation of fructose and glucose solution at a range of temperatures between 120-160°C. In this process the alpha fructose is converted to mannitol and beta fructose to sorbitol. Typically, nickel is used as active metal anchored to catalyst for the hydrogenation reaction in gas phase [13].

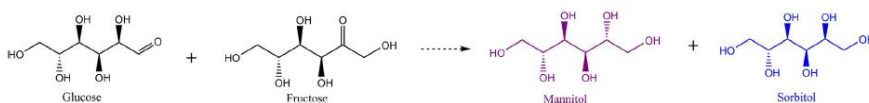


Figure 2. Hydrogenation of fructose to sorbitol and mannitol [9].

Generally, the hydrogenation of a 50/50 mixture of fructose/glucose results in approximately 25% mannitol and 75% sorbitol. This is attributable to the selectivity of nickel catalyst used in the process [14]. Actually, it's extremely difficult to

separate sorbitol and mannitol, the requirement results even higher production costs and decreased yields [10]. The commonly used technique for separating sorbitol and mannitol is crystallization [15], as both have significantly different solubilities in water. By exploiting this solubility difference, the two compounds can be separated effectively. In the crystallization process, a solution containing the mixture of sorbitol and mannitol is cooled under controlled conditions, causing the compounds to crystallize out of the solution at different rates.

Since sorbitol is more soluble in water than mannitol, it remains in the solution to a greater extent. On the other hand, mannitol has lower solubility and tends to crystallize out of the solution more readily. By carefully controlling factors such as temperature, concentration, and cooling rate, it is possible to promote the preferential crystallization of either sorbitol or mannitol. The crystals formed during the cooling process can then be separated from the remaining solution through filtration or centrifugation.

Fructose can be obtained from various sources, such as corn or beet sugar, and is typically converted to glucose using an acid catalyst before hydrogenation. The hydrogenation reaction can be carried out in a batch or continuous process, with typical temperatures ranging from 80 to 180°C and pressures ranging from 1 to 100 atm [16]. The reaction time and catalyst loading can also be adjusted to optimize the yield and selectivity to mannitol. In the first step of the hydrogenation process, fructose is dissolved in water and reacted with a small amount of acid to promote its conversion to glucose. The glucose is then further reacted with hydrogen gas and the catalyst at elevated temperatures and pressures to produce mannitol. The quality of the catalyst is a critical factor in the hydrogenation process. Raney nickel, a fine-grained solid composed mostly of nickel derived from a nickel aluminum

alloy, is a commonly used catalyst due to its high activity and selectivity, but other catalysts such as palladium on carbon or platinum on carbon may also be used. The choice of catalyst will depend on various factors, such as cost, availability, and performance [14].

Mannitol can also be produced by the oxidation of sorbitol [17], which involves the use of oxidizing agents such as nitric acid or hydrogen peroxide. However, this method may result in lower yields and require more complex reaction conditions compared to the hydrogenation of fructose. When mannitol produced by chemical methods is typically of high purity and can be used in various applications, such as pharmaceuticals, food, and personal care products. However, it may be more expensive compared to mannitol produced by biological methods, such as fermentation. [14]. Therefore, the choice of production method will depend on various factors, such as cost, product quality, and sustainability.

1.4 SOLUBILITY OF D-MANNITOL

Mannitol is a sugar alcohol commonly used in various industries, including pharmaceuticals, food, and cosmetics. It is a white, crystalline powder and with a sweet taste [18]. According to the literature, mannitol has a relatively medium solubility in water, of approximately 22 g/100 mL [9], [19] at 25°C. This high solubility makes it a useful excipient in pharmaceutical formulations, where it is often used as a bulking agent, sweetener, or tablet coating material. Mannitol is also soluble in ethanol, methanol, and propylene glycol, but it is insoluble [9] in most non-polar solvents, such as chloroform and ether-like compounds.

Overall, the medium solubility of mannitol in water and other common solvents makes it a useful ingredient in various applications, but its solubility behavior can be complex and may need to be carefully considered in certain formulations. The solubility of mannitol can be affected by several factors, including temperature, pH, and the presence of other solutes. For example, the solubility of mannitol decreases as the temperature decreases. The solubility of mannitol also increases as the pH of the solution becomes more alkaline, and it may form complexes with certain other solutes, such as proteins or salts, which can affect its solubility behavior [20]. In addition to the mentioned factors, there are several other parameters that can affect the solubility of mannitol in different solvents [21], including:

- Particle size and shape: Smaller particles have a greater surface area-to-volume ratio, which allows them to dissolve more quickly and completely than larger particles. This is because a larger particle surface area is in contact with the solvent, which allows for more efficient transfer of the solid into the solution [22]. Additionally, the shape of the particles can also influence their solubility. For example, needle-shaped crystals of mannitol may dissolve more slowly than other crystal habits [23].
- Crystal form: mannitol can exist in different crystal forms, and the solubility of each form can vary. The beta-crystal form is the most stable and is the form typically used in pharmaceutical and food applications. Other crystal forms, such as the alpha and delta forms, are less stable and may be more soluble in water and other solvents. The solubility of mannitol can also be influenced by the presence of impurities in the crystal lattice, which can affect crystal packing and alter the solubility behavior [24].

- Ionic strength: The solubility of mannitol can be influenced by the presence of other ions in the solution. This is due to the formation of ion-pair complexes between mannitol and other ions, which can decrease its solubility in water. The strength of the ionic interaction depends on the charge and size of the ion, as well as the concentration of the ions in the solution [25]. For example, the presence of calcium ions can decrease the solubility of mannitol due to the formation of calcium-mannitol complexes [26].
- pH: The solubility of mannitol can also be influenced by the pH of the solution. Mannitol is more soluble in alkaline solutions than in acidic ones, due to the ionization of the hydroxyl groups on the molecule.
- Polymers: Mannitol can form complexes with certain polymers, e.g. cyclodextrins, affecting its solubility [27], as well as improve its stability and bioavailability [10]. The formation of these complexes depends on the size and shape of the polymer and the mannitol molecule, as well as the concentration and pH of the solution [28].

Understanding these factors and their effects on the solubility of mannitol is crucial for developing effective formulations for various applications such as drug delivery systems, oral suspensions, or parenteral solutions.

2. THEORETICAL BASIS

The use of solubility models is widespread in the pharmaceutical industry, where accurate prediction of solubility behavior is critical for drug development and formulation. These models can also be used in other industries such as food, chemical, and environmental engineering. The ability to predict solubility behavior can help to optimize processes and formulations, reduce costs, and minimize waste [29], and it is essential towards the design of processes such as crystallization. There are several approaches to modeling solubility, including empirical, semi-empirical and robust thermodynamic methods. Empirical models are based solely on experimental data and do not implement knowledge on the subjacent molecular interactions, but these are only applicable for interpolation of solubility data within the explored conditions.

Commonly used a mathematical expression to model the non-linear variation of a physical or chemical property as a function of temperature is as follows [30]:

$$\ln x_{eq} = \frac{C_1}{T^2} + \frac{C_2}{T} + C_3 \quad (1)$$

In this equation " $\ln x_{eq}$ " represent the natural logarithm of the solute molar fraction " x " at equilibrium in each solvent. " T " represents the temperature in Kelvin and the coefficients " C_1, C_2, C_3 " are empirical parameters to determine by fitting the experimental data.

Semi-empirical models, on the other hand, combine experimental data with theoretical considerations to derive predictive equations. A common semi-empirical model used for describing solubility curves is the Apelblat model (Eq. 2). This model has been widely applied in the pharmaceutical industry to describe the solubility behavior of drug compounds in different solvents [31]. The Apelblat model combines both empirical and theoretical approaches, making it useful for a wide range of solutes and solvents. It assumes that the activity coefficient of the solute in the solution is a function of the mole fraction of the solute and solvent in the solution, as well as three adjustable parameters. It has been successfully used to describe the solubility behavior of a wide range of compounds, including drugs, polymers, and natural compounds.

$$\ln x_{eq} = a + \frac{b}{T(K)} + c \ln(T(K)) \quad (2)$$

where, T is the temperature, and A, B and C are constants specific to each solute-solvent system and X_{eq} is the solute molar fraction at equilibrium [32].

Another important semiempirical model is the Buchowski-Ksiazaczak model (Eq.3), also called the λh -model, which includes the parameters λ and h to be estimated and includes the melting temperature (T_m) of the solid form in the mathematical expression used to predict thermodynamic solubility.

$$\ln \left(1 + \lambda \frac{1-x_{eq}}{x_{eq}} \right) = \lambda h \left(\frac{1}{T} - \frac{1}{T_m} \right) \quad (3)$$

According to Buchowski [33], and h are the specific parameters model, to be determinate. Alternatively, λ can be interpreted as the relative deviation of solvent pressure over saturated liquid equilibrated with solid. If a solution has positive deviations from Raoult's law [34], then its λ -values are expected to be positive.

However, if a solution has negative deviations from Raoult's law due to strong non-ideality, non-positive values of λ are inevitable. Furthermore, the model that Buchowski [35] demonstrated revealed that the parameters h and λ parameters remain constant at different temperatures in neat solvents.

3. OBJECTIVES

The main aim of his project is to study the solubility of mannitol in a range of pure organic solvents, including water. Solvents of organic polar protic and polar aprotic nature are selected to delve in the nature of the interactions influencing the solubility. The experimental solubility will be determinate in the range of temperature, 25-65 °C. The following specific objectives are established:

1. To obtain experimental solubility data of mannitol in different organic solvents.
2. To discuss the rank of solubility obtained according to the functional groups of the solvents used determining the solute-solvents interactions.
3. To fit experimental solubility data to different empirical and semi-empirical model equations aiming to obtain expressions able to predict the solid liquid equilibrium composition at different temperatures.
4. To characterize the equilibrated solids in suspension and initial solid by a series of techniques (PXRD, DSC and SEM), to ensure that no polymorphic transformation occurs within the explored conditions and to determine melting point and melting enthalpy of the solid form used.
5. Determine the solid-liquid equilibrium derived thermodynamic state functions, e.g. enthalpy of solution.
6. To compare the obtain result with those available in the literature.

4. EXPERIMENTAL SECTION

4.1 EXPERIMENTAL MATERIALS

Table 1 summarizes some physicochemical properties of the solvents used in the solubility determinations along with those of solid d-mannitol:

Table 1. Properties of solvents used in solubility determination of mannitol [33].

| SOLVENT | MW [g/mol] | T _m [K] | T _b [K] | ρ [g/cm ³] | μ [cP] | δ [MPa] ^{1/2 a} | E _T ^{N b} |
|------------|---------------|-----------------------|-----------------------|---------------------------|-----------|-----------------------------|-------------------------------|
| D-Mannitol | 182,17 | 169 | 300 | 1,51 | 1,3 | 38,5 | - |
| Methanol | 32.04 | 176 | 337.8 | 0.7918 | 0.56 | 29,60 | 0,762 |
| Ethanol | 46.07 | 159.0 | 351.4 | 0.8000 | 1.077 | 26,50 | 0,654 |
| Butanol | 74.12 | 183.3 | 390.8 | 0.8060 | 2.556 | 23,30 | 0,586 |
| 2-Butanol | 74.12 | 158.15 | 367.15 | 0.8534 | 2.556 | 20,70 | 0,590 |
| 1-Propanol | 60.09 | 146.7 | 370.3 | 0.804 | 2.26 | 24,30 | 0,630 |
| 2-Propanol | 60.09 | 184 | 355.8 | 0.7863 | 2.86 | 23,80 | 0,610 |
| Water | 18.02 | 273.15 | 373.15 | 0.997 | 1.00 | 47,8 | 1,00 |
| Acetone | 58.08 | 178.3 | 329.4 | 0.788 | 0.306 | 19,90 | 0,46 |
| TBA | 74.12 | 298 | 355.0 | 0.775 | 3.35 | 21,8 | 0,598 |

| | | | | | | | |
|----------|--------|--------|--------|--------|--------|-------|-------|
| MIBK | 100.16 | 189.15 | 389.15 | 0.802 | 0.7375 | 18,1 | 0,580 |
| Butanone | 72,11 | 187 | 353 | 0.805 | 0.400 | 18,90 | 0,490 |
| Dioxane | 88.1 | 284.9 | 374.2 | 1.0337 | 1.200 | 23,50 | 0,51 |

^a Hildebrand parameters [36]

^b Normalized solvatochromic solvent polarity parameters [41]

4.2 EXPERIMENTAL SET-UP

4.2.1 JACKETED EQUILIBRATION VESSEL

The experimental solubility determinations were performed in a glass jacketed vessel connected to a thermostatic bath filled with water. The vessel jacket was connected to the bath using silicon tubes so that it enables controlling the temperature of the equilibrated solutions. In addition, glass wool was used to isolate the external face of the vessel jacketed to minimize the loss of heat and preventing the UV-vis radiation from sunlight to contact the solution.

