NOVA SCHOOL OF
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BSc in Biochemistry

A COMPREHENSIVE SCREENING STUDY ON THE SOLUBILITY IN NADES BY USING HANSEN SOLUBILITY PARAMETERS

MASTER IN BIOORGANIC CHEMISTRY

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ABSTRACT

NADES, abbreviated from *Natural Deep Eutectic Systems*, are a promising new generation of green solvents formed by mixing two or more organic compounds, typically primary metabolites derived from plants such as alcohols, sugars, amino acids, etc. By combining these compounds in a specific molar ratio, they will interact mostly by hydrogen bonding which will lead to the formation of a translucent liquid that has a lower melting point than its constituents. Due to their significant characteristics, these systems have attracted the interest of many researchers and, therefore, have been studied in different areas, such as extraction, biomedical application, and biocatalysis among others. However, there is still a lack of information about most of its physicochemical properties, especially those necessary for a better understanding of its solubility behaviour. In this thesis, the use of Hansen Solubility Parameters (HSPs) was suggested to investigate the solubility of ibuprofen in hydrophilic and hydrophobic NADES. This evaluation was carried out using a set of theoretical models of HSPs and other parameters such as water content, polarity, dielectric constants, refractive indices, dipole moments, and Kamlet-Taft parameters. The empirical model of Hoftyzer and Van-Krevelen (HK) has demonstrated to be the most suitable one, for the theoretical determination of HSPs. Although the expected relationship between solubility and affinity was not found, it was possible with this work to gather several extremely useful information for the characterization of eutectic systems, as well as a large list containing the HSPs of various components of NADES.

Keywords: Natural Deep Eutectic Systems, Hansen solubility Parameters, Ibuprofen, solubility, polarity, Kamlet-Taft parameters

RESUMO

NADES, abreviado de *"Natural Deep Eutectic Systems"*, é uma nova geração de solventes verdes formados pela mistura de dois ou mais compostos orgânicos, tipicamente metabolitos primários derivados de plantas como álcoois, açúcares, aminoácidos, etc. Ao combinar esses compostos numa proporção molar específica, estes irão interagir principalmente por pontes de hidrogénio que levarão à formação de um líquido translúcido que possui um ponto de congelamento menor que seus constituintes. Devido às suas características, esses sistemas têm vindo a atrair o interesse de muitos investigadores e, por isso, têm sido estudados em diferentes áreas, como extração, aplicação biomédica e biocatálise. No entanto, ainda há uma grande falta de informação sobre a maioria de suas propriedades físico-químicas, principalmente as necessárias para um melhor entendimento de seu comportamento de solubilidade. Portanto, o uso dos Parâmetros de Solubilidade de Hansen (HSPs) foi sugerido para investigar a solubilidade do ibuprofeno em NADES hidrofílicos e hidrofóbicos. Esta avaliação foi realizada utilizando um conjunto de modelos teóricos de HSPs, e por outros parâmetros como teor de água, polaridade, constantes dielétricas, índices de refração, momentos dipolares e parâmetros de Kamlet-Taft. O modelo empírico de Hoftyzer e Van-Krevelen (HK) demonstrou ser o mais adequado, para a determinação teórica de HSPs. Embora não tenha sido encontrada a relação esperada entre solubilidade e afinidade, foi possível com este trabalho reunir várias informações extremamente úteis para a caracterização de sistemas eutécticos, bem como uma grande lista contendo as HSPs de diversos componentes do NADES.

Palavas chave: Natural Deep Eutectic Systems, Parâmetros de solubilidade de Hansen, Ibuprofeno, solubilidade, polaridade, parâmetros de Kamlet-Taft.

LIST OF PUBLICATIONS

Research article

C. C. Fernandes, R. Haghbakhsh, R. Marques, A. Paiva, L. Carlyle, and A. R. C. Duarte, 'Evaluation of Deep Eutectic Systems as an Alternative to Solvents in Painting Conservation', ACS Sustain. Chem. Eng., vol. 9, no. 46, pp. 15451–15460, 2021, doi: 10.1021/acssuschemeng.1c04591.

Communication in conferences

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Cláudio C. Fernandes, Reza Haghbakhsh, Alexandre Paiva, and Ana Rita C. Duarte. Use of Hansen Solubility Parameters (HSPs) to investigate the solubility behaviour of Hydrophilic and Hydrophobic NADESs. 15th of July 2022, 2nd Chemistry and Biochemistry Students meeting, Faculdade de Ciências da Universidade de Lisboa (FCUL), Portugal (oral communication).

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GLOSSARY

4NA	4-nitroaniline
AARD%	Average Absolute Relative Deviation percent
API	Active Pharmaceutical Ingredients
Bb	Beerbower
C.E.D	Cohesive Energy Density
DE	Dwamena equations
DES	Deep Eutectic Systems
DM4A	n,n-dimethyl-4-nitroaniline
DMSO	Dimethylsulphoxide
EM	Empirical Models
FTIR	Fourier Transform Infrared Spectroscopy
G	Gordon parameter
GCM	Group Contribution Method
GCM	Group Contribution Method
HB	Hydrogen Bond
HB	Hansen-Beerbower
HBA	Hydrogen Bond Accepter
HBD	Hydrogen Bond Donor

HK	Hoftyzer-Van Krevelen
HKF	Hoftyzer-Van Krevelen-Fedors
HOESY	Heteronuclear Overhauser Enhancement Spectroscopy
HPLC	High-Pressure Liquid Chromatography
HSPs	Hansen Solubility Parameters
ILs	Ionic liquids
KoS	Koenhen-Smolders
KTPs	Kamlet-Taft Parameters
NADES	Natural Deep Eutectic Systems
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser Effect Spectroscopy
NR	Nile red
OE	Original equations
RD%	Relative Deviation percent
SCF	Supercritical Fluids
SEM	Semi-Empirical Models
UV-Vis	Ultraviolet-visible
YAH	Yamamoto-Abbott-Hansen
Ymt	Yamamoto

SYMBOLS

α	Acidity parameter of Kamlet-Taft
N_A	Avogadro´s number (6.0221409 × 10^{23} mol^{-1})
δ_V	Bagley parameter
β	Basicity parameter of Kamlet-Taft
$E_T(30)$	Betaine (30) dye polarity scale/ Reichardt scale (in Kcal/mol)
k_B	Boltzmann constant (1.380649 × 10^{-23} m^2 kg s^{-2} K^{-1})
cal/cm^3	Calorie per centimetre cube
c´	Conversion factor (2.0455 $MPa^{1/2}$)
ºC	Degree Celsius (temperature unit)
ρ	Density
ε'	Dielectric constant (dimensionless)
$\Delta\delta_T$	Difference of total solubility parameter (Greenhalgh parameter)
μ	Dipole moment (in Debye)
Ra	Distance between the HPSs of the two materials
E_D	Energy from dispersion forces
E_H	Energy from hydrogen forces
E_P	Energy from polar forces
ΔH_{vap}	Enthalpy of vaporization

$\Delta_1^g H_m^0$	Enthalpy of vaporization (Kabo´s equation)
F_B	Formal concentration (g.dm^{-3})
G	Gordon parameter
δ_D	Hansen´s dispersion parameter
δ_H	Hansen´s hydrogen bond parameter
δ_P	Hansen´s polar parameter
R_0	Hansen´s sphere or radius of interaction
$\Delta\overline{\delta}$	Hoftyzer and Van Krevelen parameter
K	Kelvin (temperature unit)
KJ	Kilojoules (energy unit)
kK	KiloKaiser (1kK = 1000 cm^{-1} = 10000/ λ_{max} (nm))
γ_L	Liquid Surface Tension
λ_{max}	Maximum wavelength
MPa$^{1/2}$	Megapascal (1MPa$^{1/2}$= 10^3 Pa)
T_m	Melting temperature
μm	Micrometre
mg/mL	Milligrams per millilitre
mm	Millimetre
mN/m	Millinewton per meter
X_{Men}	Molar fraction of menthol
X_B	Molar ratio of compound B
V_m	Molar volume
Mw	Molecular weight
E_{NR}	Nile red dye polarity scale (in Kcal/mol)
μ_O	Onsager ´dipole moment (in Debye)

h	Planck´s constant ($6.62607004 \times 10^{-34}$ m^2.kg/s)
π^*	Polarizability parameter of Kamlet-Taft
w/w	Ratio measurement (weight for weight)
n_D	Refractive index
μ_S	Salem´ dipole moment (in Debye)
c	Speed of light in vacuum (299,792,458 m/s)
$X_{Men+LauA}$	Sum of the molar fraction of menthol and lauric acid
E_{coh}	Total cohesive energy or energy of vaporization
δ_T	Total solubility parameter
R	Universal gas constant (8.3145 cm^3.MPa.K^{-1}.mol^{-1})
η	Viscosity
W%	Water content (in percentage, %)
ϖ	Wavenumber (in cm^{-1})
$\bar{\upsilon}$	Wavenumber (in kK)

1

INTRODUCTION

1.1 A Greener Future!

The world is changing, but unfortunately for its worst. Hence, the scientific community is working hard to find any potential alternative to improve the conditions of our planet. In this battle against time, even small changes such as the replacement of toxic conventional organic solvents for greener solvents may play an important role, since it is well-known their negative effect on human health and the environment. In fact, in addition to climate change and the loss of biodiversity, the issue of chemical pollution was identified as the third major global challenge [1]. As result, and due to its benefits, such as waste and cost reduction, in recent years, the chemical and pharmaceutical industries are increasingly betting on green alternatives. Therefore, the scientific community has been looking for more solvents that come closer to water, the solvent ranked as the greenest. Any proposed alternative is at least expected to be cheap, abundantly accessible, non-toxic, non-polluting, and non-flammable such as water. Furthermore, to attract the attention of the chemical and pharmaceutical industries, it must have a good solubility range, as the main reason why water, although green, is not used as a single solvent in the synthesis process is because most organic compounds are not soluble in it [2].

For a solvent to be considered as green, it must meet all 12 principles of chemistry, suggested by Paul Anastas and John Warner, in 1998 [3]: 1. Prevent waste; 2. Atom economy; 3. Less hazardous synthesis; 4. Design benign chemicals; 5. Benign solvents and auxiliaries; 6. Design for energy efficiency; 7. Use for renewable feedstocks; 8. Reduce derivates; 9. Catalysis (vs. stoichiometric); 10. Design for degradation; 11. Real-Time analysis for pollution prevention; 12. Inherently benign chemistry for accident prevention. This list of established principles is extremely important, as it allows us not only to understand the impact of each solvent on the ecosystem, but also to identify potential new candidates. In this demand for sustainability, it is currently known that compounds such as supercritical fluids (SCF), ionic liquids (ILs), and deep eutectic systems (DES) have been highlighted in the field of green processes [4].

In this thesis, we will focus on one of the DES subclass, called natural DES (NADES), and on the study of some of their properties that will help us to better understand their character as a solvent. Thus, for this purpose, a set of empirical models of solubility was selected, since most of conventional analysis techniques are not prepared for these fluids, due to their nature and their relatively recent emergence [5]. This kind of approach, using computational modelling, has been increasingly employed in the scientific community mainly because of its benefits such as [6], [7]:

- No reagents are required, which contributes greatly to avoiding waste.
- Significantly reducing the resources required in the laboratory performing tests.
- Simple and practical: For models as those based on groups contribution it´s only necessary few information regarding the investigated compound (e.g., structure, molar weight, density, etc.)

In the case of solubility studies, computational studies can even help to predict whether two materials are soluble, to replace some toxic and harmful solvents, and also to understand the extent of the solvent-solute interaction. For example, Masumeh Mokhtarpour *et al.*, in 2020, used Hansen solubility parameters (HSPs) to study the solubility and solvation behaviour of 6 drugs in DES based on choline chloride [8]. Also, even more recently, Hemayat Shekaari *et al.*, used the empirical method, HSPs, to predict the solubility of antiepileptic drug phenytoin in mixtures of ethanol with DES such as Choline chloride:Glycerol (1:2) and Choline chloride:Ethylene glycol (1:2) [9]. In fact, not only in these two previous examples, but many of the authors who explore the applicability of these type of empirical models tend to focus mainly on DES-based on choline chloride, due to the fact this type of DES is very well described in the literature. This results in one of the major problematics, the lack of information regarding the other types of DES. Therefore, in this study, we intend to investigate different categories of DES, in order to provide a great and the diversified list of information related to DES solubility behaviour, which may be extremely useful for upcoming works. Furthermore, while the acronym "DES" is commonly used as an abbreviation for deep eutectic solvents in the literature, it is also recognized that not all eutectic mixtures may function as solvents [10], hence the investigated eutectic mixture will be regarded as a system here. That said, with sights set on a greener future, let´s make an overview of DES, and introduce our research subject, Natural DES (NADES).

1.2 Insight Deep eutectic systems (DES)

In short, deep eutectic system or "DES" was the term utilized by Abbot et al., in 2003, to classify a set of translucent and homogeneous liquids, which can be easy formed by mixing two or more organic compounds (solid or liquid) in a given molar ratio, where the interaction between a hydrogen-bond acceptor (HBA) compound and a hydrogen-bond donor (HBD) compound leads to charge delocalization and consequently, the decrease of the melting point [11]. When compared to the individual components, the melting point of the fluid formed is much lower. In other words, for DES formation it is necessary that the intermolecular forces, such as hydrogen-bond, are stronger than the intramolecular forces and rules the DES formation [12], [13]. For example, choline chloride and urea are both solid at room temperature and have a melting point of 302 ºC and 133 ºC, respectively. However, when mixed in a proportion of 1:2, it forms a liquid with a eutectic melting point at 12 ºC [14]. Theoretically, the "eutectic point" is defined as the lowest point on a solid–liquid phase diagram (as illustrated in **Figure 1**), where the eutectic temperature intersects with the eutectic composition. To put it in other words, this point signalizes the temperature at which a eutectic mixture is a unique composition of two or more non-miscible solid phases that, following association, form a liquid at a certain temperature [15].

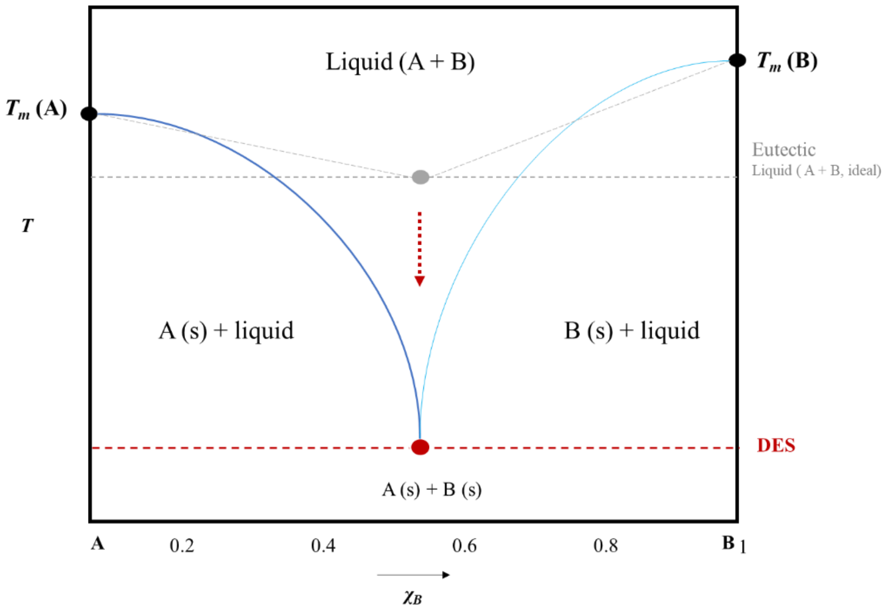


Figure 1: Schematic representation of a hypothetical DES´s solid–liquid phase diagram. (Adapted from Luís Santos [16]).

On another hand, it is also known that for thermodynamically unstable eutectic mixtures, the interaction between the constituents can be more easily affected by the environment and the geometry, which can even lead to the dissociation of the two components [17].

The determination of the DES interactions is often carried out and supported by spectroscopic methods such as Fourier Transform Infrared Spectroscopy (FTIR) and/or Nuclear Magnetic Resonance spectroscopy (NMR) [18]. In both techniques, the target functional groups are mainly hydroxyl and carbonyl, and the strategy is to compare the spectra of the individual components with the mixtures and identify bands corresponding to the O-H vibrations, in the case of using the FTIR spectroscopy, or signals representative of the interaction and/or deviation of the protons involved if it is NMR spectroscopy. Here, in addition to ^{1}H NMR spectroscopy, Nuclear Overhauser Effect Spectroscopy (NOESY) and Heteronuclear Overhauser Enhancement Spectroscopy (HOESY) are also commonly used in this characterization [19]. However, systems with high viscosity, mainly those based on amino acids and/or sugar, present spectra with low resolution, which makes it very difficult to differentiate the ^{1}H signals of each functional group. Meanwhile, in any of these techniques, the problem of low resolution, due to the high viscosity of NADES, can be solved either by modifying the environmental conditions, for example by operating at higher temperatures (e.g., 80 ºC) or diluting the systems [17].

1.3 DES Evolution and Applications

Although Abbot *et al.* have been widely referenced in the literature as the pioneers who introduced the expression “Deep Eutectic Solvents” in the scientific community, but it is also known that these mixtures exist long before, even the ILs. In fact, Frederick Guthrie, in 1884, was the first one to introduce the term “eutectic” (derivates from Greek, *ευτηκτος,*), which means easy or lowest melting, and he used it to describe “a lower temperature of liquefaction than that given by any other proportion” [20], [21]. Therefore, DES cannot be classified as a subclass of ILs or wrongly compared to it. But it is also the truth that is very difficult to distinguish them since they have similar properties such as polarity, low vapor pressure, low melting point, non-flammable, and high viscosity [15], [22], [23]. However, besides the difference in their starting material nature (organic compounds versus ions), ILs are single compounds, contrary to DES that can be binary, ternary, or quaternary mixtures. Moreover, there are some characteristics of DES that make them stand out, such as their cheaper and easier preparation method, lower toxicity of HDB compared to the metal salt of ILs, high biodegradability and biocompatibility [11], [22], [24]. Because of these remarkable features, these fluids have gained the interest of many researchers over the years, confirmed by the exponential increase of manuscript publications over the past decade, as shown in the following **Figure 2** [25]:

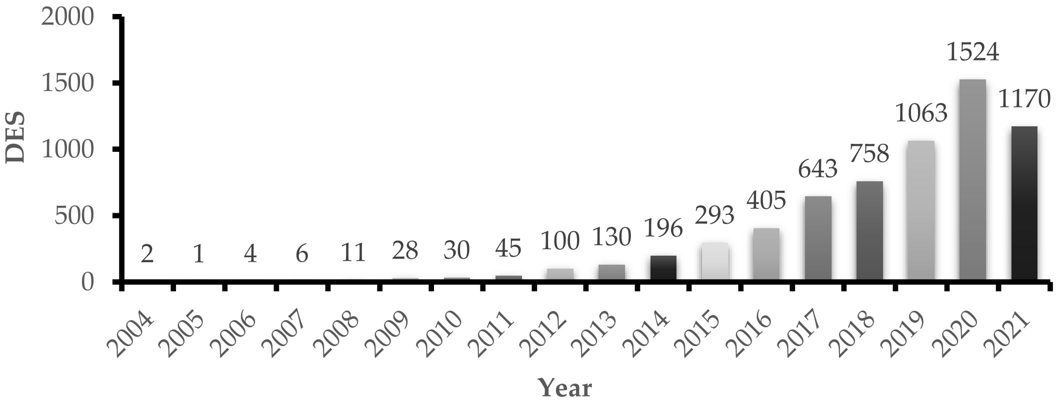


Figure 2: Number of DES articles published over the years reported by Web of Science. (Adapted from Laura Lomba [25])

DES clearly provides the scientific community with a new and interesting study object. Chemistry, electrochemistry, physic, and materials science were some of the major scientific fields that have contributed for them to stand out and slowly show their versatility, by studying its potential in the extraction process, biomedical applications, biocatalysts, cosmetic products, and therapeutic field [26]–[30]. Furthermore, this allowed, in addition to characterize and categorize the various eutectic mixture into different "subclass", according to the nature of their or application such as Natural DES (NADES) and Therapeutic DES (THEDES).

1.3.1 Natural Deep Eutectic Systems (NADES)

Due to the diversity of substances that can act as hydrogen bond donors (HBD) and/or hydrogen bond acceptors (HBA), the possibility of combining compounds that can result in DES is reported to be up to 10^6 [11]. Although, as mentioned before, initially most of the eutectic mixtures were based on the complexation of choline chloride with hydrogen donator such as carboxylic acids or urea, nowadays, other DES are being specifically designed to fulfill each desired application. When it comes to use natural primary metabolites such as sugars, terpenes, alcohols, choline derivatives, amino acids, and organic/fatty acids, this subclass of DES is denominated as Natural Deep Eutectic Systems (NADES) [12]. This thermology was suggested by Yuntao Dai et al., in 2013, who observed that many primary metabolites of plants can also change their state from solid to liquid when combined at given ratio, therefore acting as a typical deep eutectic solvent. Some of the common components used in DES or NADES formulation are shown in **Figure 3** [31]. Most of the known hydrophilic NADES are ternary and have in their constitution at least a sugar and water. Although sugars are chemically composed of various hydroxylic functional groups (-OH) that may play an important role in both HBD and HBA, in the combination of two sugars it is normally necessary an assistant compound which support the OH-OH interactions of the molecules since they are spatially quite distant. This issue is solved by introducing water as an intrinsic part of NADES. It was proven by NOESY experiments that water has a crucial role in NADES formation, by acting as a hydrogen bond mediator and thus allowing to shorten the intermolecular spatial distance between HBD and HBA. This leads to the formation of a higher-ordered hydrogen bonds network when the required quantity is added to the mixture [8], [10].