The jacketed vessel was placed on a heating/stirring plate and a Teflon-made magnetic stirrer was placed inside the solution to equilibrate. The solutions were stirred for at least 24 h at 500 rpm during the equilibration experiments.

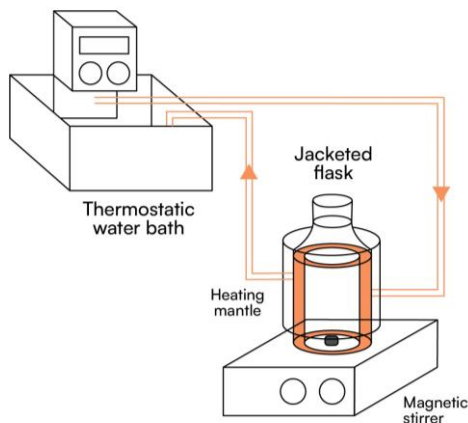


Figure 3. Experimental SET-UP used in the solubility determinations.

4.3 EXPERIMENTAL PROCEDURE

The experimental solubility data of mannitol in different studied organic solvents was determined by gravimetric analysis method. First, a solution of mannitol and the specific solvent with excess visible solids was loaded inside the equilibration vessel. Then the bath temperature was set to desired for the solubility experiments considering the difference between the bath temperature and the real solution temperature (measured by and external temperature probe) and the stirrer was switched on. Once the desired solution temperature was reached, it was confirmed that excess visible solids in suspension were always present, adding extra solid if necessary.

After 24h at the desired temperature under stirring, the agitation was stopped for at least 3 hours to let the solids in suspension to precipitate. Afterwards, samples of 10-15 mL were taken from the supernatant using polypropylene syringes. These samples were filtrated into previously weighed evaporating glass vials through 200

nm PTFE syringe filters. These samples taken were at least triplicated statistical purposes. The vials were weighted again using a precision balance (± 0.00001 g), the cap was removed and left open for the evaporation of the solvent for at least 3 weeks inside a fume hood. If necessary, some vials were placed inside an oven at 60 °C to favor the evaporation of the last amount of those solvents difficult to evaporate. When the evaporation vials were completely dry, they were weighted with the cap.

The solution will be left in these conditions for about 24h to ensure the equilibrium solid liquid. After 24 hours, the stirring is stopped for around two hours, maintaining the temperature. This procedure is to ensure that the two phases of the solution are separated, and the liquid phase can be extracted without particles in suspension.

Once the two phases are separated, the temperature of the solution is measured using a temperature sensor and proceed to sampling between 10-15 mL of solution. Previously, the sample vials are weighted and marked with a unique number. Then it proceeds to extract the solution with a syringe and a 200 nm PTFE filters into the 3 sample vials. Those sample vials are capped and weighted for a second time and after that they are uncapped and left open to evaporate at the room temperature. In case the solvent is not highly volatile, the sample vials are left in a 60°C oven to help them evaporate. When the sample vials are completely dry, they are reweighted with the cap.

After sampling at each temperature, the equilibrium vessel was refilled with the corresponding solvent, the amount of solid was adjusted if necessary and the thermostatic bath temperature was increased by 5 °C, the stirrer switched on again and let to equilibrate for another 24 h. such procedure was repeated until the

maximum explored temperature was reached, typically 65 °C, except for those solvents with lower boiling point, for which 5 °C below the boiling point was considered the maximum temperature explored in the solubility determinations.

Once the sampling at the maximum temperature explored in each solvent had been made, the solution and solids in suspension were filtered using a vacuum filtration setup. The recovered equilibrated solids in suspension were further dried at room temperature in a fume hood for another 24h and properly storage for analytical purposes. Such solids were characterized by PXRD and the diffraction patters obtained compared to those of the initial solid and those of the d-mannitol polymorphs from the Cambridge Crystallographic Data Centre (CCDC) to identify the solid form in the equilibration experiments and to ensure that no solution mediated polymorphic transformations were at play during the runs in each solvent.

4.4 CALCULATIONS AND EVALUATION

The mass ratio solubility of mannitol in each of the studied solvents (C^*) in $g_{\text{solute}}/g_{\text{solvent}}$ was calculated by means of Eq. 4, where m_1 is the mass of the solute and m_2 that of solvent.

$$C^* = \frac{m_1}{m_2} = \frac{m_{\text{vial+cap+solid}} - m_{\text{vial+cap}}}{m_{\text{vial+cap+solution}} - m_{\text{vial+cap+solid}}} \quad (4)$$

From the mass ratio solubility determined, the solubility was also expressed as mole fraction using *Equation 5*, where M_1 and M_2 are the molecular masses of solute and solvent respectively.

$$x_{eq} = \frac{C^* \cdot M_2}{C^* \cdot M_2 + M_1} \quad (5)$$

In addition, the experimental molar fraction solubility obtained were used to estimate the van't Hoff enthalpy change of solution, which simply refers to the temperature dependence of solubility [37] as follows:

$$\frac{\partial \ln x_{eq}}{\partial \ln(1/T)} = - \frac{\Delta_{\text{sol}}^{\text{vH}} H^{\circ}}{R} \quad (6)$$

5. RESULTS

5.1 CHARACTERIZATION OF MANNITOL POLYMORPHS

Figures 4 and 5 show the PXRD diffraction patterns obtained from the mannitol equilibrated solids sampled at the highest temperature evaluated. It is known that mannitol has four polymorphs: alpha, beta, gamma, and delta. The X-ray diffraction analysis provides valuable information about the crystal structure and arrangement of atoms in the mannitol samples. If the diffraction pattern matches one of the known polymorphs of mannitol, it indicates that the sample has maintained its original polymorphic form has not transformed into a different polymorph due to solvent exposure. It is evident that all the samples match the same polymorph, form beta. This can be determined by observing the specific peaks characteristic of each polymorph. For instance, the beta form exhibits a distinctive peak intensity at 18000, which is also present in the samples that were exposed to the solvent, indicating the presence of the beta form. Compared with PXRD available in the literature it can be seen that the beta form of mannitol have the same characteristic peak [38].

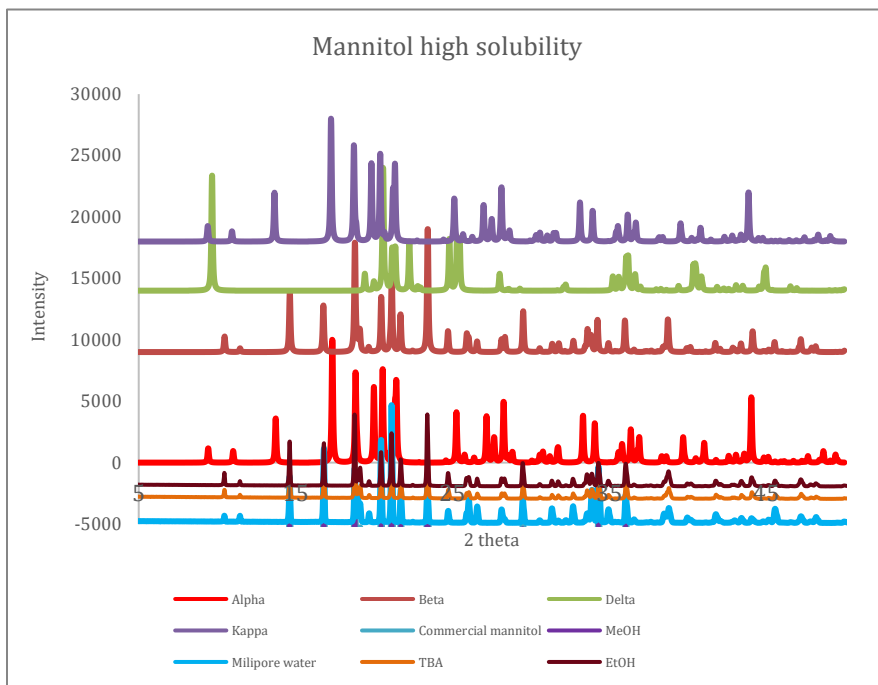


Figure 4. PXRD diffractograms collected from solid mannitol.

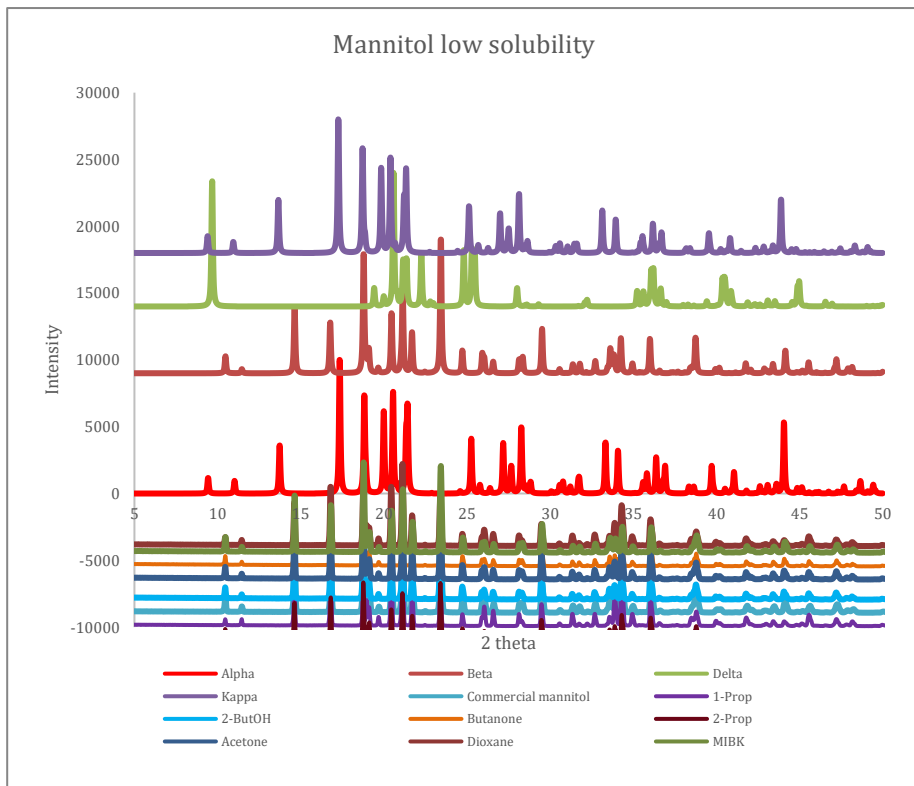


Figure 5. PXRD diffractograms collected from solid mannitol.

To better understand the morphology of mannitol, scanning electron microscopy (SEM) images have been taken, revealing the solid's shape. It is observed that the edges are not well defined, and in some instances, powder-like particles are also visible. Additionally, there is an indication of particles exhibiting a preferred orientation. This orientation is characterized by certain faces being wider on the particles, which can potentially influence the solubility of mannitol in different solvents.

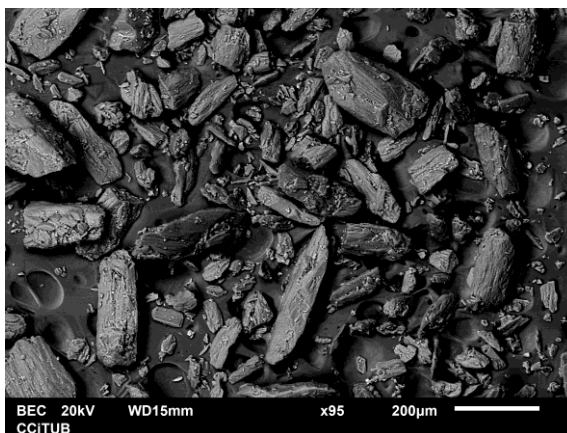


Figure 6. SEM images of the mannitol used in the solubility experiments.

The DSC (Differential Scanning Calorimetry) technique is used to measure changes in the heat absorbed or released by a sample as it undergoes controlled temperature changes. The melting point is the temperature at which a substance changes from solid to liquid at constant atmospheric pressure. To measure the melting point using DSC, a small sample of mannitol used in solubility determinations is placed in the instrument and subjected to a controlled heating program. As the temperature increases, the sample melts and absorbs or releases a specific amount of heat. This is recorded as a curve on the DSC graph, showing the heat flow as a function of temperature as follows in Fig. 7. From such an analysis, a value of $T_m = X$ was obtained as melting point, and from the area below the endothermic event, a melting enthalpy of X was determined. The parameters obtained are $166,39\text{ }^\circ\text{C}$ for the T_m and $-18,97\text{ kJ}$ for the enthalpy.

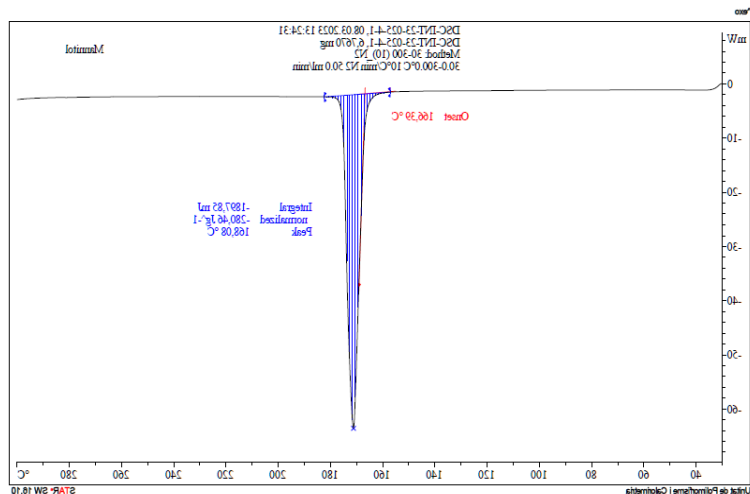


Figure 7. DSC determination the melting point of mannitol.

In the supercell packing of mannitol, the molecules are organized in a dense and ordered structure held together by hydrogen bonding. Mannitol molecules, which contain multiple hydroxyl (-OH) groups, form hydrogen bonds with neighboring hydroxyl groups in adjacent molecules. These hydrogen bonds contribute to the stability and three-dimensional structure of the mannitol crystal. They also influence its physical and chemical properties, such as solubility, stability, and reactivity. It's important to note that the formation of hydrogen bonds may vary in different polymorphs or crystallization conditions of mannitol, leading to different packing patterns and crystal properties.

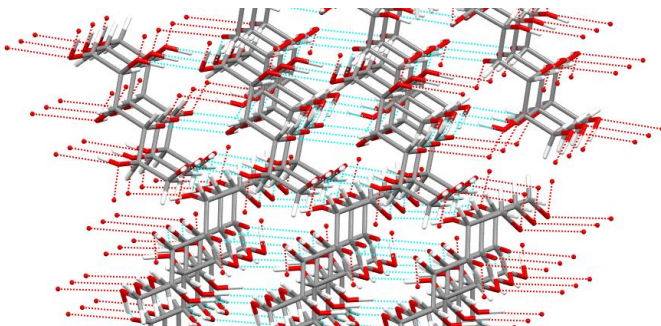


Figure 8. Supercell mannitol bonds

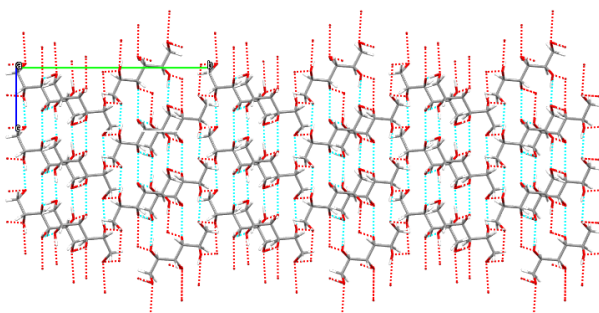


Figure 9. Supercell view along axis

5.2 SOLUBILITY DETERMINATIONS

The Hildebrand solubility parameter and solvation are related to the solubility of a substance in a solvent. If the Hildebrand solubility parameter of the solute and solvent are similar, there will be higher solubility due to a better affinity between them. Conversely, if the parameters differ significantly, the solubility may be lower due to a lower affinity between the solute and solvent.

The prediction for mannitol is Water>MeOH>EtOH>1-PropOH>2 Prop> ButOH>TBA>2 ButOH>Acetone>Butanone>MIBK.

Table 3 summarize the average solubility values obtained in different solvents. These tables show the mass fractions at temperatures ranging from 298 to 340 [K]. In this analysis, it can generally be observed that the solubility of mannitol in organic solvents increases as the temperature increases. Overall, the mass ratio solubility decreases at the higher temperature (340K) in order: H₂O > MeOH > EtOH > TBA > 1-Prop > 2-Prop > ButOH > 2-ButOH > MIBK > Dioxane > Butanone > Acetone. For the obtained solubility, water stands up with an extremely high solubility compared to other solvents.

Table 3. Mass ratio solubility of mannitol in the studied solvents

| T[K] | MeOH (10 ⁻⁴) | σ (10 ⁻⁶) | EtOH (10 ⁻⁴) | σ (10 ⁻⁶) | Tertbutanol (10 ⁻⁴) | σ (10 ⁻⁶) | MIBK (10 ⁻⁴) | σ (10 ⁻⁶) |
|--------|--------------------------|------------------------------|--------------------------|------------------------------|---------------------------------|------------------------------|--------------------------|------------------------------|
| 298,15 | 2,928 | 6,690 | 0,783 | 3,668 | 0,664 | 1,33 | 0,414 | 3,052 |
| 303,15 | 3,539 | 1,434 | 0,976 | 2,161 | 0,824 | 3,823 | 0,601 | 2,378 |
| 310,15 | 3,873 | 5,150 | 1,182 | 6,252 | 1,045 | 6,257 | 0,705 | 4,982 |
| 315,15 | 4,668 | 7,468 | 1,329 | 5,428 | 1,369 | 4,419 | 0,843 | 1,089 |
| 320,15 | 5,327 | 1,085 | 1,55 | 2,846 | 1,519 | 1,145 | 0,880 | 8,281 |
| 325,15 | 6,304 | 5,127 | 1,907 | 8,615 | 1,977 | 6,137 | 1,083 | 6,373 |
| 330,15 | 8,164 | 3,855 | 2,424 | 2,723 | 2,209 | 2,526 | 1,249 | 1,015 |
| 335,15 | 16,049 | 1,295 | 3,309 | 1,340 | 2,842 | 3,449 | 1,507 | 1,200 |
| 340,15 | 18,890 | 5,558 | 3,714 | 8,427 | 3,122 | 1,484 | 1,73 | 1,369 |

* σ represents standard deviation.

Table 3 (cont). Mass ratio solubility of mannitol in the studied solvents

| T[K] | 2-Propanol (10 ⁻⁴) | σ (10 ⁻⁶) | 1-Propanol (10 ⁻⁴) | σ (10 ⁻⁶) | Butanol (10 ⁻⁴) | σ | 2-Butanol (10 ⁻⁴) | σ (10 ⁻⁶) |
|--------|--------------------------------|------------------------------|--------------------------------|------------------------------|-----------------------------|----------|-------------------------------|------------------------------|
| 298,15 | 0,409 | 1,343 | 0,545 | 1,589 | 0,413 | 5,476 | 0,401 | 2,712 |
| 303,15 | 0,524 | 3,284 | 0,579 | 9,189 | 0,571 | 4,082 | 0,625 | 1,583 |
| 310,15 | 0,582 | 3,538 | 0,702 | 2,881 | 0,696 | 3,78 | 0,659 | 3,732 |
| 315,15 | 0,814 | 5,081 | 0,762 | 9,854 | 0,835 | 2,178 | 0,871 | 5,159 |
| 320,15 | 1,035 | 4,592 | 1,006 | 6,373 | 0,955 | 4,681 | 0,948 | 9,893 |
| 325,15 | 1,151 | 5,698 | 1,195 | 8,282 | 1,268 | 8,056 | 1,098 | 5,634 |
| 330,15 | 1,505 | 1,442 | 1,623 | 9,675 | 1,521 | 9,087 | 1,473 | 6,155 |
| 335,15 | 1,717 | 4,81 | 1,804 | 6,175 | 1,67 | 4,608 | 1,701 | 2,731 |
| 340,15 | 2,307 | 9,242 | 2,347 | 9,119 | 2,235 | 2,764 | 1,938 | 1,852 |

Table 3 (cont). Mass ratio solubility of mannitol in the studied solvents.

| T[K] | Acetone (10 ⁻⁴) | σ (10 ⁻⁶) | Water (10 ⁻⁴) | σ (10 ⁻³) | Dioxane | σ (10 ⁻⁶) | Butanone | σ (10 ⁻⁶) |
|--------|--------------------------------|------------------------------|------------------------------|------------------------------|---------|------------------------------|----------|------------------------------|
| 298,15 | 0,274 | 2,31 | 207,70 | 1,488 | 0,206 | 1,693 | 0,165 | 2,680 |
| 303,15 | 0,351 | 1,836 | 234,17 | 1,849 | 0,341 | 5,868 | 0,203 | 1,756 |
| 310,15 | 0,435 | 5,749 | 276,40 | 3,199 | 0,399 | 4,205 | 0,247 | 4,856 |
| 315,15 | 0,559 | 3,092 | 346,20 | 4,319 | 0,615 | 1,103 | 0,309 | 1,758 |
| 320,15 | 0,763 | 2,072 | 373,63 | 3,516 | 0,794 | 8,955 | 0,341 | 1,765 |
| 325,15 | 0,988 | 2,933 | 440,60 | 1,622 | 1,096 | 9,107 | 0,393 | 1,821 |
| 330,15 | - | - | 484,88 | 1,676 | 1,194 | 1,034 | 0,494 | 2,41 |
| 335,15 | - | - | 540,40 | 2,48 | 1,244 | 7,966 | 0,609 | 1,622 |
| 340,15 | - | - | 616,05 | 6,536 | 1,482 | 1,359 | 0,705 | 5,452 |

Firstly, mannitol is a polar substance, which means it has an affinity for water molecules. Mannitol molecules have hydroxyl groups (-OH) that can form hydrogen bonds with water molecules, facilitating its dissolution in this solvent. The reduced solubility of mannitol in alcohols can be attributed to several factors. Firstly, alcohols, like mannitol, contain hydroxyl groups (-OH) that can form hydrogen bonds. However, the ability of alcohols to establish hydrogen bonds with mannitol is lower than that of water. Moreover, alcohols possess larger molecular structures and exhibit lower polarity compared to water [22]. These characteristics hinder the effective interaction between mannitol molecules and alcohol molecules, leading to decreased solubility. Overall, the combination of weaker hydrogen bonding and the structural differences between alcohols and water contributes to the relatively lower solubility of mannitol in alcohols.