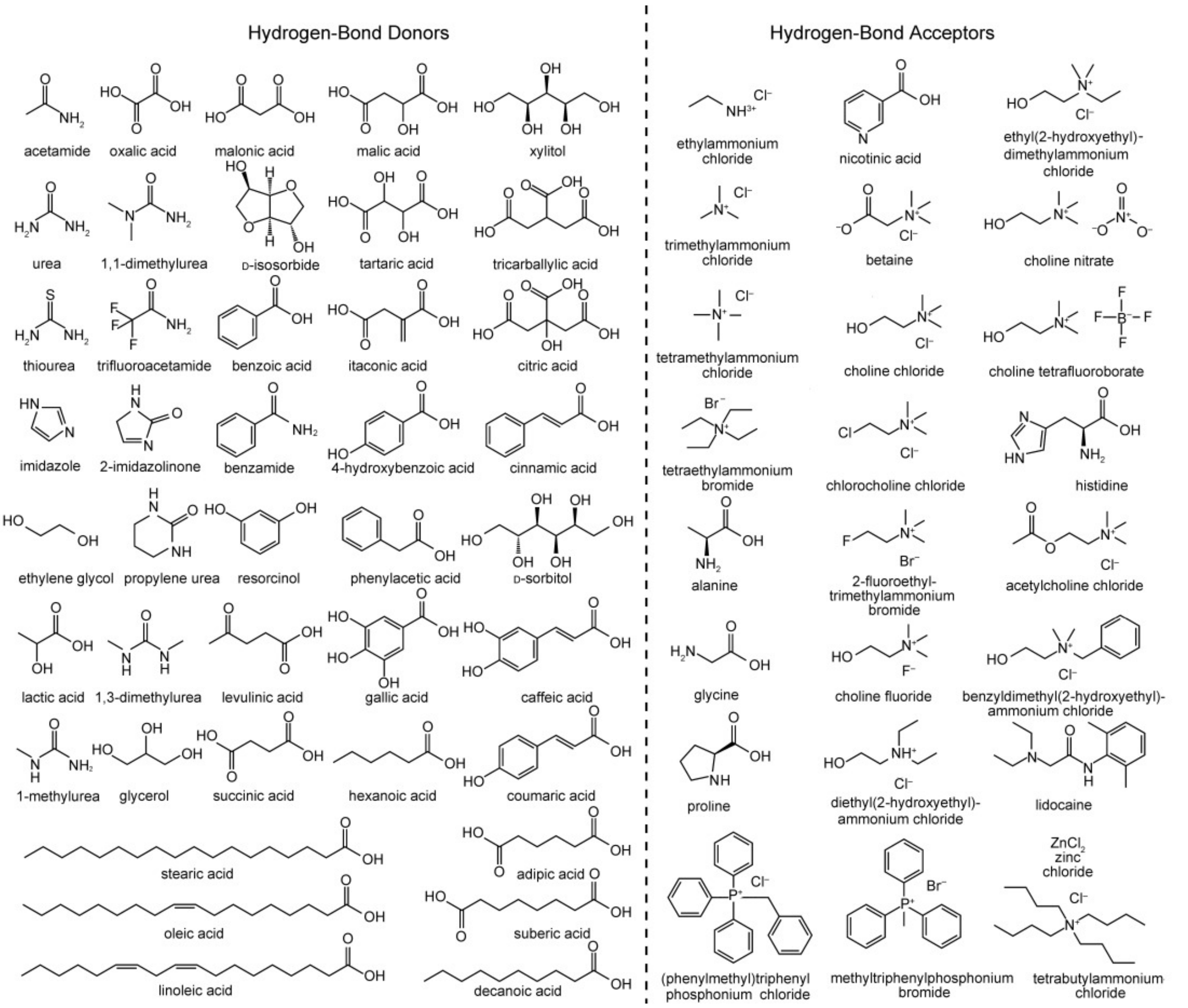


Figure 3: Chemical structure of some common hydrogen-bond donor (HBD) and hydrogen-bond accepter used in NADES formation. (Retrieved from [31])

On another hand, currently, hydrophobic mixtures based mainly on menthol, a secondary metabolite, with fatty acids (e.g., lauric acid, myristic acid, and decanoic acid) have gained a lot of attention due to their remarkable efficiency in (micro) extraction of compounds such as phytocannabinoids, polyphenols and biological macromolecules [28], [32]–[35].

1.4 Why are NADES Considered Green Solvents?

As referred previously, in section **1.1**, there are 12 principles in chemistry that need to be followed to evaluate a solvent as green. Regarding NADES features, there are many highlighted points that support the idea to classify these fluids as a new generation of green solvents: its bio-based nature, is undeniably a good indication to consider them low toxic, eco-friendly, and safer, thus, classifying them as a “green solvent” [15]. Furthermore, the yield and atom economy are considered 100%, as all initial components used are in the final blend. Thus, there are no emissions or waste during synthesis, and even if the E-factor parameter is calculated, given by the total sum of residual products divided by the total sum of the product, it is expected to be zero for the preparation of eutectic mixtures. Moreover, the preparation process occurs without any chemical reaction, but just the necessary composition, heat, and stirring, being water, the greener solvent, the only solvent used [11]. This clearly evidences the characteristics of green synthesis. Furthermore, compared to the organic traditional solvents, DES are considerably less volatile, which means that the risk of atmospheric pollution through the emission of volatile organic compounds is minimal. With all these advantageous features, it is not surprising the interest that has been noticed on the part of the scientific community.

One of the properties of NADES that is often highlighted is their high ability to solubilize compounds, for example, active pharmaceutical ingredients (API), which normally have a low solubility in solvents such as water [36]. Therefore, in this work, the use of Hansen solubility parameters (HSPs) is proposed to investigate the solubility mechanism of NADES.

1.5 Solubility Parameters

The earlier work of Scatchard et al. contributed to the development of Hildebrand and Scott´s (1950) theory, which, consequently, allowed them to a better exploration of the so-called *solubility parameter* [37], [38]. It was previously called the “Cohesion energy parameter” which is often used in studies targeting surface phenomena to describe the energy required to convert a liquid into a gas. Since evaporation all the types of bonds that unite the liquid´s molecules shall be broken, the energy of vaporization can be used to measure the total cohesive energy that holds them together in the liquid. Theoretically, the Hildebrand solubility parameter (δ_T) can be calculated using the following equation (**eqn. 1**):

$$\delta_T = \sqrt{C.E.D} = \sqrt{\frac{E_{coh}}{V_m}} = \sqrt{\frac{\Delta H_{vap} - RT}{V_m}} \qquad \text{eqn. 1}$$

Where δ_T = total solubility parameter (in $(cal/cm^3)^{1/2}$), C.E.D = cohesive energy density (also called cohesive pressure, in $cal.cm^{-3})^{1/2}$, E_{coh} = cohesive energy or energy vaporization of the compound (in $KJ.mol^{-1}$) and V_m = molar volume (in cm^3/mol). ΔH_{vap}, R, and T are the latent heat of vaporization (or also called enthalpy of vaporization), universal gas constant (8.314 $cm^3.MPa.K^{-1}.mol^{-1}$), and the absolute temperature (in Kelvins, K), respectively. ΔH_{vap} can be measured from the calorimetric or vapor-pressure analysis.

1.5.1 Hansen Solubility Parameters (HSPs): An Overview

Although Hildebrand´s solubility parameter has arguably contributed a lot to this new way of looking at solubilization between materials, a serious problem was highlighted in his theory. Hildebrand´s theory assumed that molecules can be described by a single parameter, completely ignoring the fact that polar and hydrogen-bonding interactions have a significant contribution to the association between them, which made his theory strictly applicable to nonpolar solutions, even though most solvents used are polar [38]. Meanwhile, this is still very used by researchers, even as a good base for the development of new solubility models, as the Hildebrand parameter by itself is considered completely unsuitable for real-world use [39]. Charles M. Hansen was one of the researchers who most shown interest in the Hildebrand parameter. So, during his Ph.D. thesis, in 1967, he proposed an extension approach of the single Hildebrand parameter, suggesting the division of the total energy of vaporization (E), described by Hildebrand, into three parts that represent the energetic contribution of nonpolar or dispersive forces (E_D), the energetic contribution from dipolar forces (E_P) and the energetic contribution from the hydrogen-bond interaction (E_H), as shown in **eqn. 2** [40]. The three Hansen solubility parameters (δ_D, δ_P and δ_H) emerged by dividing each of these energetic contributions by the molar volume (**eqn. 3**) of the compound, hence it is often written as **eqn. 4:**

$$E = E_D + E_P + E_H \qquad \text{eqn. 2}$$

$$\delta_D = \left(\frac{E_D}{V_m}\right)^{\frac{1}{2}} \; ; \delta_P = \left(\frac{E_P}{V_m}\right)^{\frac{1}{2}} \; ; \; \delta_H = \left(\frac{E_H}{V_m}\right)^{\frac{1}{2}} \qquad \text{eqn. 3}$$

$$\delta_t^2 = \delta_D^2 + \delta_P^2 + \delta_H^2 \qquad \text{eqn. 4}$$

Where δ_D is the dispersion contribution to the solubility parameter, δ_P, is the polar contribution to the solubility parameter, and δ_H, is the hydrogen bonding contribution to the solubility parameter. These parameters are seen as scales that quantify the contribution degree of the most common forces involved in intermolecular interactions and following the basic concept of "like dissolves like", as for Hansen, as well Hildebrand´s, claims that the high affinity between two materials means that their solubility parameters are very similar. Thus, for better understanding and visualization, HSPs are normally treated as three-dimensional coordinates that allow to locating the position of a given solvent in relation to the centre of the solute solubility sphere (e.g., polymers, fuels, drugs, or other chemicals), defined as Hansen´s sphere, interaction radius or R_0, as it can be visualized in **Figure 4** [41].

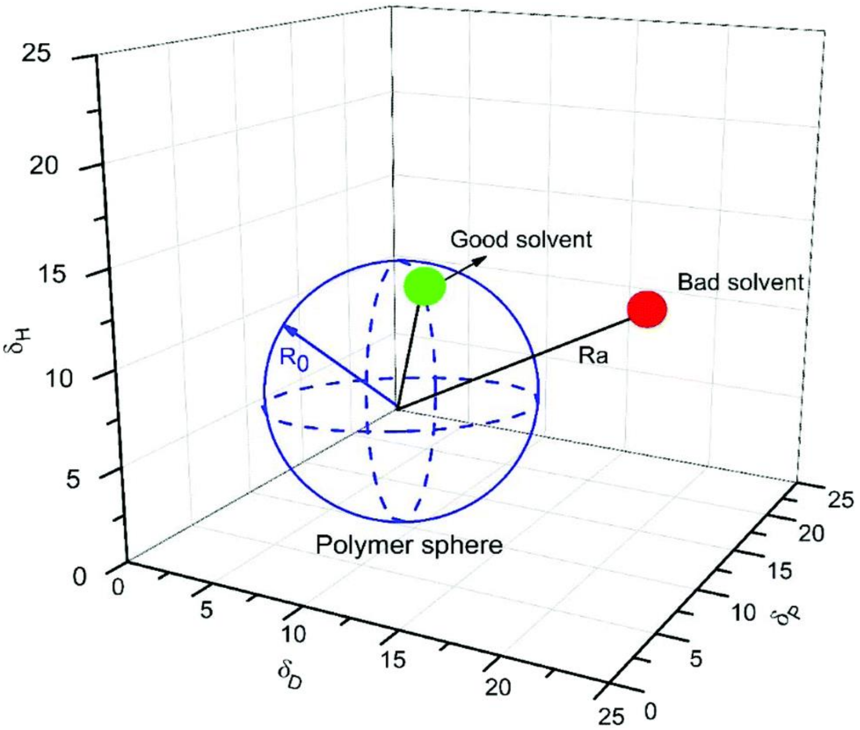


Figure 4: Hypothetical representation of Hansen´s sphere retrieved from reference [41].

Thus, knowing the HSPs of both solute and solvent, it is possible to calculate their dissimilarity factor (Ra), using the following equation (**eqn. 5**):

$$\mathrm{Ra} = \sqrt{4(\delta_D^{S1} - \delta_D^{S2})^2 + (\delta_P^{S1} - \delta_P^{S2})^2 + (\delta_H^{S1} - \delta_H^{S2})^2} \qquad \text{eqn. 5}$$

However, this equation is only valid for a pure solvent. In the case of a mixture of compounds or solvents, **eqn. 6**, presented by Jaime Lara et al., [42], is the most suitable:

$$\mathrm{Ra} = \sqrt{4(\delta_D^{S1} - \delta_D^{M})^2 + (\delta_P^{S1} - \delta_P^{M})^2 + (\delta_H^{S1} - \delta_H^{M})^2} \qquad \text{eqn. 6}$$

By the mixture rule:

$$\delta_D^M = \sum_i \varphi_i \delta_D^i \qquad \text{eqn. 7}$$

$$\delta_P^M = \sum_i \varphi_i \delta_P^i \qquad \text{eqn. 8}$$

$$\delta_H^M = \sum_i \varphi_i \delta_H^i \qquad \text{eqn. 9}$$

being,

$$\varphi_i = \frac{x_i V_i}{\sum_{j=1}^{k} x_j V_j} \qquad \text{eqn. 10}$$

Herein, the superscripts *S1* and *S2* denote solute and pure solvent, respectively, while *M*, corresponds to the mixture. φ_i, x_i, and V_i are, in turn, the volume fraction, the molar fraction, and the molar volume of component *i* in a mixture with *k* components. Finally, x_j and V_j are, respectively, the molar fraction and molar volume of component j, in a sum from component 1 to component *k*. Thus, employing **eqn. 11**, the miscibility/affinity degree can be determined through the relative energy difference (RED) calculation:

$$\mathrm{RED} = \frac{Ra}{R_0} \qquad \text{eqn. 11}$$

According to the results obtained, the following requirements are used to determine if the two materials will be likely to dissolve or not:

- If **RED > 1**: It means that the solute will **not** be soluble in the solvent.
- If **RED = 1**: It means that the solute **will be partially** soluble in the solvent.
- If **RED < 1:** It means that the solute **will be** soluble in the solvent.

Considering the fundamental principle of the NADES formation which, consequently, explains their low total vapor pressure, an experimental determination of their HSPs is somehow dubious as it requires the knowledge of their heat of vaporization. For the evaporation of any liquid to take place it is necessary the disruption of its intermolecular forces, the NADES hydrogen-bonds network certainly would be also affected in that process, making it very difficult to confirm the reliability of the results. To overcome this, researchers are increasingly adopting the use of empirical methods as they provide acceptable results. For example, more recently, Yu Chen [43] used Kabo´s empirical equation (**eqn. 12**) [44] that correlates the enthalpy of vaporization ($\Delta_1^g H_m^0$, in $\mathrm{KJ.mol^{-1}}$) with surface tension (γ_L, in $\mathrm{N.m^{-1}}$ or $\mathrm{J.m^{-2}}$), molar volume (V_m, in $\mathrm{m^3.mol^{-1}}$), and Avogadro number ($N_A = 6.022 \times 10^{23}\ \mathrm{mol^{-1}}$) to estimate the enthalpy of DES based on polyethylene glycol and then calculate the total/Hildebrand solubility parameter though **eqn. 1**.

$$\Delta_1^g H_m^0(298\ \mathrm{K}) = 0.01121\gamma_L V_m^{2/3} N_A^{1/3} + 2.4\ \mathrm{KJ.mol^{-1}} \qquad \text{eqn. 12}$$

However, historically, long before **eqn. 12** to be established, many renowned researchers such as Hansen and Skaarup, Koenhen and Smolders, Hildebrand, Beerbower, etc., had already proposed other different theoretical models that directly correlate the solubility parameters with related physicochemical properties. As these researchers' approaches do not require knowledge of the enthalpy of vaporization, they can, a priori, be used to predict the HSPs of eutectic mixtures. Examples of some of these correlations are shown in the next section. (**1.5.1.1**).

1.5.1.1 Estimation of HSPs: Semi-Empirical Models (SEM)

One of the great advantages of the subsequent correlative equations is that most of them allow the estimation of total and partial solubility parameters from the correlation with properties that are much easier to determine experimentally, such as Refractive index (n_D), dipole moment (μ) and liquid surface tension (γ_L) [45], [46]. Thus, in this thesis, this type of approach will be treated as a semi-empirical method to estimate the HSPs.

1.5.1.1.1 Dispersion Solubility Parameter (δ_D)

In general, the δ_D parameter measures the extension of the Van der Walls interactions or, in other words, the energy density that arises from dispersion bonds between molecules. This energy is present in all molecules and it regards their atomic forces; hence placing any two molecules within a few Angstroms from each other, generates a powerful attractive force between their atoms, due to the movement of electrons and, consequently, by the distribution of charges that forms an electric field which leads to the attraction of the molecules [47], [48].

Knowing that polarizability as well as London dispersion forces, are critical determinants for the interaction energy between nonpolar molecules and that polarizability is directly proportional to the Refractive index, Koenhen and Smolders [45] propose that:

$$\mathrm{\delta_{D\,(KoS)}} = 19.53\mathrm{n_D} - 11.35\ \left(\mathrm{in\ MPa^{\frac{1}{2}}}\right) \qquad \text{eqn. 13}$$

According to Koenhen and Smolders, the correlation shown in **eqn. 13** is valid for both polar and non-polar compounds, contrary to the **eqn. 14**, presented by Yamamoto-Abbott-Hansen cooperation, which is only applicable for non-polar [48].

$$\mathrm{\delta_{D\,(YAH)}} = \frac{\mathrm{n_D} - 0.784}{0.0395}\ \left(\mathrm{in\ MPa^{\frac{1}{2}}}\right) \qquad \text{eqn. 14}$$

The authors defend that this equation (**eqn. 14**) is only suitable for compounds that do not have a substantial contribution from parameters δ_P and δ_H, since in compounds such as alcohol it is hard to distinguish between the refractive index terms that are assigned to δ_D and those from δ_P and δ_H that increase density [48].

1.5.1.1.2 Polar Solubility Parameter (δ_P)

The δ_P parameter is a measure of the energy/ electrical attraction arising from dipolar intermolecular forces between molecules. Apart from certain hydrocarbons and unique compounds (e.g., in general, compounds with null dipole moment as those made exclusively of carbon and fluorine), this energy is crucial to almost every molecule [39], [47].

Böttcher [49] derived the following equation (**eqn. 15**) to predict the contribution of the substance's permanent dipoles to the C.E.D or δ_T [38]:

$$\mathrm{\delta_{P(Bot)}} = \sqrt{\left(\frac{12108}{\mathrm{V_m^2}}\frac{\varepsilon' - 1}{2\varepsilon' + \mathrm{n_D^2}}(\mathrm{n_D^2} + 2)\mu^2\right)} \times \mathrm{c}' \qquad \text{eqn. 15}$$

Where ε´and μ are the dielectric constant (dimensionless) and dipole moment (in Debye), respectively. This equation was then resigned and simplified by Hansen and Beerbower (HB) collaboration [50], who introduced **eqn. 16** [38]:

$$\delta_{\mathrm{P(HB)}} = \left(\frac{37.4\mu}{V_m^{\frac{1}{2}}}\right) \qquad \text{eqn. 16}$$

This equation is one of the most used, once after tested in several compounds it has been found to be trustworthy. Beerbower (Bb) independently [45], followed by Koenhen and Smolders (KoS), using the values obtained from Hildebrand and Hansen´s works, proposed very similar approaches (**eqn. 17** and **eqn. 18**, respectively) which establish that:

$$\delta_{\mathrm{P(Bb)}} = \left(\frac{9.5\mu}{V_m^{\frac{1}{2}}}\right) \times c' \qquad \text{eqn. 17}$$

$$\delta_{\mathrm{P(KoS')}} = \left(\frac{50.1\mu}{V_m^{\frac{3}{4}}}\right) \times c' \qquad \text{eqn. 18}$$

Here, the equations **eqn. 15**, **eqn. 17** and **eqn. 18** are expressed in $(\mathrm{cal/cm^3})^{1/2}$, therefore to obtain the result in $\mathrm{MPa}^{1/2}$ (SI unit), they result should be multiplied by the conversion factor (c' = 2.0455 $\mathrm{MPa}^{1/2}$) [38]; In case of **eqn. 16**, it is already expressed in $\mathrm{MPa}^{1/2}$. Additionally, despite the three last equations shown above (**eqn. 16** to **eqn. 18**) to estimate δ_P are clearly simpler than the Böettcher ones, the knowledge of the dipole moment (μ) of the compound is still required. In practice, the direct measurement of μ is very laborious and difficult to be determined, and it would be very complicated to use any of the four equations to estimate the δ_P parameter of NADES, since there is a clear lack of information about their μ, in the literature. Therefore, this parameter (μ) is mostly estimated using the equations derived by Debye, Kirkwood, and Onsager [51]. One of the closest approaches to this matter was carried out by Huyskens [52], investigating the μ of complexes formed by hydrogen bonds in the liquid phase through Onsager´s equation (**eqn. 19**) [53].

$$\mu_O = \sqrt{\left(\frac{9k_BT \times 10^{39}}{4\pi N_A}\right)\frac{(\varepsilon' - n_D^2)(2\varepsilon' - n_D^2)}{\varepsilon'(n_D^2 + 2)^2} \times \frac{1}{F_B}} \qquad \text{eqn. 19}$$

Here, F_B denotes the formal concentration (in mol.dm^{-3}) and k_B, the Boltzmann constant (1.38 × 10^{-23}.m^2.kg.s^{-2}. K^{-1}). Huyskens observed that Onsager's equations for pure polar liquids result in μ values that may be different from those of the gas phase. Though Kirkwood attributed such differences to the molecules' preferred orientation.