Comparing alcohols, shorter chain alcohols, such as methanol and ethanol, (matching literature determinations) [39] have a greater capacity to dissolve

mannitol compared to longer chain alcohols. This is due to several reasons, for example polarity. Shorter chain alcohols are more polar than longer chain alcohols because they have a higher proportion of hydroxyl groups relative to their size, increasing their polarity. This increased polarity facilitates the interaction and solubilization of mannitol, which is also a polar molecule, through hydrogen bonding and dipole-dipole forces.

From another standpoint, the type of alcohol affects as well the solubility [40]. Primary alcohols have a hydroxyl functional group (-OH) directly attached to a primary carbon (a carbon with only one adjacent carbon atom). Secondary alcohols have the hydroxyl group attached to a secondary carbon (a carbon with two adjacent carbon atoms). The presence of a primary carbon in primary alcohols confers greater polarity due to the primary carbon's electron deficiency and the ability to form hydrogen bonds with mannitol. This allows for stronger dipole-dipole interactions with the polar mannitol molecule, enhancing their solubility. Additionally, primary alcohols have more hydrogen atoms directly bonded to the carbon carrying the hydroxyl group, resulting in a higher number of available hydrogen bonding sites. These additional hydrogen bonding interactions further contribute to their increased solubility in mannitol. In this case, we observe a deviation from the expected behavior for TBA compared to the literature, as being a tertiary alcohol, its solubility should be lower than that of a primary alcohol.

MeOH > EtOH > TBA > 1-Prop > 2-Prop > ButOH > 2-ButOH

Furthermore, mannitol typically have a low solubility in ketone [39]. This moderate polarity may allow for limited solubility of mannitol in ketones, especially in smaller and more polar ketones [40] such as acetone (propanone) or butanone. As for the other groups mentioned, ketones and cyclic ethers are organic compounds that

have lower polarity compared to alcohols. Therefore, the solubility of mannitol in these groups will be lower compared to alcohols and water. However, the exact solubility may vary depending on the specific structure of the ketone. Ethers are compounds with low polarity, and their ability to dissolve mannitol will also be limited. However, some ethers may have slightly higher solubility than ketones and cyclic ethers due to their lower polarity. The experimental results regarding solubility in such solvents decrease in the order: MIBK > Dioxane > Butanone > Acetone.

The solubility curves obtained in the analysis of mannitol solubility are as follows:

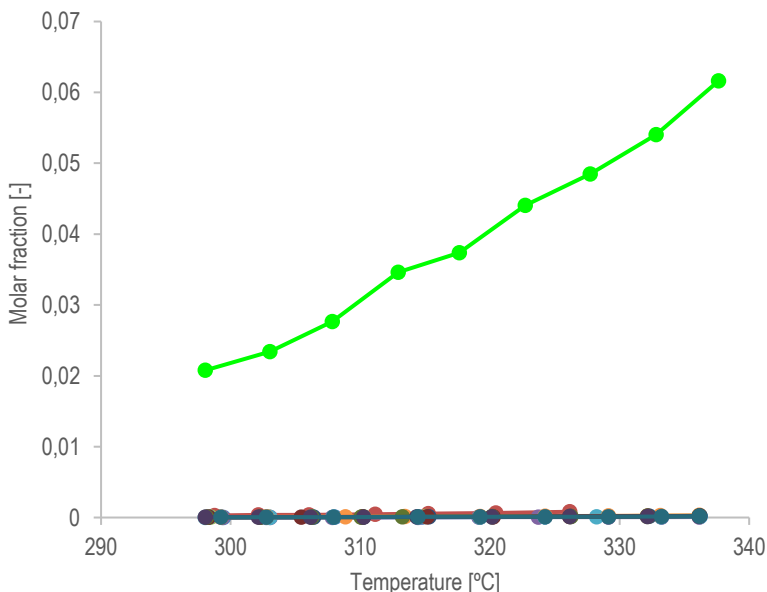


Figure 10. Molar fraction of experimental solubility data in 12 solvents studied.

As can be observed, comparing all the solubility data, water has a very high solubility in mannitol. The aim of this graph is to facilitate a visual assessment of the relative magnitude of water's solubility in comparison to the other solvents studied.

Therefore, a comparative graph of solvents with lower solubility is performed to appreciate the trend of the curves as shown in Figure 8.

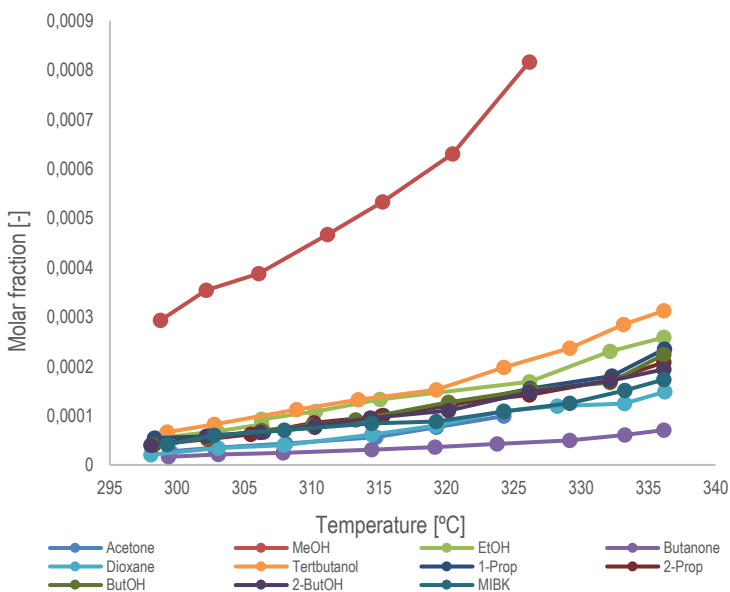


Figure 11. Molar fraction of experimental solubility data in low solubility solvents studied.

5.3 MODELING OF SOLUBILITY DATA AND THERMODYNAMIC ANALYSIS.

Three different models have been fitted to the experimental solubility data obtained at different temperatures for each solvent data. The corresponding parameters in each model, obtained by non-linear regression by minimizing the differences between experimental and calculated molar fraction solubility values, are gathered in Tables 4 and 5. To illustrate the goodness of fit, the solubility values calculated by the Modified Apelblat are plotted in Figure 12 along with the experimental data, where an excellent fitting is observed. Remarkably, the results obtained from all three models exhibit a high-quality description of the experimental reality, as it can be inferred from the mean coefficients of determination (R^2) always exceeding 0.97, and the root mean square deviations (RMSDs) for all three models are below 10×10^{-6} (Tables 4 and 5).

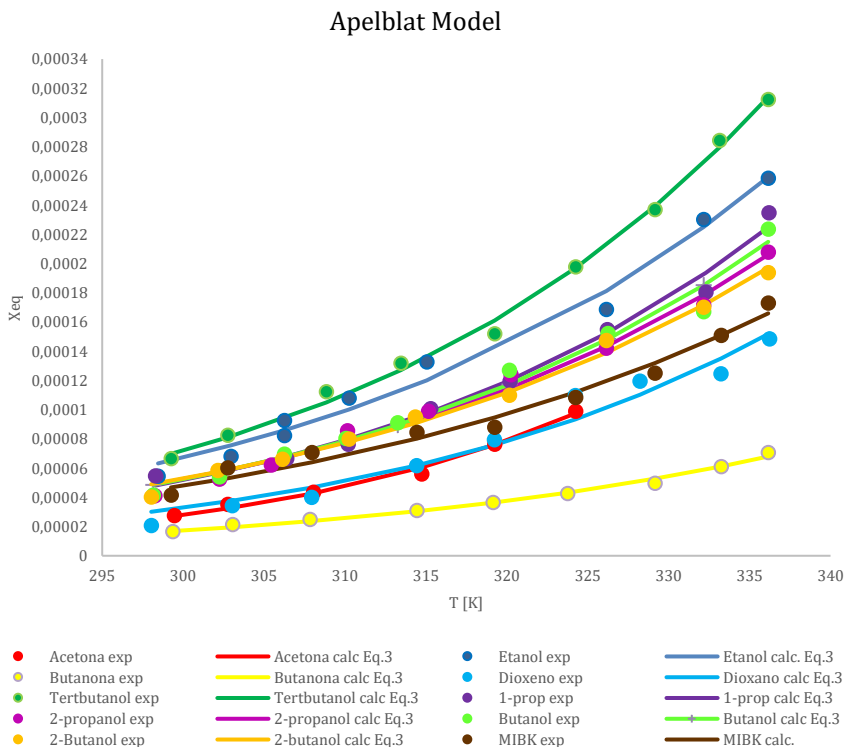


Figure 12. Apelblat modeling data of mannitol in all solvents studied.

In summary, the experimental solubility in various solvent mixtures exhibits a strong agreement with the modified data. The augmented relative differences (ARD) for the modified Apelblat equation, λh model, and Empirical Model are approximately 1%, 3%, and 2%, respectively. These results demonstrate that all three models effectively capture the solubility of mannitol across the entire temperature and composition range investigated. Among them, the modified Apelblat model provides the closest fit to the data, although all three models are useful for correlating and predicting mannitol's solubility within the explored conditions.