Salem also proposed a very useful and simpler expression (**eqn. 20**) that correlates the μ with ε′and V_m [51], [54]:

$$\mu_S = \sqrt{\frac{\varepsilon' \times V_m}{184} - 1} \qquad \text{eqn. 20}$$

Both equations will be tested here as it is still unknown their applicability in NADES field.

1.5.1.1.3 Hydrogen-Bonding Solubility Parameter (δ_H)

The δ_H parameter measures the energy from hydrogen-bonds interaction between molecules. It is also often viewed as a form of polar force since it is the consequence of a dipole-dipole attraction or electron exchange between a hydrogen atom covalently bound to a very electronegative atom (such as F, O, or N) in one molecule with a very electronegative atom in another molecule [40]. Among the three HSPs, δ_H is considered the most controversial parameter and was even pointed out by Stavroudis and Blank as a limitation of the HSPs, since Hansen's assumption did not explain the nature of all hydrogen bonding [55], in other words, according to these two authors, this single parameter does not dictate the character of a compound to act as a donor or an accepter.

Hansen, in his first approach, evaluated the possibility to determine the δ_H contribution through the energy values obtained from infrared spectroscopy among other measurements. Thus, analyzing the spectrum of various alcohol-based compounds, he found a suitable value for the energy of the OH···O bond nearly 5000 cal/mol, calculated from the wavenumber of the OH bands. Hence, he proposed that it is possible to calculate the cohesive energy density and the associated hydrogen bond solubility parameter for a solvent by assigning 5000 cal/mol of the solvent evaporation energy for each alcohol group that contains [40].

This value was then adjusted for the molecule's molar volume and its number of their alcohol groups (n), giving rise to the **eqn. 21**:

$$\delta_H = \left(\sqrt{\frac{5000 \times n}{V_m}}\right) \times c' \left(\text{in MPa}^{\frac{1}{2}}\right) \qquad \text{eqn. 21}$$

Another approach to calculate δ_H, recommended by Hansen, is to subtract the dispersion and polar contribution parameters from the total solubility parameter:

$$\delta_H = \sqrt{\delta_T^2 - (\delta_D^2 + \delta_P^2)} \qquad \text{eqn. 22}$$

The equation above (**eqn. 22**), which suggests that the remaining forces are all placed in δ_H, is in fact the most used, but it requires that reliable data is available, and still, one of the biggest challenges remain in how to get either the enthalpy of vaporization or the total solubility parameter (δ_T) for high viscous or non-volatile compounds. Yet, in exploration of the literature, a wide number of equations that correlates HSPs or δ_T (or C.E.D) with surface tension were found. A set of these correlations is organized in **Table 1**.

Table 1: Some correlations between HSPs and Surface tension, reported in the literature.

Formula	Observation	Reference	Eqn
$\delta_D^2 + k(\delta_P^2 + \delta_H^2) = 17\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)$	k = 0.80 (homologous series) k = 0.265 (for normal alcohols) k = 10.3 (for n-alkyl benzenes)	Skaarup and Hansen [38]	eqn. 23
$\delta_D^2 + 0.632\ \delta_P^2 + 0.632\ \delta_H^2 = 13.9\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)$	Applicable for non-alcohols	Beerbower [84], [45]	eqn. 24

$\delta_D^2 + \delta_P^2 + 0.06\,\delta_H^2 = 13.9\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)$	Applicable for most alcohols.		eqn. 25
$\delta_D^2 + 0.7152(\delta_P^2 + \delta_H^2) = 13.9\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)$	A modification proposed by Hansen [38].		eqn. 26
$\delta_T\,(\mathrm{cal.cm^{-3}})^{1/2} = \mathrm{k}'\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)^m$	K'= 3.741 and m = 0.5		eqn. 27
$\delta_D^2 + \delta_P^2 = 13.8\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)$	Reasonable for most compounds.	Koenhen and Smolders [45]	eqn. 28
$\delta_T\,(\mathrm{cal.cm^{-3}})^{1/2} = 4.1\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)^{0.43}$	Applicable for polar and nonpolar liquids.	Hildebrand and Scott and Lee [56]	eqn. 29
$\delta_T\,(\mathrm{cal.cm^{-3}})^{1/2} = \mathrm{k}'\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)^m$	k' = 3.74 and m = 1: If $nOH + nCOOH + nCOH = 0$; Otherwise: k' = 5.927 and m = 0.45	Sheldon [57]	eqn. 30
$\delta_T\,(\mathrm{cal.cm^{-3}})^{1/2} = 4.0\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)^{0.59}$	Used in cellulose polymer.	Jarray [58]	eqn. 31
$\delta_T\,(\mathrm{cal.cm^{-3}})^{1/2} = 4.0\left(\frac{\gamma_L}{V_m^{\frac{1}{3}}}\right)^{0.5}$	For IL it is often used the molecular volume, V_{mol}, ($V_{mol} = V_m/N_A$).	Gordon [59]	eqn. 32

For example, knowing the surface tension and the two other HSPs of a compound, δ_D, and δ_P, the δ_H may be calculated using any of the four first equations (**eqn. 23** to **eqn. 26**), shown in **Table 1**. Besides, δ_H can also be predicted by calculating the δ_T parameter, using the equations (**eqn. 27** to **eqn. 32**), and following the **eqn. 22**. Still in this list, it is essential to highlight the approach of Gordon (**eqn. 32**) as one of the most important and appropriated for this investigation. This is mainly due to the fact that the Gordon parameter (G) allows the evaluation of non-volatile compounds, i.e., those that tend to decompose before the vaporization such as DES, IL´s, and polymers; additionally, comparatively to the enthalpy of vaporization, it is much easier to be measured; therefore, it is commonly suggested as an alternative for C.E.D [60].

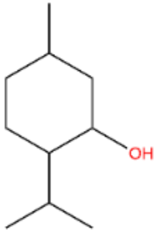
Besides surface tension, the correlations between HSPs/ δ_T and properties such as intrinsic viscosity and activation energy of viscosity are also reported, and they have been employed in the field of green solvents such as ILs [61]–[63]. However, since these kinds of correlations are not included in this study, this introduction will not be going into depth in this topic.

In general, it is still difficult to estimate the HSPs from the semi-empirical models, because, as mentioned before, most of the desired physicochemical properties are not available. Therefore, alternative authors are increasingly adopting the use of empirical models, especially those based on the group contribution methods (GCM).

1.5.1.2 Estimation of HSPs: Empirical Models (EM)

Many empirical models have been developed over the years, and this has certainly made it easier today to estimate the solubility parameters. Currently, there are various satisfactory models that are widely recommended in the absence of experimental data, namely, those proposed by Hansen and Beerbower [38], Hoftyzer and Van Krevelen [64], Fedors [65], Stefanis and Panayiotou [66], [67], Hoy [68], and Yamamoto [48], [69]. They are all based on the group contribution method (GCM), meaning that each functional group present in the molecular structure serves a purpose that is represented in each property. For example, using the table provided by Stefanis and Panayiotou [66], with the values assigned to the contribution of the various functional groups, the HSPs of DL-Menthol can be estimated by decomposing the molecule into its different constituent groups, as it can be seen in **Table 2** (see more information about empirical models in the appendix, section **A. 2**).

Table 2: Stefanis and Panayiotou´s first-order group contribution of DL-Menthol´s HSPs.

Structure	**Groups**	n_i	δ_{di}	δ_{pi}	δ_{hbi}
	CH3	3	-123.01	-1.6444	-0.7458
	CH2	3	1.82	-0.3141	-0.3877
	>CH-	4	82.94	0.6051	-0.2064
	-OH	1	-0.3462	1.1404	7.1908
	∑	-	-61.78	-2.40	3.13

Since no second-order group contribution it´s being assumed for this calculation, Stefanis equations can be rewritten as:

$$\delta_D = \left(\sum n_i \delta_{di} + 959.11\right)^{0.4126} = 16.53\ \mathrm{MPa}^{1/2}$$

$$\delta_P = \left(\sum n_i \delta_{pi} + 0.76134\right) = 5.22\ \mathrm{MPa}^{1/2}$$

$$\delta_H = \left(\sum n_i \delta_{hbi} + 0.77003\right) = 10.84\ \mathrm{MPa}^{1/2}$$

$$\delta_T = \sqrt{\delta_D^2 + \delta_P^2 + \delta_H^2} = 20.45\ \mathrm{MPa}^{1/2}$$

where n_i is the frequency with which group *i* appears and δ_{di}, δ_{pi} and δ_{hbi} are, respectively, the dispersion, polar, and hydrogen bond contributions of group *i*. According to Hansen [38], the solubility parameters of L-Menthol are: δ_D = 16.6 MPa$^{1/2}$, δ_P = 4.7 MPa$^{1/}$2, δ_H = 10.6 MPa$^{1/2}$ and δ_T = 20.25 MPa$^{1/2}$. The value of the average relative deviation percent, AARD% (**eqn. 33**), between the three predicted and experimental HSPs is 4.48%, which shows a good agreement between the results.

$$\mathrm{AARD\%} = \frac{100}{\mathrm{N}} \sum_{\mathrm{i}}^{\mathrm{N}} \left| \frac{\delta_{\mathrm{i,exp}} - \delta_{\mathrm{i,cal}}}{\delta_{\mathrm{i,exp}}} \right| \qquad \text{eqn. 33}$$

$$\mathrm{RD\%} = 100 \left(\left| \frac{\delta_{\mathrm{T,exp}} - \delta_{\mathrm{T,cal}}}{\delta_{\mathrm{T,exp}}} \right| \right) \qquad \text{eqn. 34}$$

Furthermore, comparing the δ_T values from the two methods, through their relative deviation percentage, RD% (**eqn. 34**), it is possible to observe that the difference between them is lower than 1%, confirming even more the reliability of the empirical method.

In general, a set of models were here presented, which could be used to estimate the HSPs, however, none of them has shown how to determine the R_0 parameter. This is because, in practice, the R_0 is the most problematic parameter, as it must be determined experimentally using a set of organic solvents with known HSPs and classify them as "good" or "bad", according to their solubility capacity [47]. However, most of these listed solvents are toxic, expensive, and hard to manage due to their high volatility, which leads to the requirement of many new approaches to evaluate the affinity/miscibility degree.

1.5.1.3 Assessment of the Miscibility

Another great advantage brought by the empirical models was to eliminate the need to have the R_0 parameter and therefore the necessity to build a 3D-plot to describe the interaction between solute and solvent. The reason for this is that some authors have proposed other alternative methods for the assessment of the degree of solubility between materials [70].

Bagley [71], for instance, assumes that the miscibility evaluation can also be done using a 2D graph. This conclusion was drawn after he observed that, contrarily to δ_H, the parameters δ_D and δ_P have similar thermodynamic properties, which allowed him to introduce a new combined solubility parameter, δ_V (**eqn. 35**):

$$\delta_{\mathrm{V}} = \sqrt{\delta_{\mathrm{D}}^2 + \delta_{\mathrm{P}}^2} \qquad \text{eqn. 35}$$

Thus, the Bagley's 2D-plot is built by correlating δ_V as a function of δ_H, and the evaluation is then proceeded using the relative distance in the Bagley´s plot, called $Ra_{(V)}$, calculated by the following equation (**eqn. 36**):

$$Ra_{(V)} = \sqrt{4(\delta_V^{S1} - \delta_V^{S2})^2 + (\delta_H^{S1} - \delta_H^{S2})^2} \qquad \text{eqn. 36}$$

Such a relationship (δ_V Vs δ_H) has been particularly helpful to understand how well solvents and polymers dissolve in each other [71], and according to the Bagley, these substances are only miscible if $Ra_{(V)} \leq 5.6$ MPa$^{1/2}$.

Another solubility threshold value was suggested by Hoftyzer and Van Krevelen (HK) who described the mixing between materials using $\Delta\bar{\delta}$, and introduced the following condition, expressed in **eqn. 37**, to consider that two materials are miscible [64]:

$$\Delta\bar{\delta} = \sqrt{(\delta_D^{S1} - \delta_D^{S2})^2 + (\delta_P^{S1} - \delta_P^{S2})^2 + (\delta_H^{S1} - \delta_H^{S2})^2} \leq 5\ \mathrm{MPa}^{1/2} \qquad \text{eqn. 37}$$

The δ_T parameter can also be an assessment of solubility (**eqn. 38**). In fact, this approach, proposed by Greenhalgh *et al.* [72], is apparently one of the most frequently employed [70].

$$\Delta\delta_T = \left|\delta_T^{S1} - \delta_T^{S2}\right| \qquad \text{eqn. 38}$$

After studying the solubility of a series of compounds, Greenhalgh found that only combinations with $\Delta\delta_T < 7\ \mathrm{MPa}^{1/2}$ are more likely to solubilize and that a $\Delta\delta_T > 10\ \mathrm{MPa}^{1/2}$ indicates that the mixing is unlikely to occur. Hansen, on the other side, claims that using the Hildebrand total solubility parameter the materials are only likely to dissolve each other if $\Delta\delta_T < 1.8\ (\mathrm{cal/cm}^{\frac{3}{2}})^{\frac{1}{2}}$ [38].

In general, although HSPs is unquestionably a very powerful tool for this investigation, it is also a fact that only by itself is not enough to explain the dissolution phenomena, mainly for compounds such as complex as NADES. Certainly, more tools are needed to explain the Lewis acidic/basic properties of these substances. Therefore, to further support and enrich this study, an assessment of the solvatochromic behaviour of NADES was also carried out.

1.6 Solvatochromism

Any chemical compound used in UV/visible/near-IR absorption spectroscopy is inevitably subjected to interference from its surrounding's dynamic process. For example, the so-called “probes” or “dyes” are compounds that can variate their colour depending on the solvent used [73]. *Arthur Hantzsch* denominated this phenomenon as “solvatochromism” [74]. Since the vast majority of molecules do not have this property, some theories have been used to explain its mechanism. According to *Otto Witt´s* theory (1876), there are two peculiar characteristics to identifying dyes: first, is the presence of some groups such as nitro, quinoid and azo, also known as chromophores (typically electron-withdrawing), which are responsible for to imparts colour when absorbing light within the visible region of the spectra; the second essential requirement is the presence of auxochromes (normally electron-donating), that are a group of atoms next that may assist the chromophores and deepen the colour, by changing their ability to absorb light [23]. Although its great contribution to understanding the mechanism of dyes, the earlier Witt´s theory was overtaken by the modern electronic structure theory, which states that the colour of dye that is exhibited is a consequence of the excitation of π-electrons ($\pi \rightarrow \pi^*$) by visible light [24]. Dyes usually present large variations in the permanent dipole moment of their excited state, which lead them to produce different spectra of colours, as the polarity of different solvents [20]. Thus, each solvent has a different effect on the ground and the first excited state of the light-absorbing molecule, resulting in a change in the size of the energy transition gap and consequently the solvatochromism phenomena [20]. Depending on its solvation strength, it can even lead to significant changes in the intensity, shape, and position of the probe's absorption bands [74]. Among the various solvatochromic dyes currently known, the Reichardt dye (pyridinium N-phenolate betaine or Betaine dye 30), Nile Red (NR), n,n-dimethyl-4-nitroaniline (DMNA), and 4-nitroaniline (4NA), as shown respectively in **Figure 5**, **I**, **II**, **III** and **IV**, and as can be seen, all of then contain at least an aromatic ring, which allows the transition $\pi \rightarrow \pi^*$. Reichardt dye and NR are two of the most widely used dyes for determining the polarity of traditional organic solvents, ionic liquids as well other mixers such as DES [75], [76].

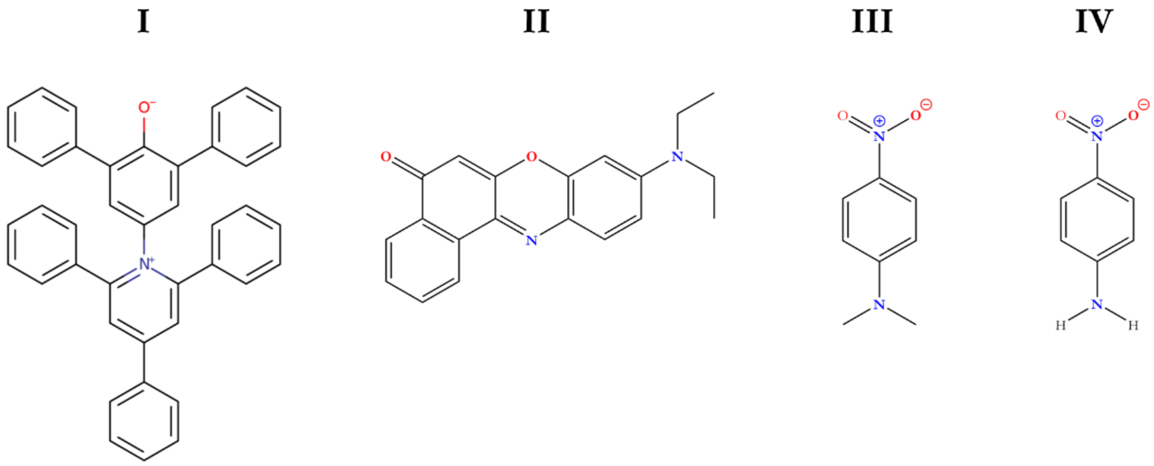


Figure 5: Molecular structure of the solvatochromic probes: I, II, III, IV correspond to pyridinium N-phenolate betaine (Reichardt´s dye or Betaine dye 30)), Nile red (NR), n,n-dimethyl-4-nitroaniline (DM4A) and 4-nitroaniline (4NA) dyes, respectively.

Reichardt´s dye belongs to a peculiar class of compounds that exhibit a "negative solvatochromism "shift (also called blue or hypsochromic shift, **Figure 6 (a)**) of Uv/vis/near-IR absorption band [20]. This is because of its zwitterionic nature in its ground state, which is highly dipolar than its excited state, therefore much better stabilized as the polarity of the solvent increases; thus, the transition energy shifts to higher energy, resulting in absorption at the lowest wavelength in the UV-visible spectrum [74], [77]–[79]. One of the concerns related to the use of Reichardt stain is its high sensitivity to solvents capable of donating hydrogen bonds (HBD), which, in an acidic medium, makes its phenolate group susceptible to protonation and, consequently, to loss of response to the solvent, as well as its ability to act as a polarity indicator [79], [80].

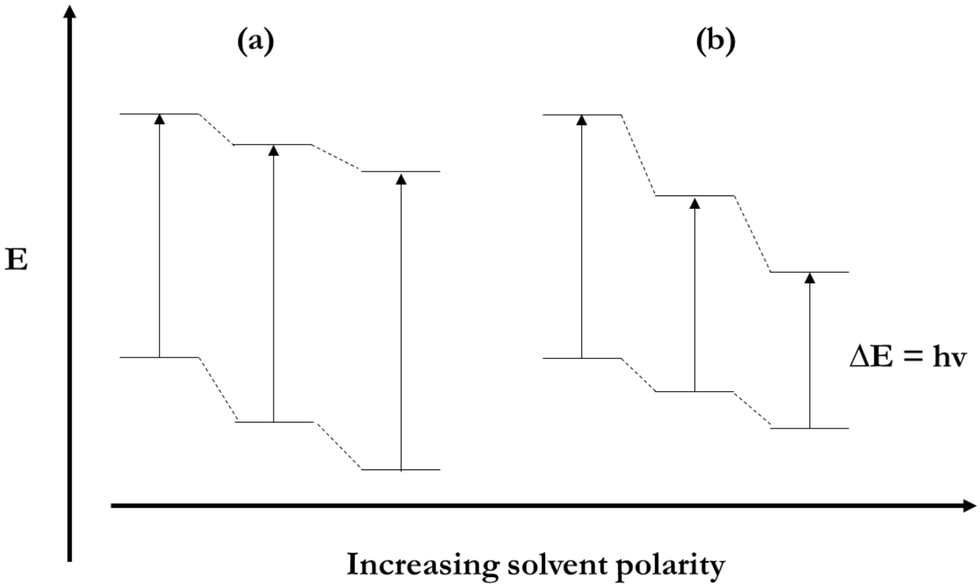


Figure 6: Schematic representation that explains the solvent polarity effect on transition energy, adapted from reference [79]. (a) represents the negative solvatochromism (hypsochromic shift) and (b) is the positive solvatochromism (bathochromic shift).

NR, contrary to betaine dye 30, exhibits a "positive solvatochromism" shift (red or Bathochromic shift, **Figure 6 (b)**), meaning that the increase of solvent polarity stabilizes rather its excited state (larger dipole moment) than its ground state. Hence, the transition energy is shifted to lower energy, which consequently causes absorption to occur at the longer wavelength of the visible spectrum [73], [74], [77]–[79], [81]–[84].

1.6.1 Polarity scales: $E_T(30)$ and E_{NR}

In addition to its characteristics as a photochemically stable substance with strong fluorescence and low basicity, NR dye, unlike Reichardt´s dye, is soluble in non-polar media and stable in extremely acidic media, which allows it not to suffer losses in molar absorptivity, and not to be significantly affected by hydrogen bonding solvents [80]. Therefore, the $E_T(30)$, described as Reichardt´s dye polarity scale, often is replaced by the NR scale, E_{NR} (see **eqn. 39**), which in fact, will be the polarity scale used in this study [85].

$$\mathrm{E_T(30)} = \mathrm{E_{NR}} = \mathrm{hc\nu_{max}N_A} = (2.8591 \times 10^{-3})\nu_{max} = \frac{28591.5}{\lambda_{max}} \qquad \text{eqn. 39}$$

Where $E_T(30)$ and E_{NR}, are the molar transition energy or electrophilicity (in Reichardt and Nile red dye scale, respectively, in Kcal/mol); h, c, ν, N_A and λ_{max} are Planck´s constant (6.63×10^{-34} m^2.kg/s), speed of light in vacuum (3.00×10^8 m/s), wavenumber, Avogadro´s number (6.02×10^{23} mol^{-1}) and maximum wavelength (in nm).

1.6.2 Kamlet-Taft Parameters (KTPs)

DM4A and 4NA, like NR, show positive solvatochromism. These two, in combination with $E_T(30)$ or E_{NR}, are commonly used to calculate Kamlet-Taft parameters (KTP) of DES [75]. Therefore, it is an essential tool to be applied in this instigation, since it allows describe the solvent's activities, evaluating their properties such as dipolarity/polarizability (π*), hydrogen-bond donor ability or acidity (α) and hydrogen-bond acceptor ability or basicity (β). This approach, using multiparameter linear polarity parameters, was developed by Kamlet, Abboud e Taft, analyzing the specific intermolecular interaction (e.g., dipole/dipole, coulombic, and hydrogen-bonding) between more than 45 dyes in approximately 200 different solvents [54], [29].

1.6.2.1 Dipolarity/polarizability scale (π*)

The π* parameter provides, in simultaneous, an estimation of the solvent´s dipolarity and polarizability, by measuring, simultaneously, the non-specific intermolecular interaction (dispersive/ van der Waals interactions, dipole-dipole e dipole-induced) involved in solute-solvent and the ability of the solvent to stabilize a nearby charge or dipole through nonspecific dielectric interactions [20]. The π* scale, when normalized, using the DM4A probe wavenumber obtained from pair cyclohexane (π* = 0.0) and DMSO (π* = 1.0), is calculated through the **eqn. 40**:

$$\pi^* = \frac{\bar{\upsilon}_{\mathrm{solvent}} - \bar{\upsilon}_{\mathrm{cyclohexane}}}{\bar{\upsilon}_{\mathrm{DMSO}} - \bar{\upsilon}_{\mathrm{cyclohexane}}} \qquad \text{eqn. 40}$$

Where, DMSO is dimethylsulfoxide and, $\bar{\upsilon}$ (in kK), is the wavenumber ($\bar{\upsilon} = 10^7/ \lambda_{max}$ (nm)). The **eqn. 40** can be simplified to give the **eqn. 41** [28]:

$$\pi^* = 0.314\,(27.52 - \varpi_{\mathrm{DM4A}})$$ eqn. 41

Being ϖ, also the wavelength, in in cm^{-1}(ϖ = 1/ ($\lambda_{\max}$ (nm) × 10^{-4})). π* is considered the heart of KTP and, therefore, over the years it has been correlated with different physico-chemical properties. For example, Marcus [86], in 1991, provides a set of equations that establish a relationship between the π* of aliphatic, polyhalogenated aliphatic, and aromatic solvents with their dipole moment (μ), as shown, in **eqn. 42**, **eqn. 43** and **eqn. 44**, respectively [87]:

$$\pi^* = 0.03 + 0.23\mu$$ eqn. 42

$$\pi^* = 0.27 + 0.35\mu$$ eqn. 43

$$\pi^* = 0.56 + 0.11\mu$$ eqn. 44

Bekareks [87] also made a great contribution, proposing a novel approach to estimate the π* parameter of aliphatic and aromatic solvents (**eqn. 45** and **eqn. 46**, respectively), through a linear correlation with their dielectric constant (ε′) and refractive index (n_D).

$$\pi^* = -0.573 + 14.65\frac{(\varepsilon' - 1)(n_D^2 - 1)}{(2\varepsilon' + 1)(2n_D^2 + 1)}$$ eqn. 45

$$\pi^* = -0.058 + 8.08\frac{(\varepsilon' - 1)(n_D^2 - 1)}{(2\varepsilon' + 1)(2n_D^2 + 1)}$$ eqn. 46

1.6.2.2 Hydrogen-bond donor ability scale (*α*)

The Kamlet-Taft *α* parameter is related to the acidity of or the capacity of a solvent to donate charge. Its estimation is usually made using the **eqn. 47**, which is not suitable for this study, due to the acid character of the hydrophobic NADES. Therefore, *α* scale will be evaluated using the equation proposed by Dwamena et al (**eqn. 48**) [76].

$$\alpha = 0.0649 * \left(E_T(30)\right) - 0.72\pi^* - 2.03$$ eqn. 47

$$\alpha = \frac{19.967 - 1.024\pi^* - \varpi_{NR}}{1.6078}$$ eqn. 48

1.6.2.3 Hydrogen-bond acceptor ability scale (β)

The basicity of a HBA solvent or its capacity to function as an electron-pair donor, through a specific dye-solvent, can be measured through the β parameter. It is usually done using the **eqn. 49**, presented by Kamlet-Taft [88]. This equation is one of the most employed and it has been even used in the study of solvents such as ILs and DES [76], [84]. So, the β parameter of the desired solvent can be estimated if the maximum absorption number waves of the indicator´s pair, such as DM4A/4NA, in the reference´s solvents DMSO and cyclohexane are known.

$$\beta = \frac{0.76(\Delta\bar{\upsilon}_{\text{solvent}} - \Delta\bar{\upsilon}_{\text{cyclohexane}})}{\Delta\bar{\upsilon}_{\text{DMSO}} - \Delta\bar{\upsilon}_{\text{cyclohexane}}}$$ eqn. 49

Where $\Delta\nu = \nu_{\text{(n,n-dimethyl-4-nitroaniline)}} - \nu_{\text{(4-nitroaniline)}}$.
Commonly, **eqn. 49** is simplified and written as **eqn. 50** [28]:

$$\beta = \frac{1.035\varpi_{DM4A} + 2.64 - \varpi_{4NA}}{2.80}$$ eqn. 50

Among all the shown dyes, 4NA (4-nitroaniline) is considered the special one, because contrary to NR, betaine dye 30 or DM4A it can be used both to measure the HBA and HBD ability of a solvent. This is only possible because, as can be seen by its chemical structure (see **Figure 5 (IV)**), 4NA contains an amine group that allows it to act also as HBD, while the oxygen and nitrogen atoms present in the other indicators (see **Figure 5 (IV)**) can only provide them the HBA´s behaviour. Thus, knowing the π*, the 4NA dye can also be used to measure the basicity, following the **eqn. 51**, as proposed by Marcus [86]:

$$\beta = 0.358\ (31.10 - \varpi_{4NA}) - 1.125\pi^*$$ eqn. 51

The KTPs are, undoubtedly, a fundamental tool for this investigation, since they provide a set of bases that may help to better explaining of NADES solubility behaviour. Moreover, it has also been used to identify and classify potential switchable solvents and explore them as an alternative to hazardous solvents [89], [90]. Functions that will certainly serve the purpose of this thesis.

1.7 Aim of the Thesis

The main purpose of this thesis is to evaluate the applicability of HSPs in NADES field, using a set of famous theoretical models. Thus, to achieve this goal, the following steps were followed:

1st. List a set of systems that allow the most comprehensive study of NADES, involving the evaluation of both hydrophilic and hydrophobic systems as well the effect of changing the ratio or HDB component.

2nd. Prepare and characterize NADES using a set of experimental parameters (solvatochromic, density, viscosity, water content, etc) that can be used to explain the effect on the solubility and utilize some of them to estimate HSPs using the semi-empirical models (**SEM**) established by Koenhen and Smolder, and Yamamoto- Abbott-Hansen, along with the empirical models (**EM**) proposed by Stefanis and Panayiotou, Hoftyzer - Van Krevelen – Fedors, Hoy, and Yamamoto.

3rd. Evaluate these models and use the experimental data on the solubility of a chosen compound in NADES to screen and validate the relative affinity predicted by the theoretical models of HSPs.

4th. Provide fundamental data of NADES physicochemical properties.

The illustration in **Figure 7** provides a more comprehensive view of each step of this work.

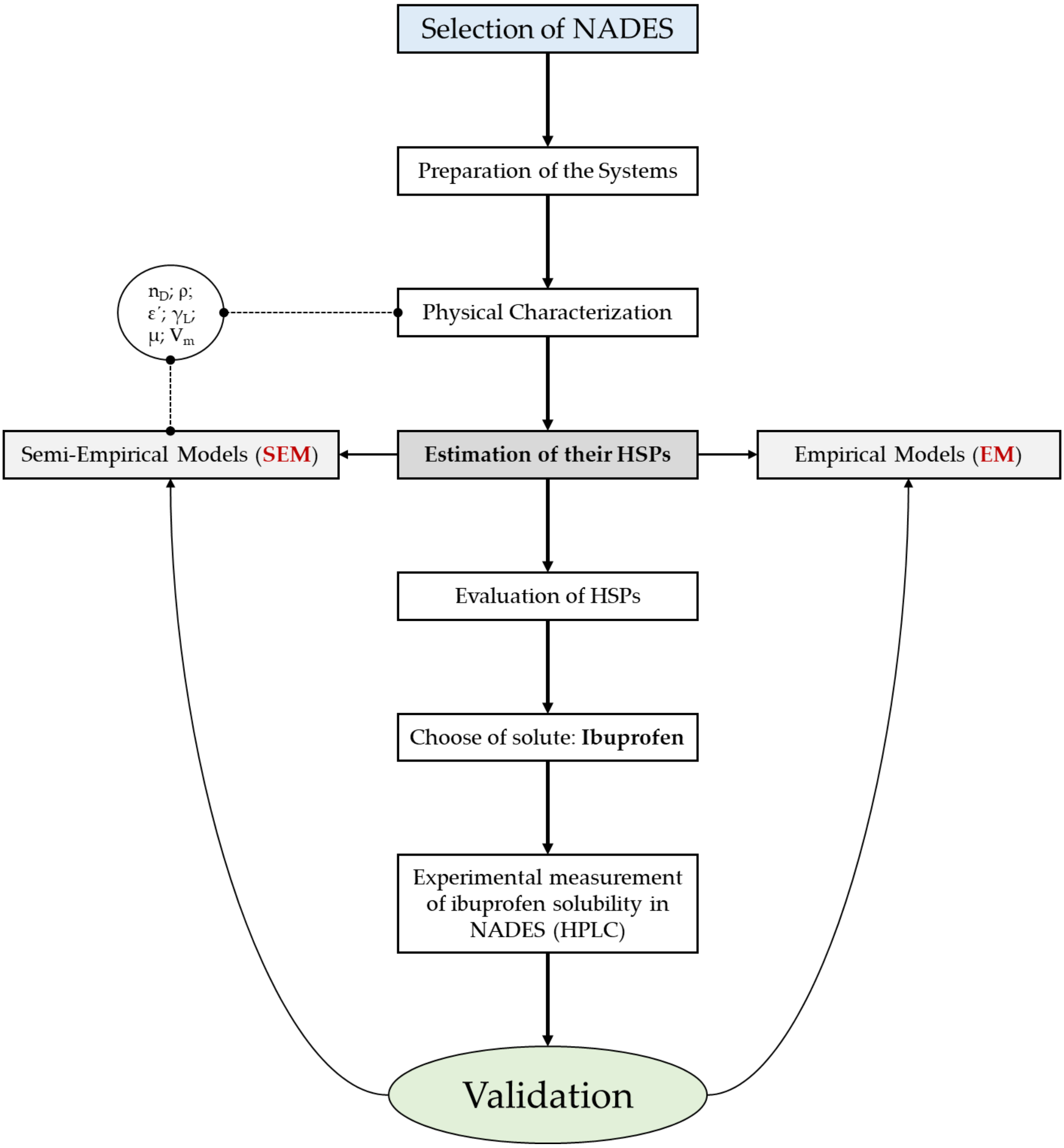


Figure 7: Schematic representation of the workplan carried out in this thesis.

2

MATERIALS AND METHODS

2.1 Chemicals

A short description of the chemical products used in this work is listed in **Table 3**. Here, information on the compound´s CAS number, as well their purity, melting point and supplier can be found. In addition, it is also shown the abbreviated name of NADES´s components (in parentheses, in bold), which will be used more often as work progresses to refer to a specific compound.

Table 3: Information on the organic compounds used in this work.

Chemical name	CAS no.	Purity (%)	Melting point (ºC)*	Brand	Supplier
4-Nitroaniline (**4NA**)	100-01-6	99.0	147	Sigma-Aldrich	Laborspirit
Acetic acid (glacial)	64-19-7	≥ 99.0	16.2	Sigma-Aldrich	Laborspirit
Betaine	107-43-7	≥ 99.0	310	Sigma-Aldrich	Laborspirit
Borneol	464-45-9	97.0	206-209	Sigma-Aldrich	Laborspirit
Choline Chloride	67-48-1	98.0	302-305	Alfa Aesar	Laborspirit
Cyclohexane (**CHx**)	110-82-7	99.5	4-7	Riedel-de Haën	N/A
D-(+)-Sucrose	57-50-1	99.5	185-187	Sigma-Aldrich	Normax
D-(-)-Fructose	57-48-7	≥ 99.5	119-122	Sigma-Aldrich	Laborspirit
D-(+)-Glucose anhydrous	50-99-7	≥ 97.5	150-152	Merck	Laborspirit

Chemical name	CAS no.	Purity (%)	Melting point (ºC)*	Brand	Supplier
Decanoic acid	334-48-5	≥ 98.0	27-32	Sigma-Aldrich	Laborspirit
DL-Menthol	89-78-1	> 95.0	34-36	Sigma-Aldrich	Laborspirit
Dimethyl Sulfoxide (**DMSO**)	67-68-5	N/A	18.4	Corning	Enzifarma
D-Sorbitol	50-70-4	98.0	97 - 100	Sigma-Aldrich	Laborspirit
Ethanol (**EtOH**)	64-17-5	99.8	-114	Fisher chemical	Enzimatic
Ethylene glycol (**EG**)	107-21-1	≥ 99.5	-13	Carlo Erba	Laborspirit
Glycerol (**Gly**)	56-81-5	99.5	20	Scharlau	Laborspirit
Hexane (**Hx**)	110-54-3	96	-95	Carlo Erba	Laborspirit
Ibuprofen (**Ibu**)	15687-27-1	99.0	77-78	Alfa Aesar	Laborspirit
Lactic acid	50-21-5	≥ 85.0	18	Sigma-Aldrich	Laborspirit
Lauric acid	0143-07-07	≥ 98.0	44-46	Sigma-Aldrich	Laborspirit
Levulinic acid	123-76-2	≥ 97.5	30-33	Sigma-Aldrich	Laborspirit
L-Proline	147-85-3	99.0	228	Alfa Aesar	Laborspirit
Methanol	67-56-1	99.0	-98	Sigma-Aldrich	Laborspirit
Myristic acid	544-63-8	98.0	52-54	Sigma-Aldrich	Laborspirit
N, N-Dimethyl-4-nitroaniline (**DMNA**)	100-23-2	98.0	163-165	Alfa Aesar	Laborspirit
Nile red (**NR**)	7385-67-3	≥ 98.0	203-205	Sigma-Aldrich	Laborspirit
Propan-1-ol (**1-prOH**)	71-23-8	99.5	-127	Carlo Erba	Laborspirit
Propan-2-ol (**2-prOH**)	67-63-0	99.5	-89.5	Sigma-Aldrich	Laborspirit
Thymol	89-83-8	≥ 98.5	48-51	TCI	Laborspirit
Trehalose	6138-23-4	≥ 99.0	203	Hayashibara	Hayashibara
Urea	57-13-6	98.0	132-135	N/A	Normax

N/A = Not Available

* Melting points information were obtained from *Chemical Book* website reference [91].

2.2 NADES Preparation

The NADES described in **Table 4** were prepared following the conventional method described by Dai *et al.* [19]: Mixing the NADES components, previously weighted in an analytic balance BAKEABS 220-4N, and letting them to stir with temperature ≤ 65 ºC, until forming a typically viscous and translucid liquid. Although it is a very simple method, when it comes to working with compounds such as choline chloride and amino acids two precautions should be carefully considered before or during NADES preparation:

- Choline chloride (Chcl): Due to its hygroscopic characteristic, the choline chloride used to prepare systems such as Chcl:EG (1:2), Chcl:Gly (1:2), and Chcl:Ure (1:2) must be stored and dried at least 24h before its use, in an oven vacuum, at 60 ºC, to avoid moisture adhesion and consequently a possible water interference.
- Amino acids: For eutectic mixtures of proline-based such as (e.g., Bet:Suc:Pro:W (5:2:2:21), Glc:Pro:Gly:W (3:5:3:20), and Pro:Gly:Sorb:W (1:1:1:13)), the temperature must be adjusted to ≤ 40 ºC, because of the degradation process. Furthermore, these systems also showed some photosensitivity as they degrade (becoming darker and darker over time) when exposed to light.

For a better analysis, the systems were subdivided into two categories, hydrophobic and hydrophilic. The choice criterion was based on the hydrophilic/hydrophobic nature of its constituents and the presence of water as a component of the system.

Table 4: NADES investigated in this work.

Components				**Molar ratio**	**NADES**	**Mw (g/mol)**	**ID***
A	**B**	**C**	**D**				
Betaine	Glucose	Water		5:2:10	Bet:Glc:W (5:2:10)	66.24	**B1**
Betaine	Glycerol	Sucrose	Water	2:3:1:5	Bet:Gly:Suc:W (2:3:1:5)	85.72	**B2**
Betaine	Sorbitol	Water		3:1:10	Bet:sorb:W (3:1:10)	50.98	**B3**
Betaine	Sucrose	Proline	Water	5:2:2:21	Bet:Suc:Pro:W (5:2:2:21)	62.63	**B4**
Choline chloride	Ethylene glycol			1:2	Chcl:EG (1:2)	87.92	**C1**
Choline chloride	Glycerol			1:2	Chcl:Gly (1:2)	107.94	**C2**
Choline chloride	Urea			1:2	Chcl:Ure (1:2)	86.58	**C3**
Fructose	Glucose	Sucrose	Water	1:1:1:10	Fru:Glc:Suc:W (1:1:1:10)	67.90	**F1**
Glucose	Proline	Glycerol	Water	3:5:3:20	Glc:Pro:Gly:W (3:5:3:20)	56.54	**G1**
Glycerol	Fructose			4:1	Gly:Fru (4:1)	109.71	**G2**
Glycerol	Fructose	Sorbitol	Water	1:1:1:3	Gly:Fru:Sorb:W (1:1:1:3)	84.74	**G3**

Components				Molar ratio	NADES	Mw (g/mol)	ID*
A	B	C	D				
Glycerol	Glucose			4:1	Gly:Glc (4:1)	109.71	**G4**
Glycerol	Glucose	Sorbitol	Water	1:1:1:3	Gly:Glc:Sorb:w (1:1:1:3)	84.74	**G5**
Glycerol	Sucrose	Sorbitol	Water	2:1:2:10	Gly:Suc:Sorb:W (2:1:2:10)	71.40	**G6**
Glycerol	Trehalose	Sorbitol	Water	2:1:2:10	Gly:Tre:Sorb:W (2:1:2:10)	71.40	**G7**
Proline	Glycerol	Sorbitol	Water	1:1:1:13	Pro:Gly:Sorb:W (1:1:1:13)	108.16	**P1**
Trehalose	Fructose	Water		1:2:13	Tre:Fru:W (1:2:13)	155.82	**T1**
Trehalose	Glucose	Water		1:2:14	Tre:Glc:W (1:2:13)	164.26	**T2**
Menthol	Acetic acid			1:1	Men:AcetA (1:1)	161.60	**M1**
Menthol	Borneol			7:2	Men:Bor (7:2)[a]	159.47	**M2**
Menthol	Decanoic acid			1:1	Men:DecA (1:1)	159.82	**M3**
Menthol	Decanoic acid			2:1	Men:DecA (2:1)	168.17	**M4**
Menthol	Decanoic acid			4:1	Men:DecA (4:1)	170.95	**M5**
Menthol	Decanoic acid			7:2	Men:DecA (7:2)	164.27	**M6**
Menthol	Lauric acid			2.7:1	Men:LauA (2.7:1)	165.08	**M7**
Menthol	Lauric acid			2:1	Men:LauA (2:1)	163.26	**M8**
Menthol	Lauric acid			4.5:1	Men:LauA (4.5:1)	161.16	**M9**
Menthol	Lauric acid			4:1	Men:LauA (4:1)[a]	171.28	**M10**
Menthol	Lauric acid			5.3:1	Men:LauA (5.3:1)	166.27	**M11**
Menthol	Lauric acid			8:1	Men:LauA (8:1)	136.19	**M12**
Menthol	Lauric acid	Decanoic acid		2:1:1	Men:LauA:DecA (2:1:1)[a]	170.69	**M13**
Menthol	Lauric acid	Decanoic acid		4:1:1	Men:LauA:DecA (4:1:1)[a]	164.28	**M14**
Menthol	Levulinic acid			1:1	Men:LevA (1:1)	153.24	**M15**

Components				Molar ratio	NADES	Mw (g/mol)	ID*
A	B	C	D				
Menthol	Myristic acid			4:1	Men:MyrA (4:1)	154.25	**M16**
Menthol	Myristic acid			8:1	Men:MyrA (8:1)	155.06	**M17**
Menthol	Thymol			1:1	Men:Thy (1:1)	155.59	**M18**
Menthol	Thymol			2:1	Men:Thy (2:1)[a]	38.97	**M19**
Menthol	Thymol			4:1	Men:Thy (4:1)[a]	58.55	**M20**
Menthol	Thymol			8:1	Men:Thy (8:1)	58.55	**M21**

[a] Systems investigated in our last work [92]. Some data will be used in this thesis.