Table 4. Significant parameters obtained from thermodynamical analysis.

| | Water | MeOH | EtOH | 1- Propanol | 2- Propanol | TBA |
|-----------------------------------|----------|--------|---------|----------------|----------------|--------|
| C1 | -1116000 | -27,84 | -19,55 | -21,68 | -19,92 | -21,61 |
| C2 | 4260 | -5133 | -3796 | -4142 | -3853 | -4138 |
| C3 | -5,624 | 8,771 | 3,032 | 3,919 | 2,972 | 4,237 |
| TSSR * 10⁶ | 11,44 | 0,303 | 0,0594 | 0,0334 | 2,894 | 2,013 |
| λ | 265,2 | 5376 | 20,71 | 50,73 | 55,03 | 69,33 |
| h | 10,574 | 0,944 | 183,328 | 81,722 | 76,201 | 59,698 |
| TSSR * 10⁹ | 8272 | 0,461 | 0,568 | 0,377 | 3,980 | 0,0224 |
| A | -51,97 | -99,27 | -77,28 | -83,39 | -78,5 | -83,30 |
| B | 0,137 | 0,137 | -0,227 | -5,368 | -0,245 | -0,560 |
| C | 8,449 | 15,95 | 11,86 | 12,89 | 12,03 | 12,93 |
| TSSR * 10¹⁰ | 11,44 | 38939 | 0,0595 | 0,0334 | 2,894 | 2,012 |

Table 5. Significant parameters obtained from thermodynamical analysis.

| | Butanol | 2-Butanol | Dioxane | MIBK | Butanone | Acetone |
|-----------------------------------|---------|-----------|---------|--------|----------|---------|
| C1 | -20,70 | -18,99 | -22,81 | -18,99 | -19,79 | -27,82 |
| C2 | -3980 | -3707 | -4316 | -3488 | -3849 | -5035 |
| C3 | 3,390 | 2,492 | 4,042 | 1,668 | 1,849 | 6,290 |
| TSSR * 10⁶ | 5,847 | 1,883 | 6,358 | 2,959 | 0,228 | |
| λ | 54,94 | 12,14 | 59,90 | 12,23 | 11,93 | 368,8 |
| h | 76,12 | 305,6 | 72,34 | 308,4 | 339,9 | 13,33 |
| TSSR * 10⁹ | 0,6199 | 1,523 | 0,5688 | 32,55 | 0,033 | 0,0369 |
| A | -80,68 | -75,81 | -86,97 | -71,94 | -79,45 | -102,1 |
| B | -0,250 | -0,222 | -0,775 | -4,511 | -0,148 | 0,137 |
| C | 12,42 | 11,57 | 13,44 | 10,87 | 12,01 | 16,06 |
| TSSR * 10¹⁰ | 5,847 | 1,883 | 6,358 | 2,959 | 0,228 | 0,3034 |

In Van't Hoff analysis, the Van't Hoff enthalpy change ($\Delta_{\text{sin}}^{\text{vH}}H^\circ$) of solution can be determined from the slope of a plot of x_{eq} vs. $1/T$, as shown in Equation 6. Figure 10 displays the Van't Hoff plots of solubility for all studied solvents. Although it has been demonstrated that a Van't Hoff plot can exhibit nonlinear behavior [27], the solvents in this study exhibit nearly linear trends over the investigated temperature range. The linear coefficient of determination (R_2) consistently exceeds 0.97. The positive values of the Van't Hoff enthalpy (Table 8) indicate an increase in solubility with temperature. The Van't Hoff enthalpies of the solutions fall within the range of 30-40 kJ/mol for most solvents, except for water and MIBK, which show significantly lower values of 23.19 and 28.15 kJ/mol, respectively, and dioxane, which exhibits a higher value of 41.92 kJ/mol. There is no clear relationship observed between the length of the carbon chain of the primary alcohol, as mentioned in the literature [27], and the Van't Hoff enthalpy of solution.

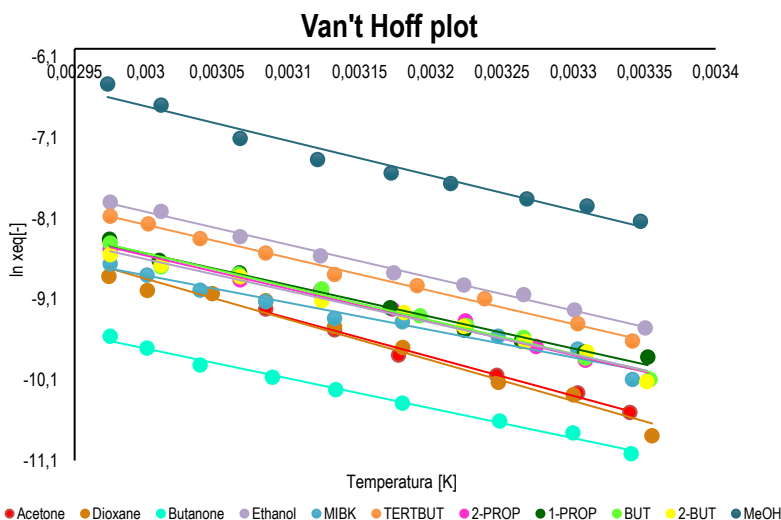


Figure 13. van't Hoff plot of solubility for all the solvents studied.

Table 6. Van't Hoff Enthalpies with Standard Errors and Regression Coefficients obtain from solubility curves.

| | ΔH [KJ/mol] | R ² |
|------------|---------------------|----------------|
| Water | 23,19 \pm 0,71 | 0,993 |
| Methanol | 32,67 \pm 2,27 | 0,978 |
| Ethanol | 33,88 \pm 0,91 | 0,994 |
| Acetone | 39,97 \pm 2,03 | 0,987 |
| 1-Propanol | 32,65 \pm 1,37 | 0,986 |
| 2-Propanol | 34,18 \pm 1,56 | 0,984 |
| Butanol | 34,52 \pm 1,56 | 0,984 |
| 2-Butanol | 32,64 \pm 1,55 | 0,982 |
| TBA | 34,06 \pm 0,90 | 0,994 |
| Dioxane | 41,92 \pm 2,55 | 0,971 |
| MIBK | 28,15 \pm 1,93 | 0,974 |
| Butanone | 30,75 \pm 1,02 | 0,991 |

In this case they are interactions based on the electrostatic forces between the ions of the solute and the molecules of the solvent. If these electrostatic forces are not strong enough to overcome the attractive forces between the ions in the solid solute, more energy is required to separate the ions and allow the formation of the solution. This results in a high and positive enthalpy of dissolution, which in turn leads to lower solubility.

As observed, water, which exhibits the highest solubility, has the smallest value of enthalpy. This observation supports the information found in the literature [39]. It can be noted that solubility shows an inversely proportional trend to the enthalpy value in all solvents except for MIBK, Butanone, 1-PropOH, and 2-ButOH. These four solvents deviate from the expected values reported in the literature, showing lower values. Several factors could contribute to these discrepancies:

- Additional intermolecular interactions, such as stronger hydrogen bonds or dipole-dipole forces, between the solute and the solvent that were not considered in the initial calculation or estimation of enthalpy of dissolution.
- Presence of impurities if the solute or the solvent contains impurities that can affect the intermolecular interactions during dissolution, this could contribute to a deviate value of enthalpy of dissolution.

In resume, mannitol is a polyalcohol with multiple hydroxyl groups (-OH) that have the ability to form hydrogen bonds. This makes it prone to interact with solvents that can also form hydrogen bonds.

In the case of water, it is a polar solvent capable of forming hydrogen bonds with the hydroxyl groups of mannitol. These interactions between mannitol and water facilitate its solvation, resulting in high solubility of mannitol in water.

As for alcohols, they are also polar solvents that contain hydroxyl groups. The solubility of mannitol in alcohols will depend on the ability of these alcohols to form hydrogen bonds with the hydroxyl groups of mannitol. The stronger the hydrogen bonding interactions (depending on the chain length), the higher the solubility of mannitol in alcohols.

In the case of ketones, their polarity is lower compared to water and alcohols. However, ketones can still interact with mannitol through hydrogen bonding between the carbonyl group of the ketone and the hydroxyl groups of mannitol.

Cyclic ethers have moderate polarity but do not have significant hydrogen bonding capacity. This can limit the solvation interactions between mannitol and cyclic ethers, resulting in relatively low solubility of mannitol in these solvents.

In summary, the solubility of mannitol in different solvents is influenced by the ability to form hydrogen bonds and solvation interactions between mannitol and the solvents. Solvents that can form hydrogen bonds with the hydroxyl groups of mannitol, such as water and some alcohols, will have a higher capacity to solvate and dissolve mannitol. On the other hand, solvents with lower capacity to form hydrogen bonds, such as ketones and cyclic ethers, may exhibit lower solubility of mannitol.

6. CONCLUSIONS

In the study of mannitol solubility, it has been demonstrated that temperature has an effect on solubility. As the temperature increases, the solubility also increases.

Mannitol, in general, exhibits the highest solubility in polar protic solvents, followed by polar aprotic solvents and finally non polar solvents. Within polar protic solvents, the solubility of mannitol increases with the polarity of the solvent, which, in turn, tends to increase with the shorter carbon lengths in alcohols. The reduced ability to form hydrogen bonds is a significant factor contributing to lower solubility observed in polar aprotic and non polar solvents. So in order to solubility data obtained it is conclusive that water has high solubility in mannitol, as the literature shows, followed by short chain alcohols, then ethers and ketones, except for TBA that shows an anomalous behavior in comparison to literature.

The obtained van't Hoff enthalpies of the solution fits relatively well in the solubility order except for MIBK that is lower than expected and dioxane, higher value compared to other solvents.

It has been conclusively demonstrated that mannitol retains its specific polymorphic structure despite being dissolved in various solvents and subjected to temperature variations. This unequivocally affirms the exceptional stability of mannitol's beta polymorph, establishing it as the most thermodynamically favored and persistent form observed.

Furthermore, it has been verified that the solubility models employed to predict mannitol solubility are all suitable for this study. It is true that the Apelblat model exhibited the closest fit to the experimental data, yielding the lowest error. However, it can be concluded that all three models employed in the analysis are suitable for accurate solubility predictions of mannitol. These findings underscore the reliability and applicability of solubility modeling in understanding and predicting the behavior of mannitol in various solvents and temperature conditions.

The study of the solubility of mannitol in different organic solvents in relation to biomass offers various highly relevant applications. By investigating the solubility of mannitol in different organic solvents, it is possible to determine the most suitable solvent for efficient extraction and purification of mannitol from biomass. This is essential for sustainably harnessing biomass resources and obtaining high-quality mannitol for use in industrial or pharmaceutical applications.

This information enables the selection of the most appropriate solvent for extraction, as well as the optimization of process conditions and purification of the obtained mannitol. These data are essential for developing efficient and sustainable processes that harness biomass as a raw material and enable effective production of high-quality mannitol.

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ACRONYMS

| | |
|--|-----------------------------------|
| ButOH | Butanol |
| PropOH | Propanol |
| TBA | Tert butyl alcohol |
| MIBK | Metyl isobutyl ketone |
| MeOH | Methanol |
| EtOH | Ethanol |
| $\Delta H_{\text{Sin}}^{\text{VH}} \text{H}^\circ$ | Van't Hoff enthalpy change |
| Xeq | Mannitol conversion |
| T_m | Melting temperature |
| T_b | Boiling temperature |
| SEM | Scanning Electron Microscopy |
| DSC | Differential Scanning Calorimetry |
| HMF | (hydroxymethyl)furfural |
| PXRD | Powder X-Ray Diffraction |
| PTFE | Polytetrafluoroethylene |

APPENDICES

APPENDIX I: SOLVENTS DATA

Table 2. Source of all solvents used in solubility determination.

| SOLVENT | CAS NUMBER | SOURCE | MASS FRACTION PURITY |
|------------|------------|------------------|----------------------|
| D-mannitol | 69-65-8 | Alfa Aesarr | 0,97 |
| Methanol | 67-56-1 | Fluka Analytical | 0,99 |
| Ethanol | 64-17-5 | Quimivita | 0,99 |
| Butanol | 71-36-3 | Sigma-Aldrich | 0,99 |
| 2-Butanol | 78-92-2 | PanReac | 0,995 |
| 1-Propanol | 71-23-8 | Sigma-Aldrich | 0,99 |
| 2-Propanol | 67-63-0 | PanReac | 0,998 |
| Acetone | 67-64-1 | PanReac | 0,99 |
| TBA | 75-65-0 | Fluka Chemika | 0,997 |
| MIBK | 108-10-1 | PanReac | 0,99 |
| Butanone | 78-93-3 | PanReac | 0,995 |
| Dioxane | 123-91-1 | Acros Organics | 0,995 |