* Hydrophilic systems from **B1** to **T2** and from hydrophobic systems from **M1** to **M21**.

Mw – Molecular weight

2.3 NADES characterization

To characterize and fundament the applicability of NADES as a solvent, the following set of properties were measured:

2.3.1 Water content

The measurement of NADES´s water content was carried out with a 831 Karl Fischer coulometer with a generator electrode (Metrohm) and a moisture analyzer DAB (Kern). All the measurements were performed at room temperature and the results listed in **Table A. 1 and Table A. 2** (appendix) correspond to an average of at least three measures ± their respective standard deviation. These were obtained in ppm (parts per million) and then converted to percentage, by dividing by 10^4.

2.3.2 Viscosity & Density

The dynamic viscosity and density of NADES were measured using an automated rotation Stabinger Viscometer-Densimeter, model SVM 3001 from Anton Paar. Furthermore, to avoid a possible degradation of proline-based eutectic systems, their viscosities and densities were measured in the temperature range of 293.15 to 313.15 K, with steps of 5/5 K. For the others, where this condition does not apply, it was selected a temperature range of 293.15 to 333.15

K and steps of 10/10 K. The values presented in **Table A. 1 and Table A. 2** correspond to an average of triplicates with their respectively standard deviation.

2.3.3 Refractive index

The Refractive index measurement was performed at room temperature, using a monochromatic Abbe-2WAJ Refractometer with an accuracy of ± 0.0002 n_D (see **Table A. 1** and **Table A. 2**). The methodology consists in dropping a few drops of the sample in the refractometer and with the help the two handwheels, move them in order to place the horizontal line, seen through the eyepiece, in the center of the circle. During all the measurements the equipment should be pointed in the direction of the light.

2.3.4 Dielectric constant

The measurement of dielectric constants (or relative permittivity) was obtained at room temperature, performing the protocol established by R. Craveiro *et al.* [85]. With an Alpha-N impedance Analyzer from Novocontrol, GmBh at a frequency range from 10−1 Hz to 1 MHz, using the Dielectric Relaxation Spectroscopy (DRS) method. For this technique, few drops of the sample were placed between 2 stainless steel electrodes of Au (10 mm diameter) in a BDS 1200 parallel plate capacitor and using two silicon spacers (50 μm) to prevent contact between the electrodes.

2.3.5 Surface Tension

NADES′ Surface tension (also called the interfacial tension, in mN/m units) was obtained using the pendant drop-method, following the procedure described by Decaro junior *et al.* [93]. To form the pendant droplets, it was used a needle (with an exterior diameter of 0.52 mm) connected to a Hamilton® graduated syringe (up to 5 μL of volume). The analysis was then carried out, at room temperature, using a OCA20 tensiometer, from Dataphysics, armed with a CCD high-speed and high-definition camera to capture droplet formation. The SCA20 software was used to automate the apparatus and handle the images that were captured on a computer. At least three pendant droplets were created for each spraying NADES and were analyzed by the software using the Young-Laplace equation.

2.3.6 Fourier transform infrared (FTIR) spectroscopy

The FTIR spectrum of each studied NADES was obtained using a PerkinElmer Spectrum Two equipment (Waltham, MA, USA) with attenuated total reflection (ATR) in the Transmittance mode and in a wavenumber range of 400–4000 cm^{-1} [94].

2.4 Solvatochromic Method

Before starting the spectroscopic analysis, stock solutions of each dye (NR, DM4A, and 4NA) were prepared by dissolving 1mg of the probe in 1mL of ethanol and stored in ambered glass vials [78]. Following, the determination of both, polarity and KTPs, was carried out following the methodology explained by Amos K. Dwamena *et al.* [76]: The samples were prepared in cuvettes of plastic (length: 1.5 cm, from Laborspirit), through a diluting of 1:200 (5 μL of the dye solutions in 1000 μL of NADES) and analyzed, at room temperature, using a Thermo Scientific™ GENESYS™ 50 Vis/UV-Vis Spectrophotometer. The samples stained with NR were read in a wavelength range of 400-650 nm, while those marked with DM4A and 4NA in a range of 300-450 nm, and the calculations of polarity and KTPs were made using the wavelength of the maximum absorption applied, in turn, in equations showed in section **1.6.1** and **1.6.2**.

2.5 Solubility Measurement: HPLC

The solubility of ibuprofen in NADES was quantified by high-pressure liquid chromatography (HPLC), following the protocols described by P. Joana *et al.* [95], and L. Ascar *et al.*, with some adaptations [96]. Each system was initially saturated with an excess of ibuprofen and allowed to stir at 298.15 K for 24 hours. For the hydrophobic systems, the supernatant was collected with hydrophobic syringe filters PTFE (pore size: 0.45 μm and diameter: 4 mm), non-sterile, from Laborspirit, and the filtrated transferred to thread HPLC vials with

Label (2 mL, clear glass, 12 × 32mm). In the case of hydrophilic systems, due to their high density, before filtration, the samples were diluted in water at a 1:1 (w/w) ratio, while hydrophobic systems were diluted 1000× with acetonitrile. For the chromatographic separation, a Dionex (Summit model) equipped with a column Agilent Eclipse XDB - C18 (250 mm × 4.6 mm, and particle size of 5 μm) was used. The analysis was carried out at room temperature, using a mixture of buffer K_2HPO_4 pH 6.8 (H_3PO_4) : acetonitrile (65:35). 10 μL of each sample were injected at a flow rate of 0.7 mL/min. The quantification proceeded using the absorbances of solutions detected at 222 nm. The calibration curves were made using each NADES as standard.

3

RESULTS AND DISCUSSION

3.1 Water Content on NADES

Eutectic mixtures are strongly ruled by hydrogen bond interactions, which implies that their physicochemical properties can be easily modified in the presence of highly polar solvents such as water. This is due to the fact that water molecules can act either as HBD or HBA, therefore they can disrupt the HBA/HBD hydrogen bonding network of NADES [97], [98]. Hence, before initializing any assay that targets the evaluation of the applicability of a given system, it is extremely important the knowledge of its water content (W%).

The systems under research were organized in the graph shown in **Figure 8**, by descending order of W%, and considering the results, it was possible to take out some information:

- As expected, the majority of the hydrophilic systems had a higher amount of water than hydrophobic ones, being **P1** and **M12** found, respectively as the extremes in this scale.
- By examining the substitution´s effect on the HBD compound, it is possible to observe that the $W\%_{C3} > W\%_{C2} > W\%_{C1}$. The same effect was also reported by Al-Murshedi *et al.* [94], who argue that, compared to ChCl:EG (**C1**) or ChCl:Gly (**C2**), the two components of the system ChCl:Ure (**C3**) have a greater preference for interacting with water than with each other. In addition, the effect of replacing glucose with fructose was also evaluated in analogous systems, in this case, **G2**/**G4**, **G3**/**G5,** and **T1**/**T2**. What was concluded is that despite the variation of the W% is not linear, the difference observed between their values is not very significant.

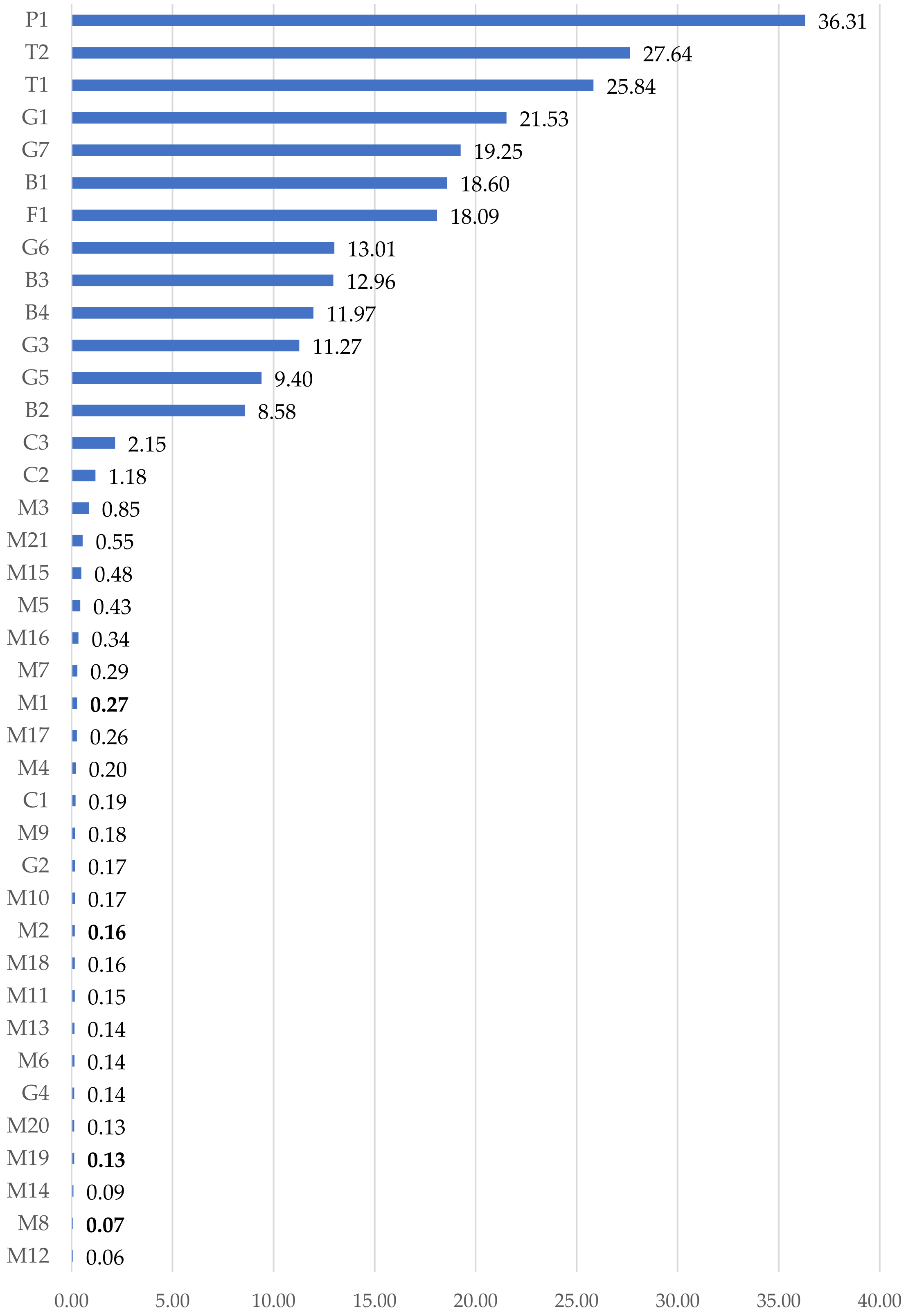


Figure 8: Water content (W%) of the investigated NADES at room temperature.

- Regarding the hydrophobic mixtures, the results show that the water content does not have a direct relationship with the HBD fraction, and it varies from system to system. Another interesting observation was that even though myristic acid (MyrA, $C_{14}H_{28}O_2$) is clearly the more lipophilic compound presented when mixed with menthol the formulated NADES seems to contain more water than other mixtures such as Men:LauA, Men:DecA, and even Gly:Glc (4:1); revelling once more the unpredicted behaviour of NADES.
- In addition, comparing the W% of **M1**, **M2**, **M18** and **M19** (Men:DecA (1:1), Men:DecA (2:1), Men:Thy (1:1) and Men:Thy (2:1), respectively) with the results reported by Van Osch *et al.* [99] for these same systems (**M1** = 0.022%; **M2** = 0.028%; **M18** = 0.031%; **M19** = 0.031%), it was possible to observe that the values obtained in this work (in bold, in **Figure 8**) are relatively higher.

3.2 Evaluation of NADES´ Viscosity and Density

Shear viscosity is a property that quantifies the capacity of a fluid to resist deformation at a given shear rate. In other words, it is related to transport properties, which affects, consequently, the electrical conductivity and leads to the quickflow of a fluid with low viscosity , whereas a fluid with higher viscosities takes longer to flow [100], [101]. On the other hand, density is defined as the mass of a compound per unit volume. Density along with viscosity, are two of the most important parameters that characterize eutectic mixtures, as they provide a good basis for understanding their interactions at the molecular level, in the liquid phase, which may even explain the solubility behaviour of each system.

For a better analysis of the dynamic viscosity (η) and density (ρ), the NADES were separated into two groups according to their nature: hydrophilic systems (**Figure 9**) and hydrophobic systems (**Figure 10**) (all data are listed in the appendix**, Table A. 1** and **Table A. 2**). At the viscosity level, both systems were found to be much more viscous than water. Furthermore, except for **P1** and **C1** mixtures, all the other hydrophilic systems are significantly more viscous than hydrophobic ones. The cause is normally associated with the extensive network of hydrogen bonds created between the components of hydrophilic NADES, such as sugars, which results in a decrease in the mobility of free species within the NADES [102]. In addition, the existence of an inherently very viscous component such as glycerol in a mixture with negligible W%, perfectly justifies the position of **G4** and **G2** as the most viscous systems being used in this research. At the same time, the high W% of **P1** may explains its low viscosity.

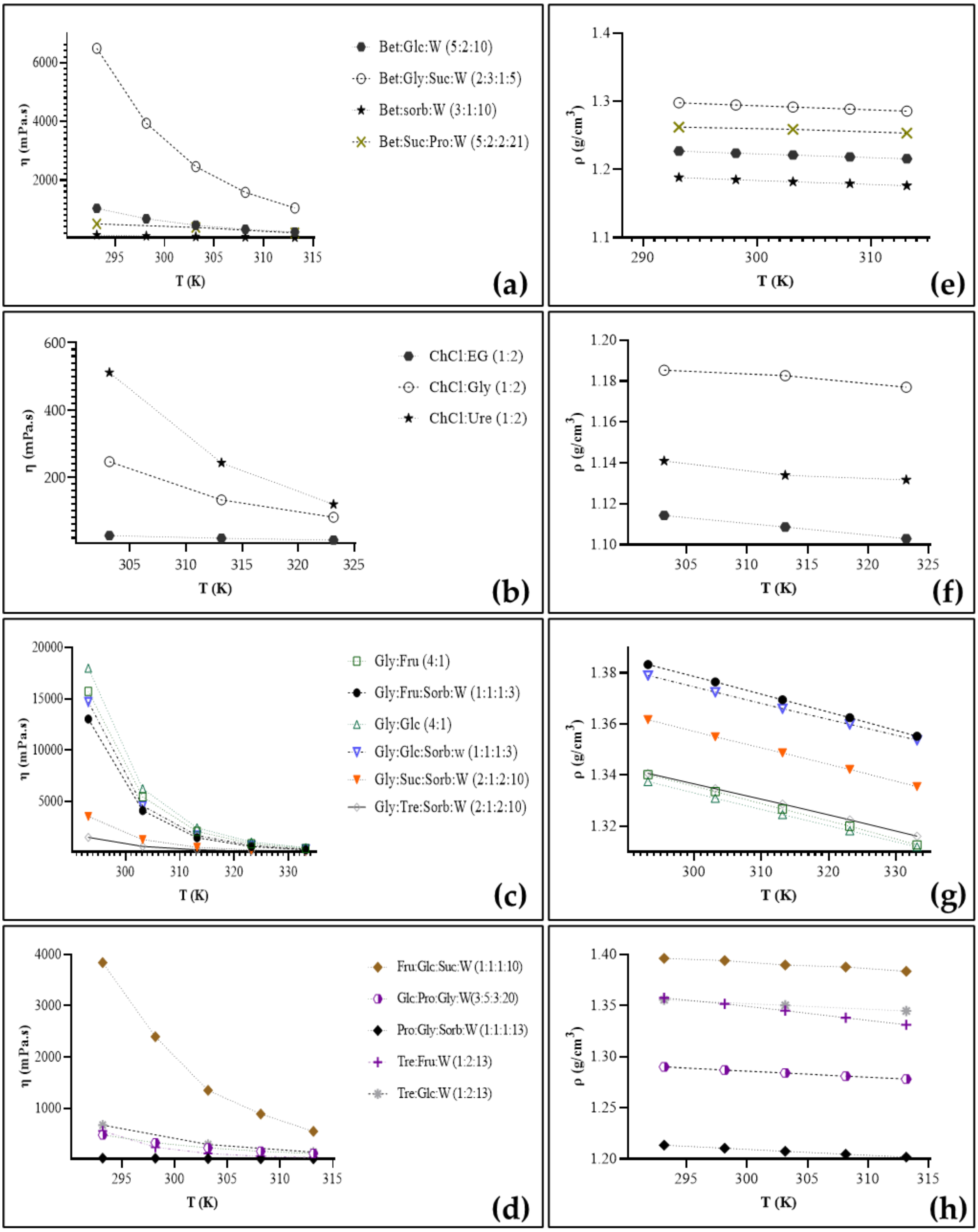


Figure 9: Variation of the dynamic viscosity of hydrophilic NADES (from (a) to (d)) and their respective density (from (e) to (h)) at different temperatures.

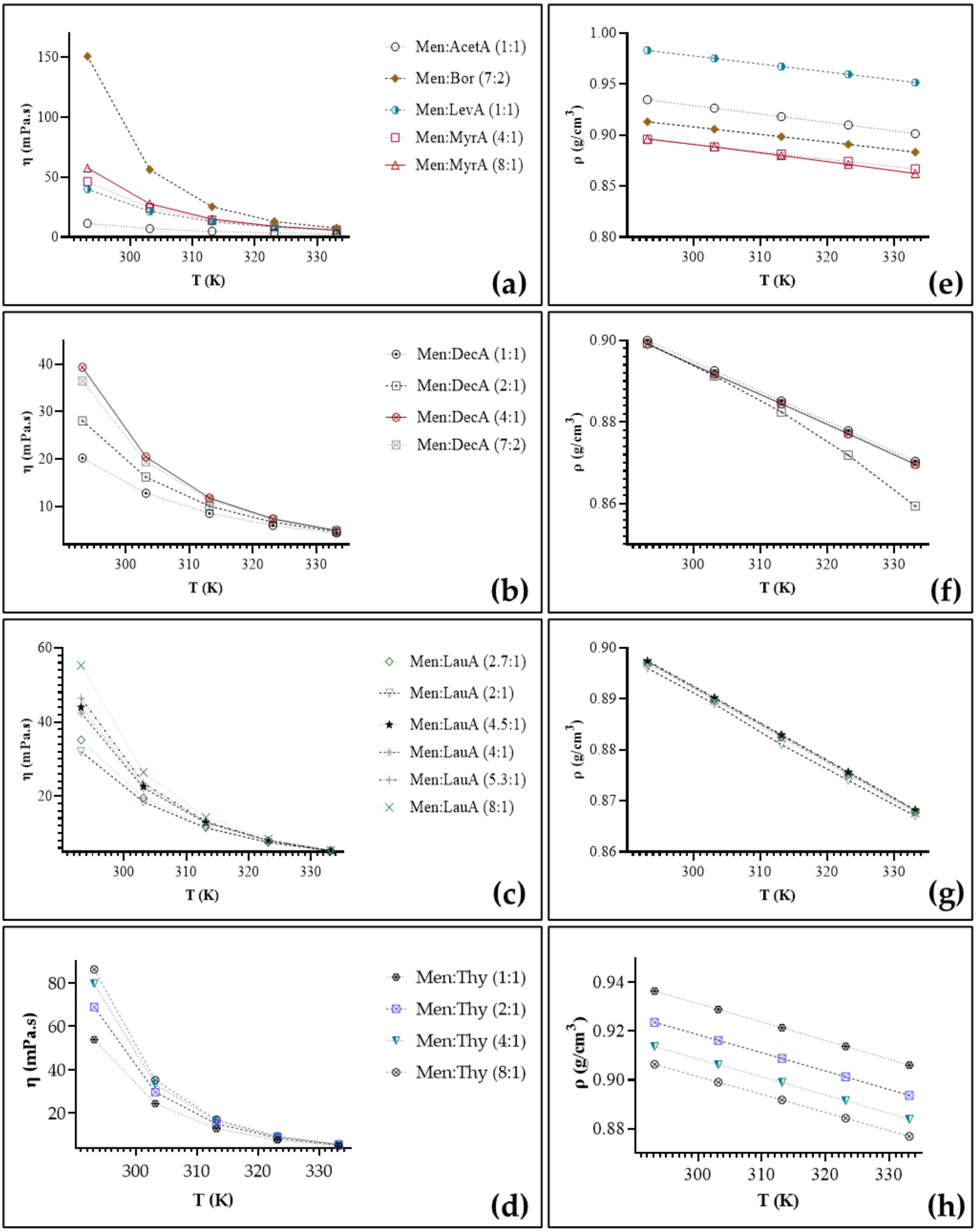


Figure 10: Variation of the dynamic viscosity of hydrophobic NADES ((a) to (d)) and their respective density ((e) to (h)) at different temperatures.