APPENDIX II: SOLUBILITY EXPERIMENTAL DATA

Experiment 1. Water

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 109 | 24,9 | 10,4479 | 16,5753 | 11,5315 |
| 110 | 24,9 | 10,4345 | 17,0895 | 11,6173 |
| 111 | 24,9 | 10,3984 | 17,0768 | 11,5712 |
| 112 | 29,9 | 10,452 | 16,6314 | 11,6001 |
| 113 | 29,9 | 10,3804 | 17,0934 | 11,7215 |
| 114 | 29,9 | 10,4318 | 17,0636 | 11,7592 |
| 115 | 34,7 | 10,4203 | 15,6308 | 11,5912 |
| 116 | 34,7 | 10,3783 | 16,8226 | 11,825 |
| 117 | 34,7 | 10,4353 | 17,0982 | 11,908 |
| 118 | 39,8 | 10,3885 | 16,6777 | 11,982 |
| 119 | 39,8 | 10,3655 | 15,0383 | 11,7412 |
| 120 | 39,8 | 10,4179 | 17,0966 | 12,085 |
| 121 | 44,5 | 10,4666 | 17,8986 | 12,5764 |
| 122 | 44,5 | 10,37788 | 16,9399 | 12,2301 |
| 123 | 44,5 | 10,3546 | 15,9515 | 11,9214 |
| 124 | 49,6 | 10,4036 | 16,787 | 12,4321 |
| 125 | 49,6 | 10,3397 | 17,066 | 12,475 |
| 126 | 49,6 | 10,2457 | 16,9948 | 12,3989 |
| 127 | 54,6 | 10,3227 | 16,9247 | 12,5307 |
| 128 | 54,6 | 10,3582 | 15,8009 | 12,4436 |
| 129 | 54,6 | 10,3781 | 16,9932 | 12,6668 |
| 130 | 59,7 | 10,4519 | 17,0746 | 12,9255 |
| 131 | 59,7 | 10,3684 | 17,4688 | 12,8 |
| 132 | 59,7 | 10,4552 | 17,4478 | 12,966 |
| 133 | 64,5 | 10,4786 | 16,9835 | 12,9471 |
| 134 | 64,5 | 10,4179 | 17,4522 | 12,9762 |
| 135 | 64,5 | 10,4143 | 16,5537 | 12,9797 |

Experiment 2. Methanol

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 1 | 25,6 | 10,3788 | 19,8248 | 10,3941 |
| 2 | 25,6 | 10,4175 | 20,2529 | 10,434 |
| 3 | 25,6 | 10,4494 | 20,2652 | 10,466 |
| 19 | 29 | 10,4215 | 19,5005 | 10,4389 |
| 20 | 29 | 10,4355 | 19,8574 | 10,455 |
| 21 | 29 | 10,3585 | 19,425 | 10,377 |
| 37 | 32,9 | 10,3866 | 19,3949 | 10,4062 |
| 38 | 32,9 | 10,398 | 19,8091 | 10,419 |
| 39 | 32,9 | 10,4455 | 19,3563 | 10,465 |
| 55 | 38 | 10,3122 | 19,3606 | 10,3396 |
| 56 | 38 | 10,4221 | 20,0457 | 10,4473 |
| 57 | 38 | 10,4509 | 20,1957 | 10,477 |
| 73 | 42,1 | 10,2794 | 19,5441 | 10,308 |
| 74 | 42,1 | 10,4166 | 19,9459 | 10,4453 |
| 75 | 42,1 | 10,4957 | 20,3767 | 10,525 |
| 91 | 47,3 | 10,4456 | 19,7507 | 10,479 |
| 92 | 47,3 | 10,1890 | 19,8228 | 10,2236 |
| 93 | 47,3 | 10,3246 | 19,5046 | 10,3571 |
| 109 | 53 | 10,1785 | 19,6415 | 10,2225 |
| 110 | 53 | 10,3985 | 19,5037 | 10,4405 |
| 111 | 53 | 10,1809 | 18,8769 | 10,221 |
| 127 | 59 | 10,388 | 19,4859 | 10,4353 |
| 128 | 59 | 10,4091 | 15,2349 | 10,459 |
| 129 | 59 | 10,428 | 15,2344 | 10,47 |
| 145 | 63,2 | 10,3138 | 16,334 | 10,367 |
| 146 | 63,2 | 10,2137 | 17,4715 | 10,2667 |
| 147 | 63,2 | 10,2198 | 13,4751 | 10,25 |

Experiment 3. Acetone

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 165 | 26,3 | 10,3994 | 19,8659 | 10,4005 |
| 166 | 26,3 | 10,4147 | 20,2885 | 10,4156 |
| 167 | 26,3 | 10,4543 | 15,3973 | 10,4547 |
| 177 | 29,6 | 10,4537 | 20,1090 | 10,4548 |
| 178 | 29,6 | 10,4344 | 20,2084 | 10,4355 |
| 179 | 29,6 | 10,4228 | 20,1005 | 10,4238 |
| 192 | 34,9 | 10,5095 | 19,9042 | 10,5109 |
| 193 | 34,9 | 10,4927 | 20,2075 | 10,4939 |
| 194 | 34,9 | 10,4194 | 15,2721 | 10,4207 |
| 207 | 41,6 | 10,1593 | 19,4908 | 10,161 |
| 208 | 41,6 | 10,4218 | 19,9193 | 10,4234 |
| 209 | 41,6 | 10,3306 | 18,0906 | 10,3324 |
| 222 | 46,1 | 10,4726 | 19,6667 | 10,4748 |
| 223 | 46,1 | 10,4114 | 19,7734 | 10,4137 |
| 224 | 46,1 | 10,3042 | 19,7594 | 10,3064 |
| 237 | 51,1 | 10,4131 | 18,9458 | 10,4158 |
| 238 | 51,1 | 10,2014 | 19,759 | 10,2043 |
| 239 | 51,1 | 10,5425 | 19,8654 | 10,5451 |

Experiment 4. Dioxane

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 162 | 24,9 | 10,4537 | 22,7183 | 10,4542 |
| 163 | 24,9 | 10,4344 | 22,8694 | 10,4349 |
| 164 | 24,9 | 10,4228 | 16,8702 | 10,4231 |
| 180 | 29,9 | 10,3554 | 22,7377 | 10,3561 |
| 181 | 29,9 | 10,4388 | 16,9259 | 10,4393 |
| 182 | 29,9 | 10,3946 | 16,8064 | 10,3951 |
| 195 | 34,8 | 10,4387 | 20,9088 | 10,4395 |
| 196 | 34,8 | 10,3839 | 19,0393 | 10,3847 |
| 197 | 34,8 | 10,4988 | 16,8628 | 10,4993 |
| 210 | 41,3 | 10,2774 | 16,195 | 10,2781 |
| 211 | 41,3 | 10,4206 | 16,9504 | 10,4216 |
| 212 | 41,3 | 10,3724 | 16,7209 | 10,3731 |
| 225 | 46,1 | 10,4105 | 16,7123 | 10,4114 |
| 226 | 46,1 | 10,382 | 16,6422 | 10,3831 |
| 227 | 46,1 | 10,3984 | 16,7212 | 10,3995 |
| 240 | 51,1 | 10,4153 | 22,6232 | 10,4178 |
| 241 | 51,1 | 10,2227 | 16,5614 | 10,2242 |
| 242 | 51,1 | 10,2669 | 16,567 | 10,2684 |
| 252 | 55,1 | 10,3136 | 16,514 | 10,3152 |
| 253 | 55,1 | 10,4551 | 16,6061 | 10,4567 |
| 254 | 55,1 | 10,4788 | 16,7816 | 10,4802 |
| 264 | 60,1 | 10,3605 | 16,1399 | 10,3624 |
| 265 | 60,1 | 10,3688 | 15,9833 | 10,3709 |
| 266 | 60,1 | 10,3545 | 16,1589 | 10,3549 |
| 276 | 63,1 | 10,1742 | 20,3173 | 10,177 |
| 277 | 63,1 | 10,3197 | 16,734 | 10,3217 |
| 278 | 63,1 | 10,271 | 16,0031 | 10,2729 |

Experiement 5. Butanone

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 171 | 26,2 | 10,4159 | 20,0886 | 10,4163 |
| 172 | 26,2 | 10,3189 | 19,7726 | 10,3193 |
| 173 | 26,2 | 10,4229 | 15,3005 | 10,4231 |
| 186 | 29,9 | 10,4835 | 20,3163 | 10,484 |
| 187 | 29,9 | 10,3549 | 20,0679 | 10,3554 |
| 188 | 29,9 | 10,3600 | 15,4486 | 10,3603 |
| 201 | 34,7 | 10,4763 | 20,0288 | 10,4769 |
| 202 | 34,7 | 10,4271 | 19,9234 | 10,4277 |
| 203 | 34,7 | 10,4639 | 15,3903 | 10,4642 |
| 216 | 41,3 | 10,1695 | 19,5235 | 10,1702 |
| 217 | 41,3 | 10,3102 | 20,1727 | 10,311 |
| 218 | 41,3 | 10,3295 | 15,0723 | 10,33 |
| 231 | 46 | 10,3432 | 19,3017 | 10,344 |
| 232 | 46 | 10,3987 | 20,0379 | 10,3995 |
| 233 | 46 | 10,4284 | 20,1279 | 10,4294 |
| 246 | 50,6 | 10,3470 | 19,7089 | 10,3479 |
| 247 | 50,6 | 10,4589 | 20,2018 | 10,4599 |
| 248 | 50,6 | 10,4643 | 20,2040 | 10,4655 |
| 258 | 56 | 10,1918 | 19,5245 | 10,1929 |
| 259 | 56 | 10,4356 | 19,7578 | 10,4368 |
| 260 | 56 | 10,4373 | 19,8079 | 10,4385 |
| 270 | 60,1 | 10,4289 | 19,8216 | 10,4303 |
| 271 | 60,1 | 10,3657 | 20,0156 | 10,3672 |
| 272 | 60,1 | 10,4274 | 20,0004 | 10,4289 |
| 285 | 63 | 10,4172 | 20,5713 | 10,4189 |
| 286 | 63 | 10,1973 | 20,0071 | 10,199 |
| 287 | 63 | 10,2000 | 20,0110 | 10,2019 |

Experiment 6. Ethanol

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 4 | 25,3 | 10,4667 | 19,3826 | 10,4696 |
| 5 | 25,3 | 10,3603 | 20,4688 | 10,3633 |
| 6 | 25,3 | 10,3633 | 20,157 | 10,3663 |
| 22 | 29,8 | 10,3661 | 19,3215 | 10,3695 |
| 23 | 29,8 | 10,3409 | 19,5308 | 10,3445 |
| 24 | 29,8 | 10,4328 | 17,1415 | 10,436 |
| 40 | 33,1 | 10,4073 | 19,4477 | 10,4116 |
| 41 | 33,1 | 10,4027 | 18,6245 | 10,4067 |
| 42 | 33,1 | 10,3609 | 19,4656 | 10,3649 |
| 58 | 37,1 | 10,4057 | 20,0674 | 10,4099 |
| 59 | 37,1 | 10,3958 | 20,3893 | 10,4012 |
| 60 | 37,1 | 10,3852 | 20,1887 | 10,3902 |
| 76 | 41,9 | 10,2812 | 19,2678 | 10,2866 |
| 77 | 41,9 | 10,2659 | 19,5712 | 10,2717 |
| 78 | 41,9 | 10,4082 | 20,1836 | 10,4142 |
| 94 | 47,1 | 10,4778 | 18,8729 | 10,4838 |
| 95 | 47,1 | 10,1968 | 19,5429 | 10,2040 |
| 96 | 47,1 | 10,2883 | 18,7887 | 10,2949 |
| 112 | 53 | 10,1624 | 17,418 | 10,1699 |
| 113 | 53 | 10,1926 | 19,5467 | 10,1996 |
| 114 | 53 | 10,2297 | 18,5097 | 10,237 |
| 130 | 59 | 10,3949 | 19,8165 | 10,4021 |
| 131 | 59 | 10,5624 | 15,3667 | 10,5685 |
| 132 | 59 | 10,375 | 15,2095 | 10,3815 |
| 148 | 63 | 10,3947 | 19,8751 | 10,4037 |
| 149 | 63 | 10,2173 | 16,3432 | 10,2263 |
| 150 | 63 | 10,4081 | 16,4171 | 10,4169 |