At the density level, contrary to the hydrophilic systems, all the hydrophobic systems exhibit a density lower than water. Furthermore, the results also show that both the nature and the molar fraction of HBD have a significant effect on viscosity or density. For example, unlike the viscosity of the Men:Thy system (**M18**-**M21**), which increases with decreasing of the HBD (thymol) fraction, its density increases linearly with the HBD fraction. However, in the case of the Men:LauA system(**M7**-**M12**), both viscosity and density increase with the decreasing of HBD fraction. Being the density of a compound entirely related to its atomic weight, and which consequently dictates its shape, packing, and possible interactions [102], this means that a hydrophobic system such as Men:Thy has a better packaging and molecular arrangement, the higher the percentage of thymol, whereas an HBD like lauric, decanoic or myristic acid has the opposite effect.

Figure 11 shows the type of relationship that was found to exist between the W% and proprieties such as viscosity(a), density (b), and molar volume (c).

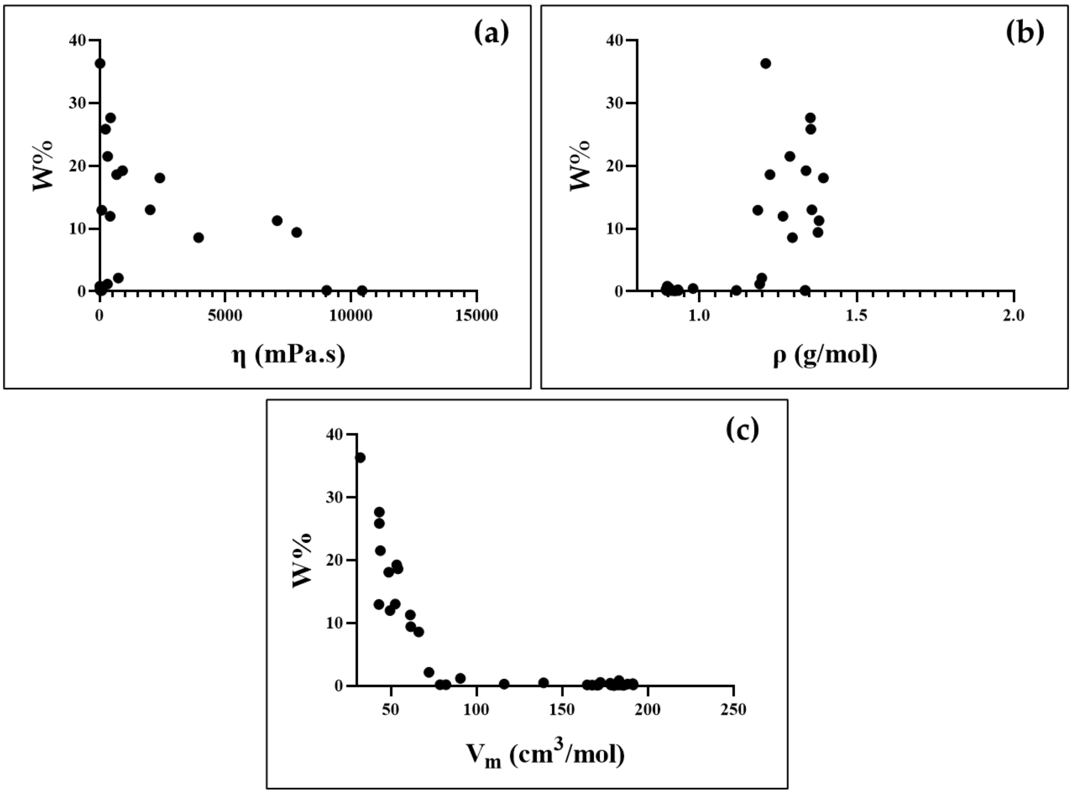


Figure 11: Correlation between W% and viscosity (**a**), density (**b**), and molar volume (**c**).

As it can be noticed, both η and ρ, exhibit no significant dependence with W%. Meanwhile, the V_m, calculated by dividing the molecular weight of each system by its ρ, at 298.15K, shows an exponential decay type relationship, which indicates that the larger the V_m the W% is smaller. But such a relationship is predictable as hydrophobic systems have no water in their constitution and have higher molecular weight than hydrophilic ones (see appendix, **Table A. 1** and **Table A. 2**).

3.3 The HSPs of NADES

In order to guarantee the effectiveness of all the semi-empirical models (**SEM**) used, as well as the empirical models (**EM**) under study, StP, HK, HKF, Hoy and Ymt, their applicability in a group of common organic solvents was first analyzed. This methodology was used before the calculation of each one of NADES's HSPs. The idea was to test the described models on solvents often used and that have already most of their data available, including experimental data of HSPs. This allowed the evaluation of their relative deviation from the experimental data and the identification of the more suitable models to predict each of the parameters.

3.3.1 Estimation of δ_D Parameter

As stated earlier, the refractive index (n_D) is required to estimate semi-empirically the δ_D parameter. Using the values, taken from the literature, it was possible to estimate the dispersive contribution of the selected organic solvents. According to the findings (**Table 5**), in general, any of the models could be used to estimate the δ_D parameter, as they all show a very small deviation from the experimental values.

Table 5: Comparison between the δD parameter of organic solvents, determined by different models.

Organic Solvents	n_D	δ_D						
		SEM		**EM**				**EXP**
		YAH	**KoS**	**StP**	**HK**	**HKF**	**Ymt**	**Hansen** [38]
Water	1.3330 [103]	13.90	14.69	N/D*	N/D*	N/D*	N/D*	15.50

Organic Solvents	n_D	δ_D						
		SEM		**EM**				**EXP**
		YAH	**KoS**	**StP**	**HK**	**HKF**	**Ymt**	**Hansen** [38]
MeOH	1.3284 [104]	13.78	14.60	15.82	15.57	14.48	14.69	15.10
EtOH	1.3614 [103]	14.62	15.24	15.83	15.41	15.10	15.20	15.80
1-prOH	1.3850 [103]	15.22	15.70	15.85	15.65	15.46	15.50	16.00
2-prOH	1.3772 [103]	15.02	15.55	15.49	14.76	14.87	14.97	16.00
EG	1.4318 [103]	16.40	16.62	16.58	17.17	18.39	17.08	17.00
Gly	1.4672 [105]	17.30	17.31	16.97	17.10	17.81	17.72	17.40
CHx	1.4266 [103]	16.27	16.52	17.07	15.00	16.77	16.83	16.80
Hx	1.3750 [103]	14.96	15.51	15.10	14.59	14.61	14.88	14.90
AARD%		4.99	2.77	2.13	3.87	3.95	2.33	-

* N/D - Not determined (no group contribution for this compound)

Regarding the SEM, the Koenhen-Smolders model (KoS, **eqn. 13**[I]) showed better agreement with Hansen's experimental data than the Yamamoto-Abbott-Hansen model (YAH, **eqn. 14**[II]**)** with an AARD% of 2.77 and 4.99, respectively). On the other hand, among all the models, the empirical model of StP was found to have the lowest deviation error (2.13%), and therefore can be indicated as the most appropriate to calculate δ_D.

The results obtained from the n_D' measurement are also listed in **Table 6** and as can be observed, all the systems presented higher values than water ($n_{D(NADES)} \geq 1.4416$). Systems that are hydrophilic showed slightly higher values than those that are hydrophobic. It would be expected due to their intrinsic complexity that contributes greatly to the light retention, and therefore making it considerably more difficult to allow light propagation. Still in **Table 6**, the results obtained from the prediction of NADES′ δ_D parameter using the two methods referred (SEM and EM) were listed.

[I] $\delta_{D\,(KoS)} = 19.53 n_D - 11.35$

[II] $\delta_{D\,(YAH)} = (n_D - 0.784)/0.0395$

Table 6: Refractive index (n_D) and δ_D parameter of NADES predicted using theoretical models.

NADES	**n_D** [a]	**δ_D**					
		SEM		**EM**			
		YAH	**KoS**	**StP**	**HK**	**HKF**[ψ]	**Ymt**[*]
B1	1.4762	17.48	17.45	16.45	18.47	14.90	15.99
B2	1.4865	17.73	17.64	16.74	16.79	17.24	16.74
B3	1.4598	17.10	17.16	16.08	16.41	15.44	15.92
B4	1.4824	17.59	17.54	17.44	16.71	16.81	16.31
C1	1.4764	17.44	17.42	16.09	17.73	16.93	15.67
C2	1.4677	17.65	17.58	16.35	17.62	16.80	16.17
C3	1.4779	18.13	17.95	16.94	18.38	18.70	16.00
F1	1.4849	17.78	17.69	18.84	19.88	18.49	17.31
G1	1.4799	17.63	17.57	17.46	19.31	17.51	17.25
G2	1.4911	17.90	17.77	17.57	19.58	17.96	17.87
G3	1.4924	17.80	17.70	17.80	19.71	18.31	17.78
G4	1.4913	17.92	17.79	17.58	19.52	17.61	17.86
G5	1.4923	17.80	17.70	17.80	19.64	17.77	17.77
G6	1.4849	17.66	17.59	18.17	16.85	19.17	17.46
G7	1.4776	17.47	17.44	18.14	16.80	19.91	17.47
P1	1.4413	16.65	16.81	16.87	16.66	17.48	16.87
T1	1.4735	17.25	17.27	18.55	19.50	20.55	17.17
T2	1.4742	17.35	17.35	18.53	19.43	20.06	17.17
M1	1.4407	16.65	16.81	16.34	17.70	17.76	15.75
M2	1.4667	17.31	17.32	16.82	18.31	18.69	15.78
M3	1.4497	16.89	16.99	16.19	17.04	17.38	15.99
M4	1.4533	16.96	17.05	16.30	17.37	17.76	15.90
M5	1.4569	17.05	17.12	16.39	17.64	18.07	15.82
M6	1.4561	17.04	17.11	16.38	17.59	18.02	15.83
M7	1.4564	17.06	17.13	16.33	17.40	17.85	15.88
M8	1.4550	17.00	17.08	15.92	16.28	17.70	15.92

NADES	**n_D [a]**	**δ_D**					
		SEM		**EM**			
		YAH	**KoS**	**StP**	**HK**	**HKF ψ**	**Ymt***
M9	1.4585	17.11	17.17	16.39	17.60	18.07	15.83
M10	1.4593	17.09	17.15	16.38	17.56	18.02	15.84
M11	1.4583	17.09	17.15	16.41	17.66	18.13	15.81
M12	1.4591	17.11	17.17	16.45	17.77	18.25	15.78
M13	1.4513	16.91	17.01	16.18	16.98	17.35	16.01
M14	1.4547	17.01	17.09	16.29	17.31	17.73	15.91
M15	1.4538	16.97	17.06	15.86	17.81	17.97	15.77
M16	1.4608	17.34	17.34	16.37	17.44	17.97	15.86
M17	1.4604	17.11	17.16	16.44	17.70	18.22	15.79
M18	1.4923	17.96	17.82	16.95	18.04	19.11	16.04
M19	1.4818	17.70	17.62	16.81	18.04	18.92	15.92
M20	1.474	17.50	17.46	16.70	18.05	18.77	15.83
M21	1.4682	17.34	17.34	16.62	18.05	18.68	15.77

SEM – Semi-empirical models; **EM** – Empirical models; **YAH** – Yamamoto-Hansen-Abbott model (**eqn. 14**); **KoS** – Koenhen-Smolders model (**eqn. 13**); **StP** – Stefanis-Panayiotou model; **HK** - Hoftyzer-Van Krevelen model; **HKF** - Hoftyzer-Van Krevelen model-Fedors; **Ymt** – Yamamoto model.

[a] More information in appendix, **Table A. 1** and **Table A. 2**.

* An empirical model based on group contribution was also developed by the Yamamoto-Abbott-Hansen collaboration. The abbreviation **Ymt** was used to distinguish it from the semi-empirical model **YAH**.

ψ Extension of the HK approach using the molar volume calculated with the Fedors´s group contribution. This approach is very useful for compounds whose molar volume is unknown (see **Table A. 12**, appendix).

The results showed no significant differences between the δ_D calculated by the different theoretical models. Thus, up to this point, any of the used models could be considered valid since there is no experimental data available to compare and determine which one is the most accurate.

3.3.1.1 Correlating n_D with W%

Rozas *et al.* [106] recently investigated the correlation between W% and n_D and reported that there is no linear relationship between them, as it was also confirmed in this work (**Figure 12**).

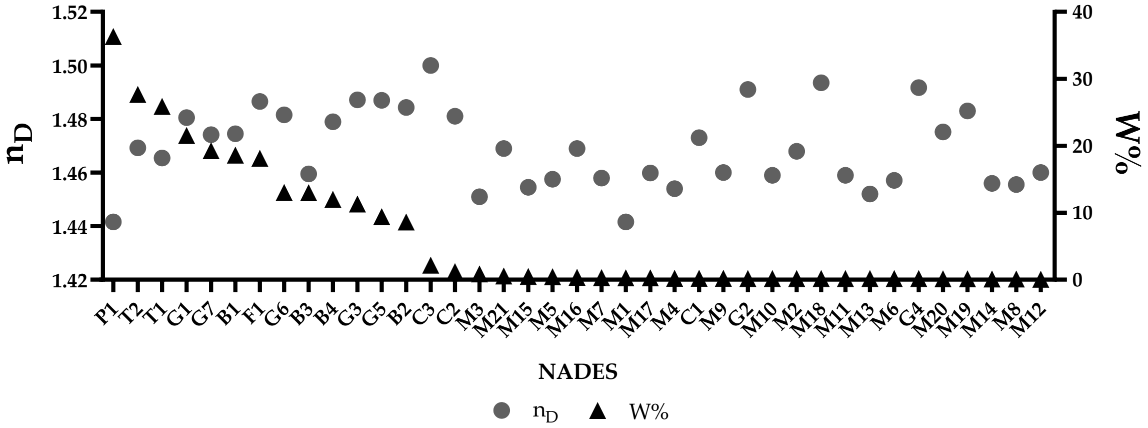


Figure 12: Correlation between the refractive index (n_D) and water content (W%).

The hypothesis here suggested, is that the various water molecules present in the medium (mainly in hydrophilic systems) will act separating and surrounding each species of the mixture and allowing a better travel of the light through the liquid, decreasing, consequently, the n_D. Furthermore, taking into account that the polarizability influences how much energy is required for interactions between nonpolar molecules (London dispersion forces) and that it explains why n_D is directly correlated with the δ_D parameter [45], the same behaviour is expected if δ_D parameter, calculated semi-empirically, is correlated with W%, as it can be confirmed in **Figure 13**.

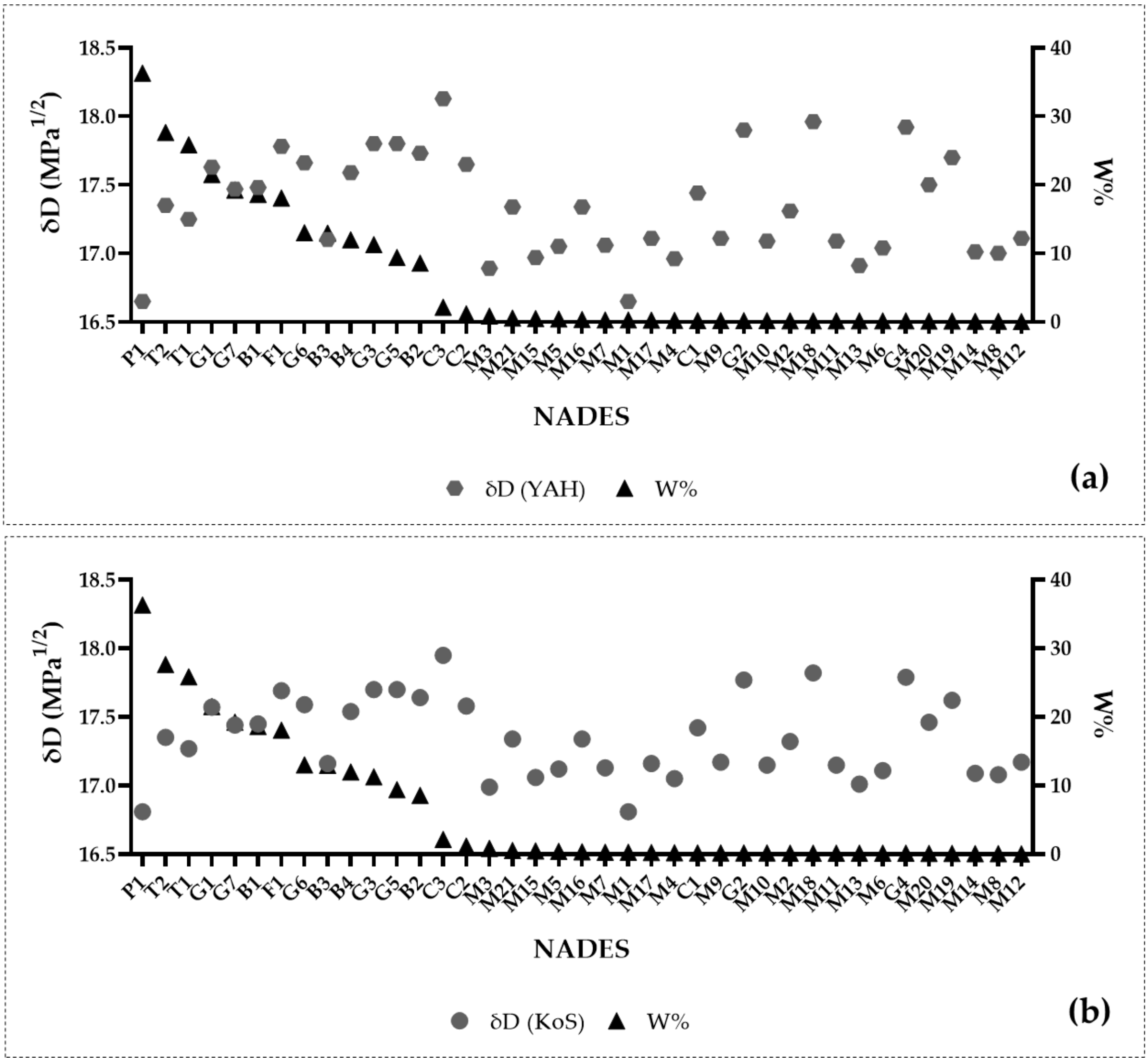


Figure 13: Correlation between the dispersion parameter (δ_D) determined semi-empirically and water content (W%): **(a)**, using by model of Yamamoto-Abbott-Hansen (YAH, **eqn. 14**) and **(b)**, using the model of Koenhen-Smolders (KoS, **eqn.** 13).

3.3.2 Estimation of δ_P Parameter

To determine the permanent dipole´s contribution to the C.E.D. of a given compound, using the SEM, its dipole moment (μ) should be known. Theoretically, μ is commonly determined using Debye´s theory, however, that treatment is considered incorrect as it assumes that the reaction field generated by the dipole cannot affect its direction [52]. This was the reason that allowed Onsager to establish his equation shown previously (**eqn. 19**[III]), which emerged as a correction of Debye´s assumption. Furthermore, taking into account the non-volatile nature, the liquid-phase state, as well the presence of hydrogen-bonds clusters in the compounds under study, the Onsager´s and Salem´s methods (μ_O, (**eqn. 19**), and μ_S (**eqn. 20**[IV]), respectively) show to be the most appropriate to be used in this investigation [53], [54]. By predicting the δ_P parameter of organic solvents (preliminary test) using the semi-empirical and empirical models (SEM and EM, respectively), it was observed that the results obtained from the semi-empirical models differ a lot from the experimental ones, as it can be confirmed in **Table 7**.

Table 7: Comparison between the experimental (Exp.) and theoretical (SEM and EM) value of δP parameter calculated for organic solvents

Solvent	**V_m[a] (cm³/mol)**	**Exp. [38]**	**SEM**				**EM**			
		δ_P	$\delta_{P(Bot)}$	$\delta_{P(HB)}$	$\delta_{P(Bb)}$	$\delta_{P(KoS)}$	$\delta_{P(StP)}$	$\delta_{P(HK)}$	$\delta_{P(HKF)}$	$\delta_{P(Ymt)}$
Water	18.07	16.00	21.94	16.30	8.47	21.68	N/A*	N/A*	N/A*	N/A*
MeOH	40.45	12.27	11.13	11.23	5.84	12.94	7.03	12.36	11.49	6.82
EtOH	58.39	8.80	7.70	9.31	4.84	9.79	6.71	8.56	8.39	5.12
1-prOH	74.84	6.80	5.87	8.11	4.21	7.98	6.40	6.69	6.61	4.24
2-prOH	76.46	6.10	5.78	8.01	4.16	7.88	5.99	6.53	6.58	3.49
EG	73.09	11.05	5.48	8.99	4.67	7.96	9.10	12.65	13.55	8.30
Gly	55.92	12.02	14.96	19.92	10.35	19.45	10.77	11.85	12.34	8.32
CHx	131.57	0.0	0.00	0.00	0.00	0.00	5.73	0.00	0.00	1.70
Hx	108.04	0.0	0.00	0.00	0.00	0.00	3.07	0.00	0.00	1.18
AARD%			21.82	21.58	40.86	26.93	17.03	**4.67**	7.83	37.06

[a] Molar volumes were calculated using the molecular weight and density collected from the **table of organic solvents created by professor Murov** [107].
* N/A – Not available, because there are no group contribution for this compound.

[III] $$\mu_O = \sqrt{\left(\frac{9k_BT\times10^{39}}{4\pi N_A}\right)\frac{(\varepsilon'-n_D^2)(2\varepsilon'-n_D^2)}{\varepsilon'(n_D^2+2)^2}\times\frac{1}{F_B}}$$

[IV] $$\mu_S = \sqrt{\frac{\varepsilon'\times V_m}{184}} - 1$$

But, since the experimental values of their δ_P parameter are known, these SEM (listed in section **1.5.1.1.3**) were rewritted in order to calculate the dipole moment. The idea here was to determine the values of the dipole moments needed in each of these models to achieve at the values of δ_P. As it can be seen in **Table 8**, the dipole moments found are very different from those commonly reported in the literature.

Table 8: Comparison between the dielectric constants and dipole moments of literature with the results obtained in this work.

Solvent	Literature		$\mu_{(Boe)}$[c]	$\mu_{(HB)}$[c]	$\mu_{(Bb)}$[c]	$\mu_{(KoS)}$[c]	This thesis		
	ε´[104]	μ					ε´ (at 4.1 × 105 Hz)	$\mu_{(O)}$	$\mu_{(S)}$
Water	78.36	1.85[b]	1.93	1.82	3.49	2.79	78.22	3.10	2.58
MeOH	32.66	1.70[b]; 1.60[a]	2.68	1.86	3.57	3.30	34.55	3.07	2.57
EtOH	24.55	1.69[b]; 1.70[a]	2.76	1.60	3.07	3.11	34.55	3.60	3.16
1-prOH	20.60	1.68[b]	2.78	1.41	2.71	2.93	20.86	3.07	2.74
2-prOH	19.92	1.66[a]	2.51	1.26	2.43	2.63	19.39	3.01	2.66
EG	41.4	2.31[b]	6.66	2.84	5.46	6.56	38.18	3.52	3.25
Gly	42.5	4.20 [b]; 2.7[a]	4.82	2.53	4.87	5.31	44.79	4.25	4.10
CHx	2.02	0.00[b]	0.00	0.00	0.00	0.00	2.18	0.30*	0.74
Hx	1.88	0.00[b]	0.00	0.00	0.00	0.00	1.96	0.38*	0.39*

[a] Data collected from the ***"Table of organic solvents"*** created by **professor Murov** [107].

[b] Obtained from reference [38]**.**

[c] Dipole moments calculated from the semi-empirical equations (from **eqn. 15** to **eqn**. 18).

* Described by Huyskens as the *"apparent dipole moment"* [52].

Yet, while the Hansen-Beerbower approach (HB, **eqn. 16**[V]) showed to be the most similar to the expected, the dipole moment estimated through the equations of Beerbower (Bb, **eqn. 17**[VI]) and Koenhen-Smolders (KoS´, **eqn. 18**[VII]) are surprisingly very analog to those calculated using, correspondingly, the methods of Onsager and Salem. Therefore, taking into account the outcome from this preliminary analysis, only the two semi-empirical models, Bb

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[V] $\delta_{P(HB)} = \left(37.4\mu/V_m^{\frac{1}{2}}\right)$

[VI] $\delta_{P(Bb)} = \left(9.5\mu/V_m^{\frac{1}{2}}\right) \times c'$

[VII] $\delta_{P(KoS')} = \left(50.1\mu/V_m^{\frac{3}{4}}\right) \times c'$

and KoS, were studied. In addition, it was also observed that at a frequency of 4.1 × 10^5 Hz, the measured dielectric constants (ε') of the organic solvents is comparable to those described in the literature. Hence, this point was also used to evaluate the ε' of eutectic systems and can be visualized in the next two graphics of **Figure 14** (see more information in appendix**,** from **Table A. 3 – Table A. 6**).

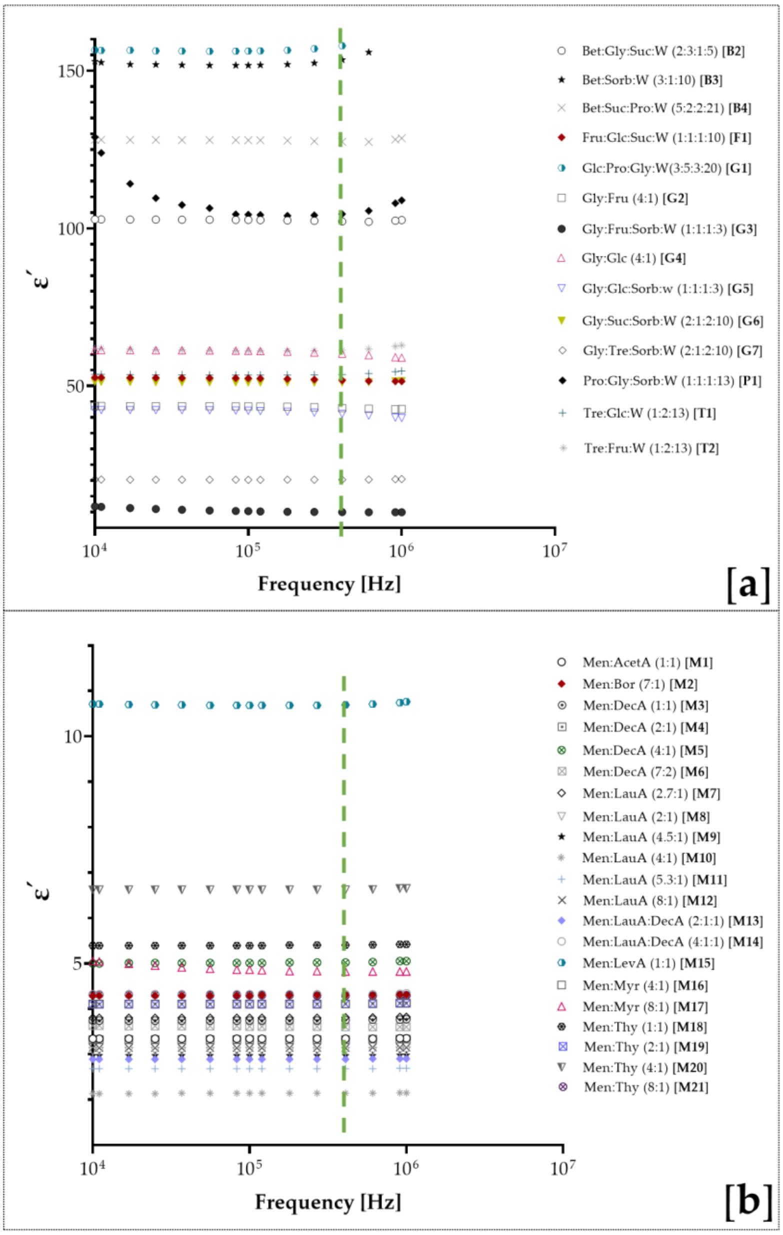


Figure 14: Dielectric constant of the hydrophilic **[A]** and hydrophobic systems **[B]** in a frequency range of 10^4-10^6 Hz. The vertical green dashed line indicates the frequency point where studied ε´ were acquired.

By analyzing the results presented in **Table 9**, as it was expected, the ε′ of all the hydrophilic systems are higher than the hydrophobics, and most of them even higher than water. This means that in the presence of an external field, systems such as those based on betaine, glycerol, fructose, or glucose are much more easily polarized than those based on menthol. In addition, ε' is often used as a relative solvent polarity scale, indicating that a solvent is more polar the higher its ε´ and therefore will dissolve more salts [108]. Thus, according to this assumption, **G1 (**Glc:Pro:Gly:W (3:5:3:20)) and **M10** (Men:LauA (4:1)) are, respectively, the more and the less polar systems found in this list.

Table 9: Dielectric constant, dipole moment and the δ_P parameter of NADES estimated using the theoretical models.

NADES	**ε´**	**μo**	**μs**	**δ_P**					
				SEM		**EM**			
				Bb	**KoS´**	**StP**	**HK**	**HKF**	**Ymt**
B1	N/D*	N/D	N/D	N/D	N/D	10.51	9.98	8.41	6.61
B2	102.20	6.01	5.98	14.36	26.41	7.44	9.85	10.11	7.44
B3	153.47	6.04	5.91	17.89	36.03	10.99	10.58	10.16	7.65
B4	127.45	5.82	5.77	16.07	31.68	14.19	9.40	9.45	7.81
C1	N/D*	N/D	N/D	N/D	N/D	8.41	10.10	9.91	5.28
C2	N/D*	N/D	N/D	N/D	N/D	9.36	9.99	9.72	5.65
C3	N/D*	N/D	N/D	N/D	N/D	11.02	11.58	12.55	6.31
F1	51.79	3.64	3.57	10.12	19.82	**19.14**	11.04	10.27	10.24
G1	157.93	6.12	6.06	**17.94**	**36.39**	12.64	10.37	9.40	9.63
G2	42.98	4.29	4.26	9.20	16.02	12.23	11.66	11.12	8.26
G3	9.97	1.69	1.53	4.19	7.13	14.91	11.63	10.81	9.43

NADES	ε´	μo	μs	δ_P					
				SEM		EM			
				Bb	KoS´	StP	HK	HKF	Ymt
G4	60.26	5.07	5.09	10.87	19.11	12.17	11.41	10.79	8.26
G5	41.12	3.63	3.57	8.98	16.65	14.79	11.35	10.27	9.40
G6	51.03	3.78	3.69	10.12	19.34	17.43	10.97	12.47	9.89
G7	20.26	2.35	2.21	6.25	11.46	17.29	10.97	**13.00**	9.85
P1	104.52	4.37	4.16	14.98	31.53	11.46	**12.15**	12.75	**11.46**
T1	61.36	3.79	3.66	11.20	22.26	18.85	11.59	12.04	10.68
T2	53.63	3.54	3.41	10.44	20.70	18.61	11.29	11.62	10.61
M1	3.34	1.05	1.05	1.89	3.05	5.58	3.95	3.87	3.30
M2	4.30	1.59	1.73	2.36	3.75	5.78	2.93	2.99	1.99
M3	3.75	1.47	1.65	2.11	3.40	4.67	2.50	2.55	2.63
M4	4.11	1.59	1.74	2.31	3.63	4.85	2.61	2.67	2.41
M5	5.02	1.87	1.96	2.72	4.13	4.99	2.70	2.77	2.23
M6	3.60	1.38	1.58	2.01	3.32	4.97	2.69	2.75	2.26
M7	3.81	1.50	1.70	2.13	3.43	4.67	2.52	2.59	2.29
M8	3.07	1.17	1.48	1.65	2.95	**2.36**	4.56	2.52	2.36
M9	2.97	1.08	1.40	1.55	2.88	4.84	2.62	2.69	2.19
M10	2.14	0.14	1.07	**0.20**	**2.19**	4.81	2.60	2.67	2.21

NADES	ε′	μo	μs	δP					
				SEM		EM			
				Bb	KoS′	StP	HK	HKF	Ymt
M11	2.68	0.89	1.29	1.28	2.66	4.89	2.65	2.72	2.16
M12	3.14	1.17	1.44	1.69	3.00	4.98	2.71	2.78	2.10
M13	2.89	1.08	1.42	1.51	2.82	4.46	**2.38**	**2.44**	2.58
M14	4.32	1.69	1.83	2.41	3.73	4.70	2.53	2.59	2.38
M15	10.69	2.71	2.66	4.46	6.73	5.81	4.95	4.93	3.45
M16	3.32	1.27	1.57	1.79	3.12	4.59	2.50	2.58	2.18
M17	4.82	1.83	1.95	2.63	4.01	4.85	2.65	2.72	2.09
M18	5.40	1.83	1.96	2.77	4.37	4.71	3.05	3.24	**1.85**
M19	4.11	1.48	1.65	2.22	3.64	4.88	2.98	3.13	1.89
M20	6.62	2.19	2.26	3.26	4.92	5.02	2.92	3.05	1.92
M21	4.29	1.59	1.74	2.36	3.74	5.11	2.89	2.99	1.94

Bb – Beerbower model (**eqn. 17**[VIII]); **KoS′**- Koenhen-Smolders (**eqn. 18**[IX])
***N/D** – not determined (equipment problems)

Using the two different models to estimate dipole moment (μ), it is noticeable a difference between them, despite, in most cases, it is not too significant. On the other hand, by analyzing the δ_P results of the two models (SEM and EM), one may infer that these relatively seem, despite being identified as different systems as the most and less polar (blue and green boxes, respectively). Yet, another approach would be to use the Hoftyzer-Van Krevelen model

---

[VIII] $\delta_{P(Bb)} = \left((9.5\mu)/V_m^{\frac{1}{2}}\right) \times c'$

[IX] $\delta_{P(KoS')} = \left((50.1\mu)/V_m^{\frac{3}{4}}\right) \times c'$

(HK) as a reference, since in the tests with organic solvents (**Table 7**), it stands out as the most adequate model.

3.3.2.1 Correlating δ_P with W%

It is inevitable not to think about water when talking about polarity, as this refers to the most polar molecule. In order to understand how it affects the δ_P, the correlations shown in **Figure 15** were established.

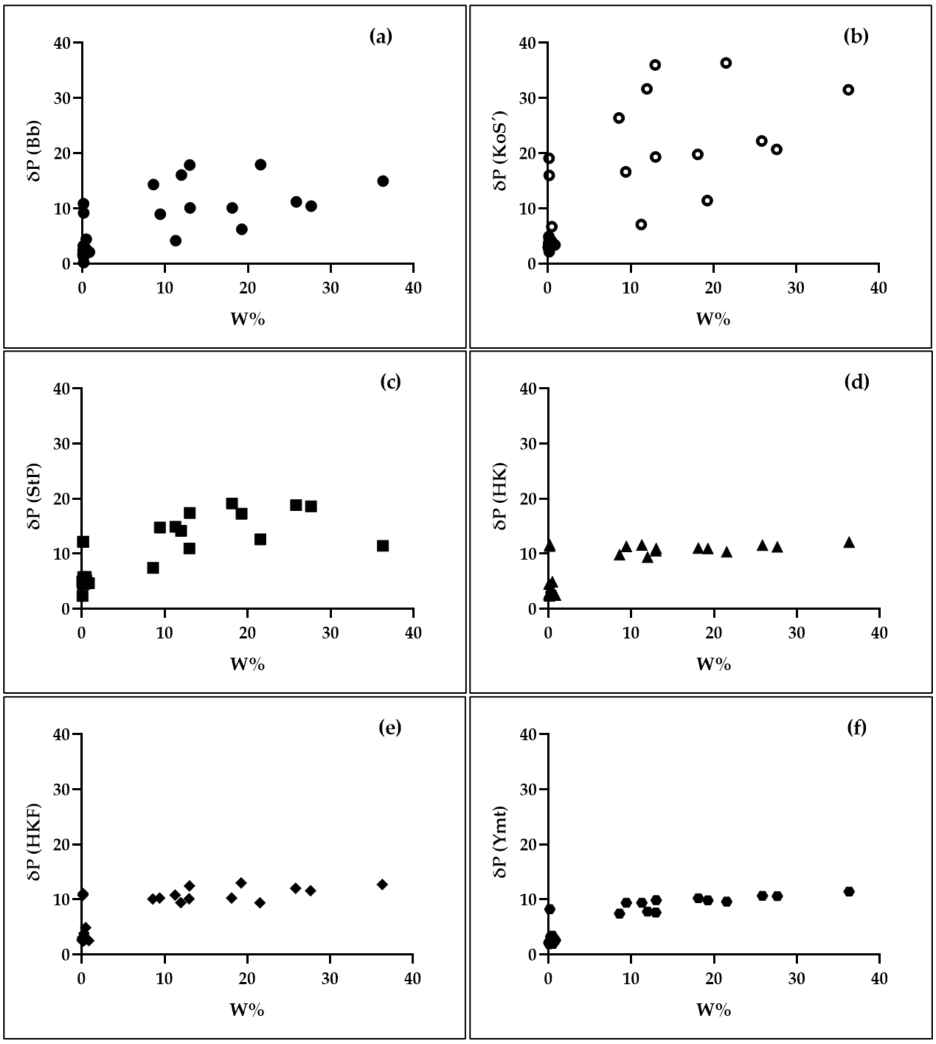


Figure 15: Relationship between the measured water content (W%) and δ_P parameter estimated using the studied models: (a) and (b) are the semi-empirical models of Beerbower (**Bb**, **eqn. 17**) and Koenhen-Smolders (**KoS´**, **eqn. 18**), respectively, and (c), (d), (e) and (f) are, in turn, the empirical models of Stefanis-Panayiotou (**StP**), Hoftyzer-Van Krevelen (**HK**), Hoftyzer-Van Krevelen-Fedors (**HKF**) and Yamamoto (**Ymt)**.

Examining the profile displayed in the six graphs above, it can be seen that despite the large fluctuations observed, there is, in general, a slight tendency of the parameter δ_P to increase with the increase in water content.

3.3.3 Estimation of δ_H Parameter

The first method proposed by Hansen to quantify the hydrogen-bond contribution for the C.E.D., was using FTIR spectroscopy. In theory, it would be necessary the knowledge of the assignment of the OH···O bond, the number of OH in the molecule as well as its molar volume. In fact, doing a preliminary test with a set of organic solvents, it was possible to confirm the reliability of such methodology (in **Table 10**).

Table 10: Evaluation of δH parameter for organic solvents using Hansen´s methodology in contrast with the ones estimated using the EM.

Solvent	δ_H (exp) [38]	$\bar{\upsilon}$(cm^{-1})	λ(nm)[a]	E_{vap}(cal/mol)[b]	$E_{vap/2}$	n	δ_H (Hansen)*	δ_H (EM)			
								StP	HK	HKF	Ymt
MeOH	**22.30**	3682[109]	2715.92	10530.52	5265.26	1	**23.34**	14.32	22.23	22.23	14.15
EtOH	**19.40**	3689[109]	2710.76	10550.54	5275.27	1	**19.44**	13.93	18.51	18.51	9.91
1-prOH	**17.40**	3689 [109]	2710.76	10550.54	5275.27	1	**17.17**	13.54	16.36	16.36	7.73
2-prOH	**17.40**	3689 [109]	2710.76	10550.54	5275.27	1	**16.99**	13.36	16.16	16.16	6.56
Gly	**29.30**	3282 [110]	3046.98	9386.35	4693.17	3	**32.46**	28.80	28.65	29.24	17.23
AARD%							**3.87**	**22.22**	**4.04**	**4.60**	**48.91**

[a] λ (nm) = (1/ $\bar{\upsilon}$ (cm^{-1})) × 10^7

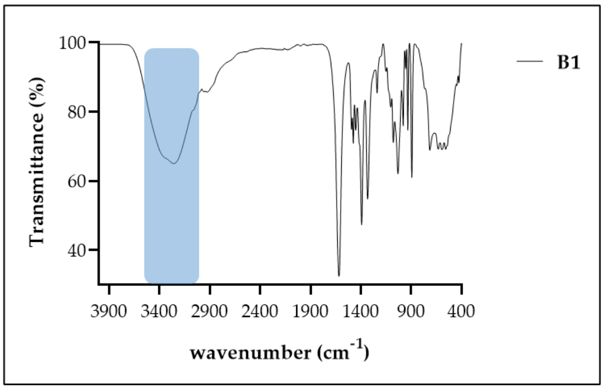
[b] E_{vap} (cal/mol) = (2.86 × 10^7)/ λ (nm)

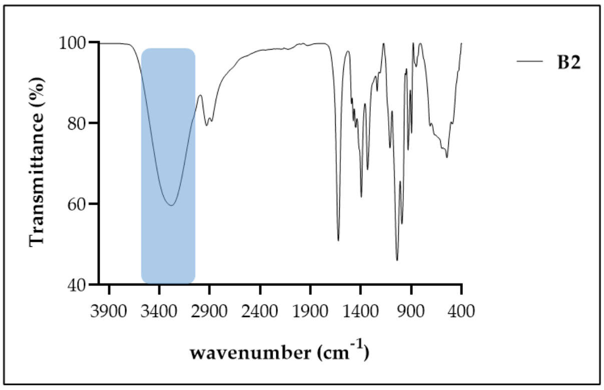
* Modification of Hansen methodology: Using the obtained energy (E_{vap}/2) instead of using the 5000 cal/mol established by Hansen in **eqn. 21**.

As can be observed, the experimental results and those estimated using the approach shared the most similarities. Furthermore, by comparing these experimental data of δ_H with the one calculated using the EM, the HK was found, once again, to be the best one.

Taking into account the polyhydroxylic nature of the various constituents of the hydrophilic NADES, their low molar volume, as well the presence of water as a fundamental component of the mixture, it would be somewhat suspicious the use the Hansen method and equation (**eqn. 21**[X]) to the assessment of NADES´s δ_H. However, since it is still unknown the NADES behaviour in this field, Hansen´s method was evaluated using then the FTIR spectrums shown in **Figure 16**.