Experiment 7. MIBK

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 168 | 26,1 | 10,3894 | 20,038 | 10,3901 |
| 169 | 26,1 | 10,4292 | 20,2104 | 10,4299 |
| 170 | 26,1 | 10,4017 | 15,3017 | 10,4021 |
| 183 | 29,6 | 10,4117 | 19,8113 | 10,4127 |
| 184 | 29,6 | 10,4027 | 20,0254 | 10,4038 |
| 185 | 29,6 | 10,4265 | 20,6733 | 10,4276 |
| 198 | 34,8 | 10,4367 | 20,0401 | 10,438 |
| 199 | 34,8 | 10,3663 | 20,2814 | 10,3676 |
| 200 | 34,8 | 10,3978 | 15,4831 | 10,3984 |
| 213 | 41,3 | 10,4149 | 20,2342 | 10,4164 |
| 214 | 41,3 | 10,3635 | 20,086 | 10,3648 |
| 215 | 41,3 | 10,3800 | 20,1893 | 10,3817 |
| 228 | 46,1 | 10,3919 | 20,2232 | 10,3935 |
| 229 | 46,1 | 10,3348 | 20,7709 | 10,3363 |
| 230 | 46,1 | 10,3416 | 20,1417 | 10,3433 |
| 243 | 51,1 | 10,4829 | 19,8364 | 10,4848 |
| 244 | 51,1 | 10,4629 | 20,2519 | 10,4649 |
| 245 | 51,1 | 10,4441 | 20,2441 | 10,4459 |
| 255 | 56 | 10,2205 | 19,5839 | 10,2228 |
| 256 | 56 | 10,4611 | 20,043 | 10,4631 |
| 257 | 56 | 10,441 | 20,1414 | 10,4432 |
| 267 | 60,1 | 10,4258 | 19,8016 | 10,4286 |
| 268 | 60,1 | 10,4009 | 20,1335 | 10,4034 |
| 269 | 60,1 | 10,4367 | 20,1795 | 10,4393 |
| 279 | 63 | 10,4317 | 20,1743 | 10,4347 |
| 280 | 63 | 10,2137 | 20,4319 | 10,2167 |
| 281 | 63 | 10,4131 | 19,4761 | 10,4162 |

Experimenta 8. Tertbutanol

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 174 | 26,1 | 10,2690 | 14,5722 | 10,2696 |
| 175 | 26,1 | 10,4074 | 14,0246 | 10,4079 |
| 176 | 26,1 | 10,3897 | 14,1159 | 10,3902 |
| 189 | 29,6 | 10,4296 | 14,9627 | 10,4304 |
| 190 | 29,6 | 10,4218 | 15,0495 | 10,4226 |
| 191 | 29,6 | 10,3336 | 14,6718 | 10,3343 |
| 204 | 35,7 | 10,4902 | 15,0474 | 10,4914 |
| 205 | 35,7 | 10,4586 | 15,2967 | 10,4596 |
| 206 | 35,7 | 10,3754 | 15,2648 | 10,3765 |
| 219 | 40,3 | 10,3773 | 14,8714 | 10,3786 |
| 220 | 40,3 | 10,4052 | 15,1799 | 10,4064 |
| 221 | 40,3 | 10,1940 | 14,5362 | 10,1952 |
| 234 | 46,1 | 10,3894 | 14,8788 | 10,3908 |
| 235 | 46,1 | 10,2715 | 15,0113 | 10,273 |
| 236 | 46,1 | 10,3765 | 15,1645 | 10,378 |
| 249 | 51,1 | 10,3825 | 15,1252 | 10,3845 |
| 250 | 51,1 | 10,4332 | 14,8496 | 10,435 |
| 251 | 51,1 | 10,2796 | 15,0727 | 10,2815 |
| 261 | 56 | 10,1466 | 14,5638 | 10,1486 |
| 262 | 56 | 10,3785 | 15,1595 | 10,3807 |
| 263 | 56 | 10,3558 | 15,4047 | 10,3586 |
| 273 | 60 | 10,4424 | 14,8265 | 10,445 |
| 274 | 60 | 10,4338 | 15,1855 | 10,4366 |
| 275 | 60 | 10,2931 | 14,9542 | 10,2958 |
| 282 | 63 | 10,3013 | 15,1543 | 10,3045 |
| 283 | 63 | 10,4012 | 14,3055 | 10,4038 |
| 284 | 63 | 10,3681 | 14,6312 | 10,3707 |

Experiment 9. 2-Propanol

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 10 | 25,1 | 10,4081 | 19,7546 | 10,4093 |
| 11 | 25,1 | 10,4222 | 19,5609 | 10,4233 |
| 12 | 25,1 | 10,3799 | 15,2503 | 10,3805 |
| 28 | 29,1 | 10,4002 | 17,1771 | 10,4012 |
| 29 | 29,1 | 10,3358 | 16,4566 | 10,3368 |
| 30 | 29,1 | 10,381 | 13,9969 | 10,3816 |
| 46 | 32,3 | 10,4259 | 19,3892 | 10,4278 |
| 47 | 32,3 | 10,4151 | 15,3067 | 10,4160 |
| 48 | 32,3 | 10,4126 | 15,1513 | 10,4134 |
| 64 | 37 | 10,3387 | 17,0456 | 10,3406 |
| 65 | 37 | 10,3619 | 18,5031 | 10,3639 |
| 66 | 37 | 10,3285 | 15,1703 | 10,3297 |
| 82 | 42 | 10,3142 | 19,5319 | 10,3170 |
| 83 | 42 | 10,3174 | 18,9743 | 10,3202 |
| 84 | 42 | 10,3631 | 15,164 | 10,3644 |
| 100 | 47,1 | 10,361 | 18,358 | 10,3638 |
| 101 | 47,1 | 10,4777 | 16,8003 | 10,4804 |
| 102 | 47,1 | 10,4081 | 19,3241 | 10,4112 |
| 118 | 53 | 10,1496 | 14,5061 | 10,1516 |
| 119 | 53 | 10,3548 | 15,4331 | 10,3571 |
| 120 | 53 | 10,4247 | 15,1813 | 10,4265 |
| 136 | 59 | 10,1855 | 19,5635 | 10,1904 |
| 137 | 59 | 10,4511 | 15,2068 | 10,4535 |
| 138 | 59 | 10,3817 | 15,4423 | 10,3844 |
| 154 | 63 | 10,1873 | 19,5347 | 10,1928 |
| 155 | 63 | 10,1947 | 18,4751 | 10,1999 |
| 156 | 63 | 10,2341 | 17,3741 | 10,2389 |

Experiment 10. Propanol

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 7 | 25,1 | 10,3578 | 19,9665 | 10,3594 |
| 8 | 25,1 | 10,369 | 20,4061 | 10,3707 |
| 9 | 25,1 | 10,3596 | 20,3611 | 10,3612 |
| 25 | 29,1 | 10,3901 | 19,546 | 10,3917 |
| 26 | 29,1 | 10,3222 | 19,8484 | 10,3239 |
| 27 | 29,1 | 10,4098 | 17,3462 | 10,4110 |
| 43 | 33,2 | 10,3768 | 19,5765 | 10,3787 |
| 44 | 33,2 | 10,3141 | 19,8443 | 10,3158 |
| 45 | 33,2 | 10,4501 | 17,7601 | 10,4517 |
| 61 | 37 | 10,3409 | 18,6828 | 10,3431 |
| 62 | 37 | 10,4105 | 20,6799 | 10,4128 |
| 63 | 37 | 10,3716 | 18,6543 | 10,3733 |
| 79 | 42,1 | 10,3357 | 14,8548 | 10,3370 |
| 80 | 42,1 | 10,3805 | 15,2912 | 10,3821 |
| 81 | 42,1 | 10,4102 | 15,385 | 10,4117 |
| 97 | 47 | 10,2855 | 18,9688 | 10,2884 |
| 98 | 47 | 10,4373 | 15,0239 | 10,4390 |
| 99 | 47 | 10,32 | 15,5558 | 10,3220 |
| 115 | 53 | 10,2038 | 14,6566 | 10,2060 |
| 116 | 53 | 10,2579 | 15,4756 | 10,2601 |
| 117 | 53 | 10,2329 | 15,1316 | 10,2353 |
| 133 | 59,1 | 10,3997 | 20,1 | 10,4049 |
| 134 | 59,1 | 10,1739 | 15,1006 | 10,1767 |
| 135 | 59,1 | 10,3552 | 15,581 | 10,3580 |
| 151 | 63 | 10,2177 | 16,7341 | 10,2223 |
| 152 | 63 | 10,3715 | 19,983 | 10,3781 |
| 153 | 63 | 10,4003 | 14,718 | 10,4035 |

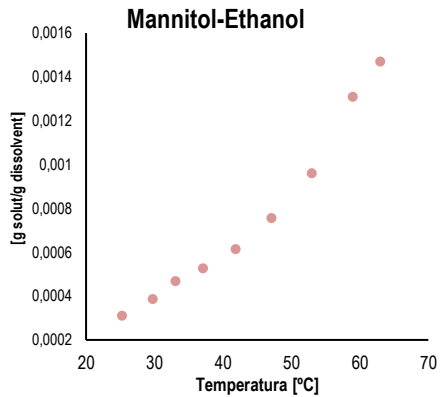
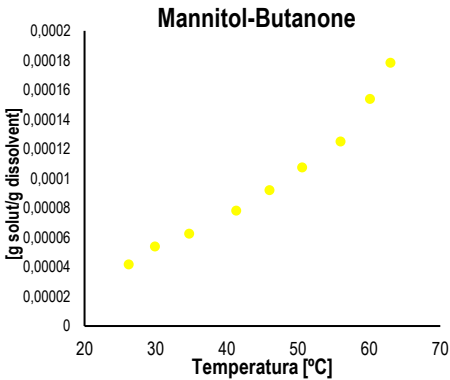
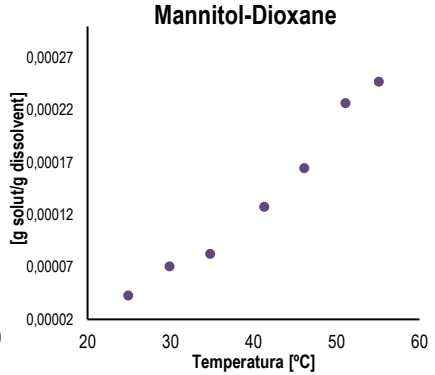
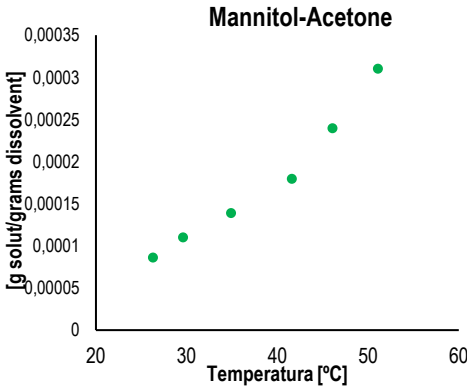
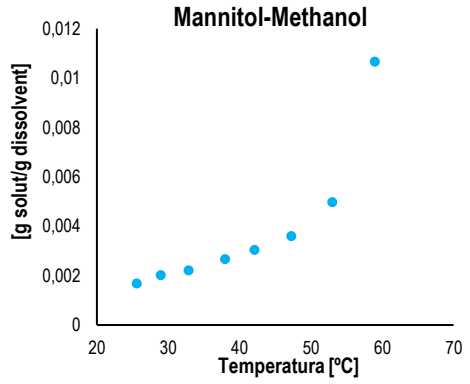
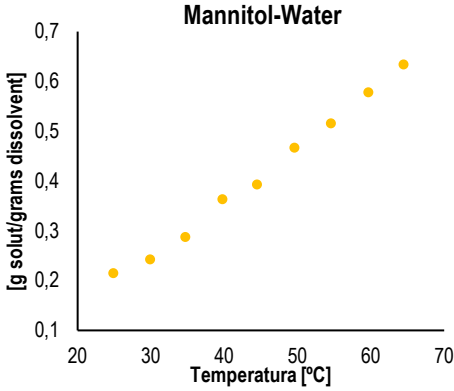
Experiment 11. Butanol

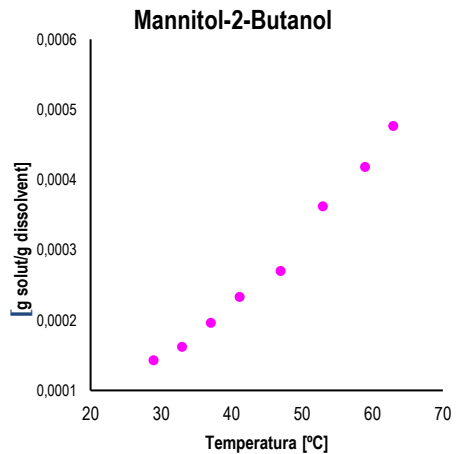
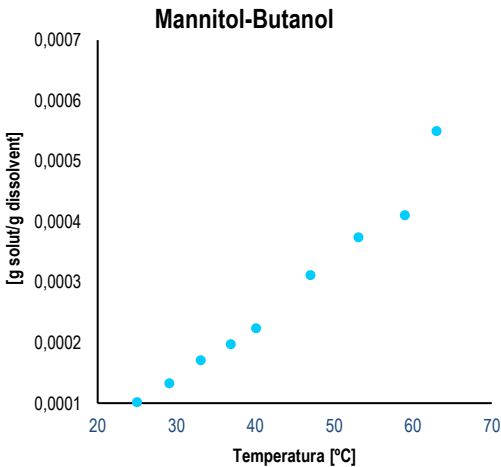
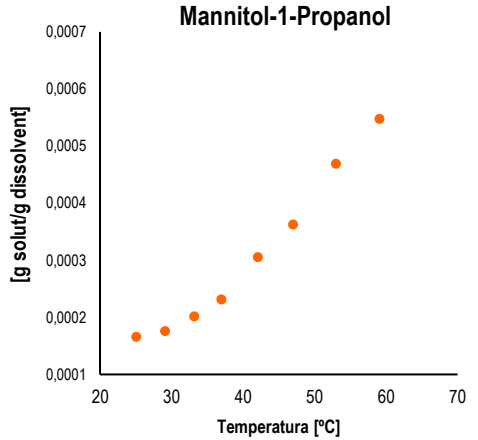
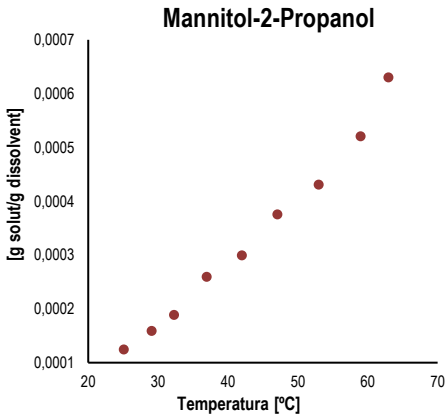
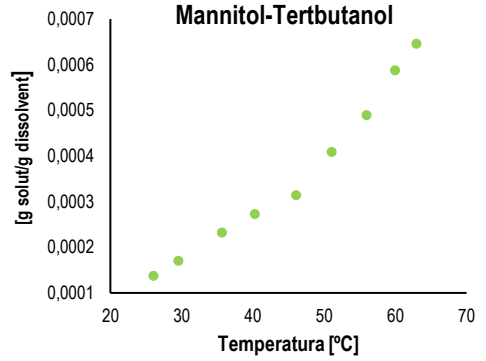
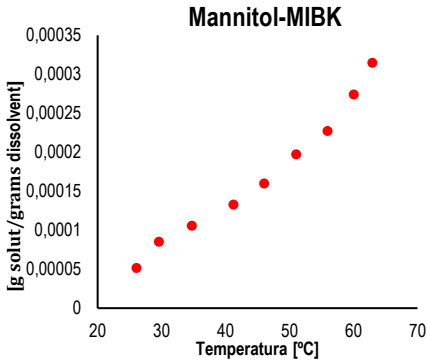
| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 13 | 25 | 10,4759 | 20,268 | 10,4769 |
| 14 | 25 | 10,4096 | 17,2377 | 10,4103 |
| 15 | 25 | 10,3829 | 15,3822 | 10,3834 |
| 31 | 29,1 | 10,3977 | 19,4028 | 10,3989 |
| 32 | 29,1 | 10,4639 | 19,8531 | 10,4650 |
| 33 | 29,1 | 10,356 | 17,1381 | 10,3570 |
| 49 | 33,1 | 10,4197 | 20,3598 | 10,4213 |
| 50 | 33,1 | 10,3653 | 20,7857 | 10,3671 |
| 51 | 33,1 | 10,4232 | 15,4426 | 10,4241 |
| 67 | 36,9 | 10,4041 | 20,3358 | 10,4061 |
| 68 | 36,9 | 10,3173 | 18,567 | 10,3188 |
| 69 | 36,9 | 10,3234 | 17,5023 | 10,3249 |
| 85 | 40,1 | 10,3926 | 18,0382 | 10,3944 |
| 86 | 40,1 | 10,2096 | 15,1681 | 10,2106 |
| 87 | 40,1 | 10,2664 | 17,5375 | 10,2681 |
| 103 | 47 | 10,3094 | 20,1722 | 10,3127 |
| 104 | 47 | 10,3088 | 15,2815 | 10,3103 |
| 105 | 47 | 10,4091 | 19,7714 | 10,4119 |
| 121 | 53,1 | 10,4516 | 14,7933 | 10,4532 |
| 122 | 53,1 | 10,3919 | 15,1589 | 10,3938 |
| 123 | 53,1 | 10,3448 | 19,0794 | 10,3479 |
| 139 | 59 | 10,4273 | 14,9801 | 10,4292 |
| 140 | 59 | 10,2292 | 15,5146 | 10,2313 |
| 141 | 59 | 10,2381 | 15,5197 | 10,2403 |
| 157 | 63 | 10,1345 | 15,734 | 10,1376 |
| 158 | 63 | 10,3217 | 15,123 | 10,3243 |
| 159 | 63 | 10,4071 | 15,471 | 10,4099 |

Experiment 12. 2-Butanol

| Vial | T(°C) | vial+cap [g] | vial+cap+solut. [g] | vial+cap+solid [g] |
|------|-------|--------------|---------------------|--------------------|
| 16 | 25,2 | 10,3544 | 17,6963 | 10,3551 |
| 17 | 25,2 | 10,4567 | 19,8641 | 10,4577 |
| 18 | 25,2 | 10,4287 | 16,7954 | 10,4293 |
| 34 | 29 | 10,3822 | 19,4177 | 10,3833 |
| 35 | 29 | 10,4170 | 16,3812 | 10,4179 |
| 36 | 29 | 10,3504 | 16,1048 | 10,3513 |
| 52 | 33 | 10,4879 | 19,7245 | 10,4893 |
| 53 | 33 | 10,4648 | 15,8018 | 10,4657 |
| 54 | 33 | 10,4397 | 15,2605 | 10,4405 |
| 70 | 37,1 | 10,3221 | 20,1906 | 10,3243 |
| 71 | 37,1 | 10,4013 | 20,1575 | 10,4033 |
| 72 | 37,1 | 10,3544 | 15,3328 | 10,3552 |
| 88 | 41,2 | 10,3656 | 20,1836 | 10,3678 |
| 89 | 41,2 | 10,3486 | 19,6717 | 10,3506 |
| 90 | 41,2 | 10,3980 | 15,3865 | 10,3993 |
| 106 | 47 | 10,3807 | 14,9289 | 10,3820 |
| 107 | 47 | 10,2078 | 15,1544 | 10,2091 |
| 108 | 47 | 10,3266 | 15,3079 | 10,3279 |
| 124 | 53 | 10,4161 | 14,9422 | 10,4178 |
| 125 | 53 | 10,4186 | 15,6242 | 10,4204 |
| 126 | 53 | 10,4997 | 15,4288 | 10,5015 |
| 142 | 59 | 10,4282 | 14,9894 | 10,4301 |
| 143 | 59 | 10,1927 | 14,8014 | 10,1946 |
| 144 | 59 | 10,4704 | 15,4066 | 10,4725 |
| 159 | 63 | 10,4721 | 17,4510 | 10,4754 |
| 160 | 63 | 10,1031 | 16,3333 | 10,1061 |
| 161 | 63 | 10,2743 | 17,0143 | 10,2775 |

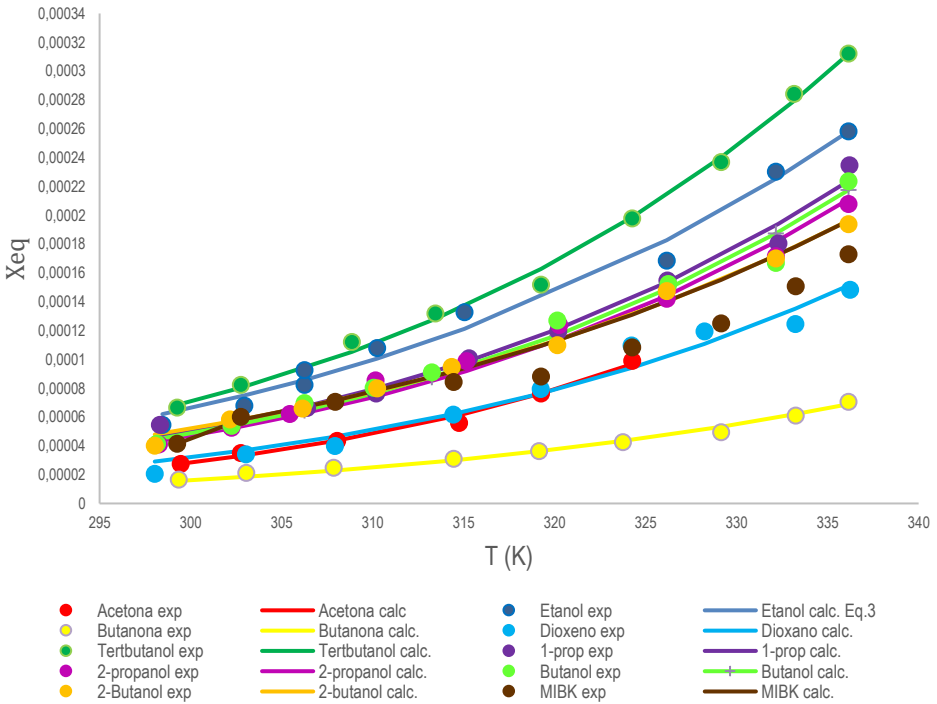
SOLUBILITY CURVES





APENDIX III: THERMODYNAMICAL ANALYSIS

Buchowski-Ksiazczak



Empirical Model