[X] $\delta_H = \left(\sqrt{(5000 \times n)/V_m}\right) \times c' \left(\text{in MPa}^{\frac{1}{2}}\right)$


B1
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})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Transmittance (%)
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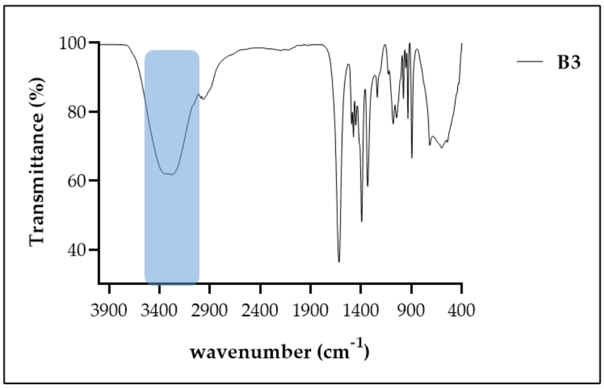
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


B3
Transmittance (%)
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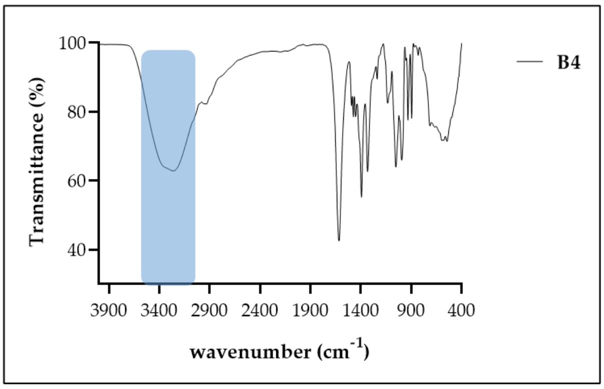
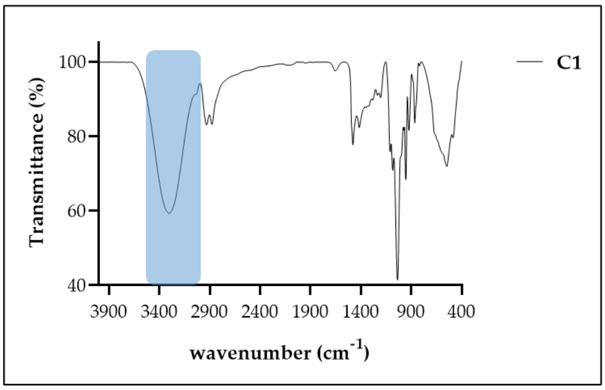
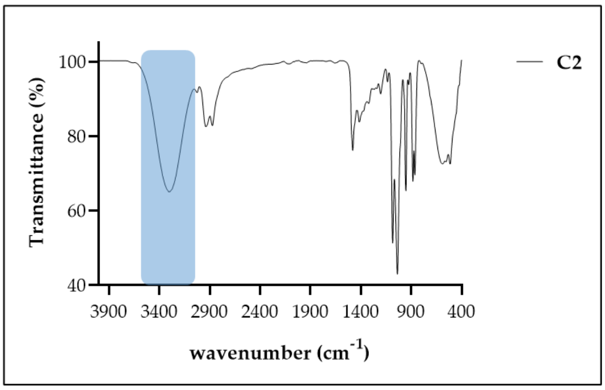
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


B4
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


C1
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


C2
Transmittance (%)
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80
60
40
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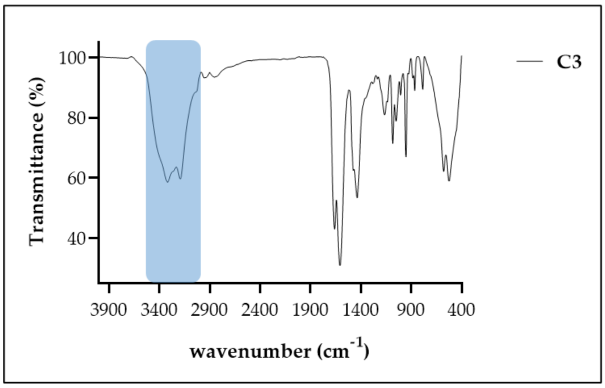
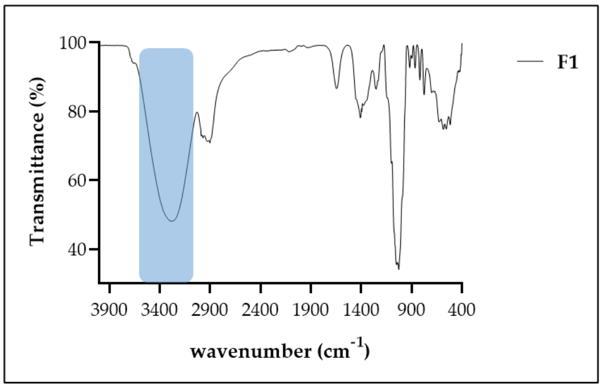
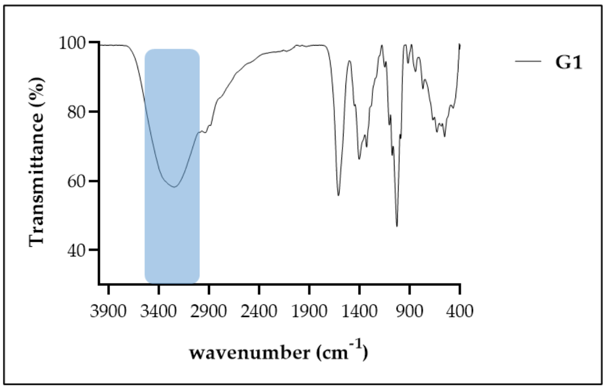
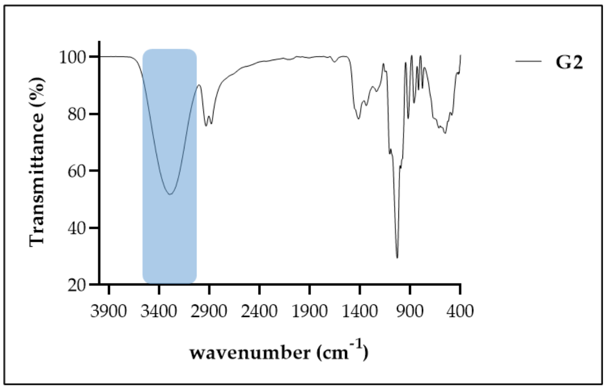
wavenumber (cm^{-1})


C3
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


F1
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


G1
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


G2
Transmittance (%)
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40
20
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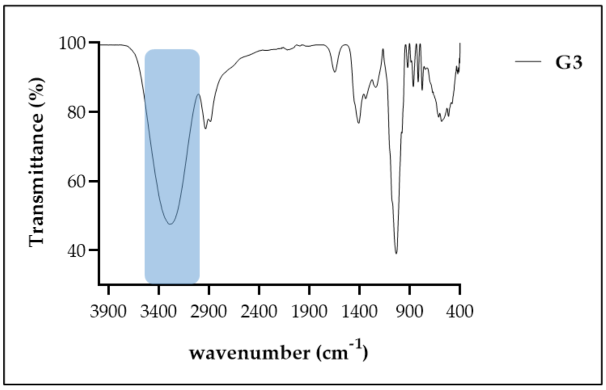
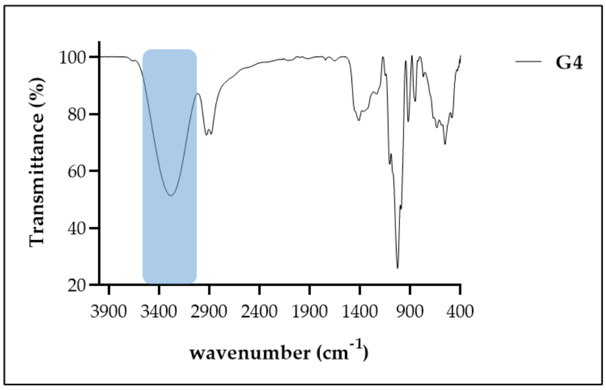
wavenumber (cm^{-1})


G3
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})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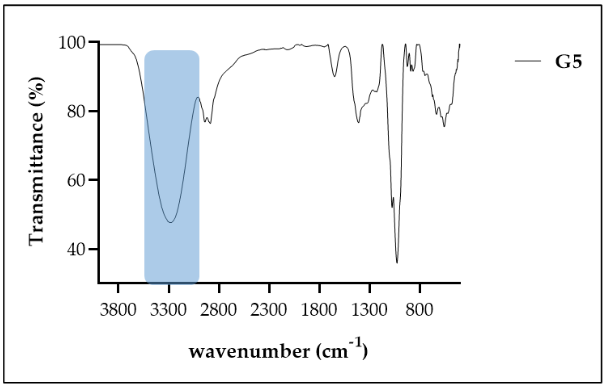
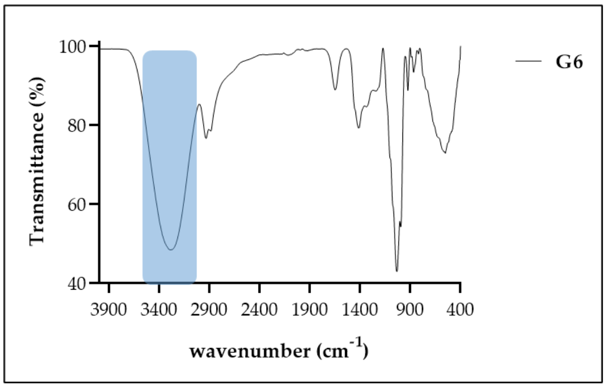
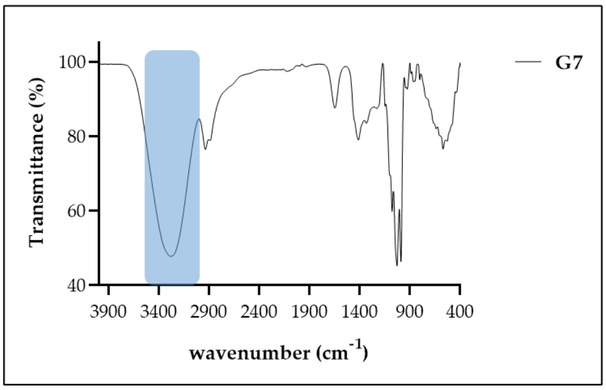
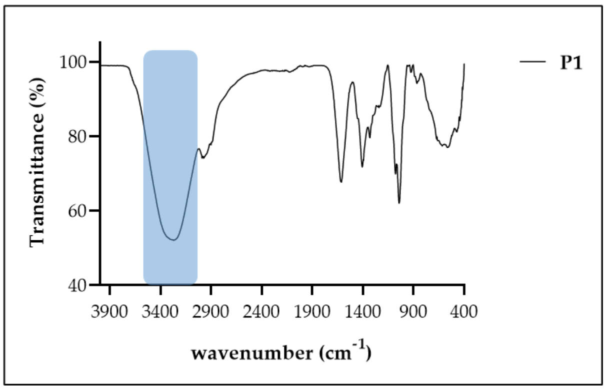
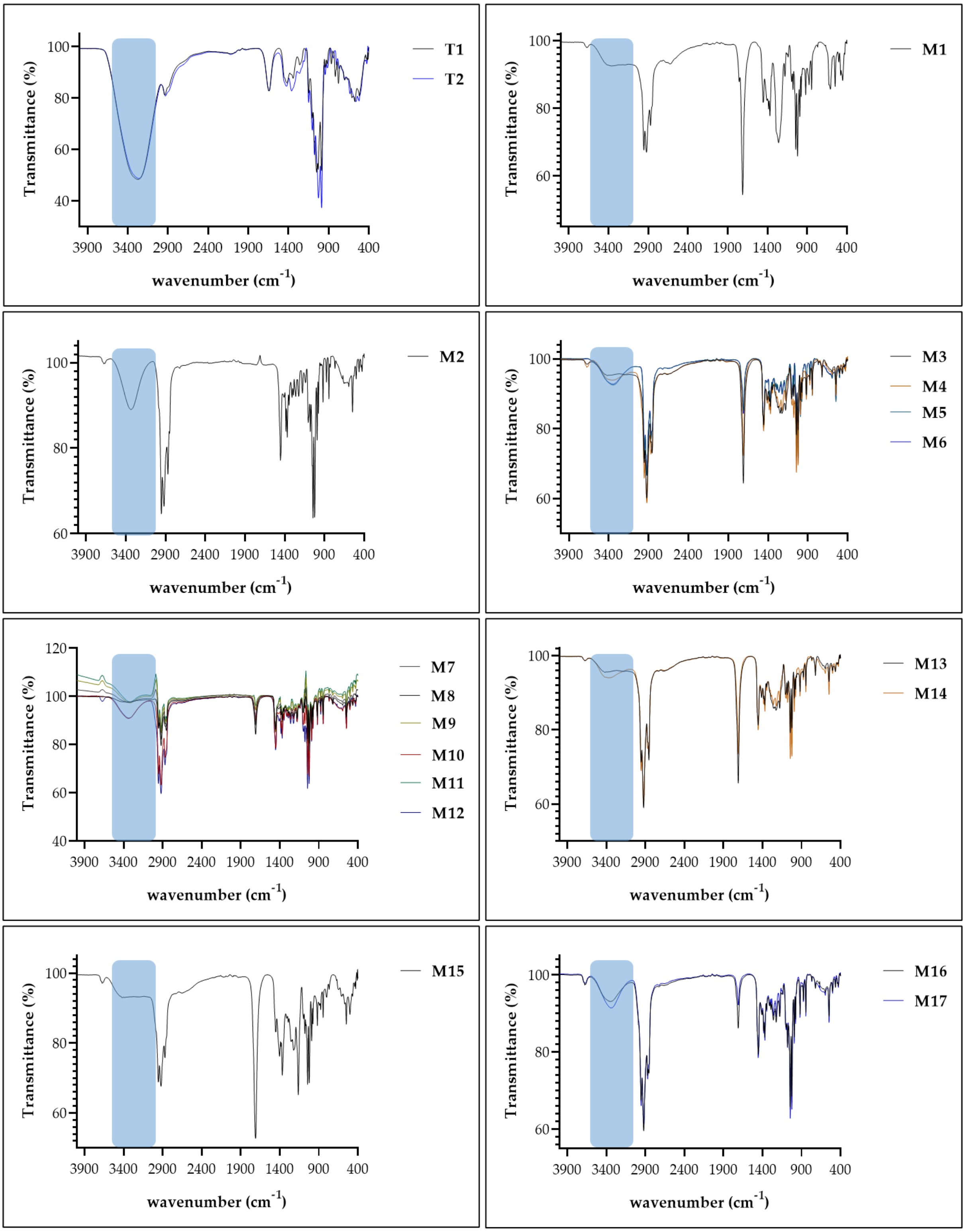
Transmittance (%)
100
80
60
40
20
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


G5
Transmittance (%)
100
80
60
40
3800 3300 2800 2300 1800 1300 800
wavenumber (cm^{-1})


G6
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


G7
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


P1
Transmittance (%)
100
80
60
40
3900 3400 2900 2400 1900 1400 900 400
wavenumber (cm^{-1})


Transmittance (%)
wavenumber (cm^{-1})
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40 60 80 100 120
T1
T2
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12
M13
M14
M15
M16
M17

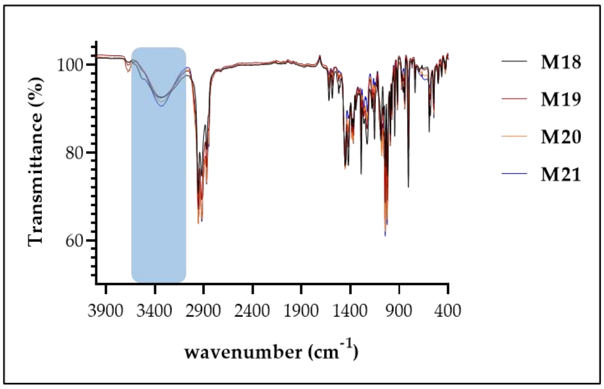

Figure 16: FTIR spectrum of NADES in the wavenumber range of 400-4000 cm^{-1}. The blue vertical rectangles highlight the bands where the wavenumbers used for the calculation were retrieved.

All calculations, as well the results achieved can be seen in appendix, **Table A. 7** and **Table A. 8**. Comparatively to the empirical models (StP, HK, HKF and Ymt), the results obtained from the Hansen method (**eqn. 21**) were found to be significantly higher (almost 3 times higher than empirical models). As there is no experimental data to validate the reliability of such a methodology, the most reasonable solution is to use empirical models (EM). So far, the EM, especially HK, have been shown a great performance in predicting the parameters, δ_D and δ_P, of organic solvents. Since they have a deviation relatively lower from the experimental than the SEM, they may work as indicative for the range of values expected when a SEM is used and, therefore they should not be ignored.

As an alternative, the set of SEM based on HSPs-surface tension correlative equations, demonstrated before in section **1.5.1.1.3** (**eqn. 23** to **eqn. 26**), were also investigated and the results are listed in **Table 11**.

Table 11: Comparison between the δ_H parameter determined using the correlation between the γ_L-HSPs (SEM) and group contribution method (EM).

NADES[c]	γ_L[a]	δ_D[a]	δ_P[a]	δ_H*						
				SEM			**EM**			
		YAH	**Bb**	**SkH**[b]	**Bb´**	**HB´**	**StP**	**HK**	**HKF**	**Ymt**
B2	54.9	8.7	7.0	24.7	23.4	21.4	15.2	24.4	24.0	7.4
B4	48.2	8.6	7.9	22.9	21.5	19.4	32.7	23.1	22.4	7.8
F1	48.4	8.7	4.9	26.1	24.9	23.1	50.9	33.0	31.6	10.2
G1	45.2	8.6	8.8	20.8	19.2	17.0	30.7	27.5	26.3	9.6

NADES[c]	γ_L[a]	δ_D[a]	δ_P[a]	δ_H*						
				SEM			EM			
		YAH	Bb	SkH[b]	Bb′	HB′	StP	HK	HKF	Ymt
G6	46.1	8.6	4.9	24.6	23.2	21.6	48.7	32.4	34.7	9.9
G7	49.3	8.5	3.1	27.3	26.2	24.5	48.7	32.4	35.5	9.8
P1	34.7	8.1	7.3	20.0	18.5	16.7	27.5	32.8	33.7	11.5
T2	47.4	8.5	5.1	26.8	25.7	23.9	50.1	33.5	34.2	10.6
M1	30.4	8.1	0.9	14.3	11.5	10.8	10.8	11.3	11.3	3.3
M2	32.8	8.5	1.2	12.1	8.0	7.5	10.9	10.8	10.9	2.0
M3	31.8	8.3	1.0	11.7	7.8	7.3	9.2	8.9	8.9	2.6
M4	31.3	8.3	1.1	11.3	7.1	6.6	9.7	9.4	9.6	2.4
M5	30.8	8.3	1.3	10.8	6.1	5.7	10.2	9.9	10.0	2.2
M6	32.0	8.3	1.0	11.8	7.8	7.3	10.1	9.8	10.0	2.3
M8	33.1	8.3	0.8	12.1	8.3	7.8	3.5	9.3	9.2	2.4
M9	32.7	8.4	0.8	12.0	8.1	7.6	10.0	9.8	9.9	2.2
M10	31.8	8.4	0.1	11.5	7.3	6.9	9.9	9.7	9.8	2.2
M11	33.1	8.4	0.6	12.4	8.6	8.1	10.1	9.9	10.0	2.2
M12	32.3	8.4	0.8	11.8	7.8	7.3	10.3	10.1	10.2	2.1
M13	33.5	8.3	0.7	12.6	9.0	8.4	8.9	8.6	8.7	2.6
M14	33.5	8.3	1.2	12.5	8.8	8.2	9.5	9.3	9.4	2.4
M15	31.5	8.3	2.2	12.7	9.2	8.5	11.2	10.7	10.8	3.5
M16	32.0	8.5	0.9	10.7	5.7	5.3	9.6	9.4	9.6	2.2
M17	32.6	8.4	1.3	11.8	7.7	7.1	10.1	10.0	10.1	2.1
M18	33.2	8.8	1.4	11.3	6.4	5.9	10.8	11.0	11.3	1.8
M19	32.3	8.7	1.1	11.2	6.3	5.9	10.8	10.9	11.1	1.9
M20	31.6	8.6	1.6	10.7	5.5	5.0	10.8	10.8	11.0	1.9
M21	31.4	8.5	1.2	11.0	6.2	5.8	10.8	10.7	10.9	1.9
AARD%				**18.6**	**23.3**	**28.4**	-	-	-	-

YAH – Yamamoto-Abbott-Hansen model (**eqn. 14**); **Bb** – Beerbower model (**eqn. 17**); **SkH** – Skaarup-Hansen model (**eqn. 23**); **Bb′** – Beerbower model (**eqn. 24**); **HB′**- Hansen-Beerbower model (**eqn. 26**). **AARD%** - average absolute relative deviation percentage.

[a] To facilitate the calculation the values of the surface tension (γ_L) are presented in mN/m and, δ_D and δ_P in (cal/cm^3)$^{1/2}$.

[b] The constant used was *k′*= 0.80.

[c] Some systems may not appear here because it was not possible to measure their surface tension.

*The final results of δ_P are written in MPa$^{1/2}$ units in order to be in the same dimension of δ_D and δ_P estimated previously.

Here, it was possible to observe that the models proposed by Skaarup and Hansen (SkH, **eqn. 23**[XI]), by Beerbower (Bb′, **eqn. 24**[XII]) and Hansen-Beerbower collaboration (HB′, **eqn. 26**[XIII]), in this same order, are the most comparable to the HK model (see more details in the appendix, **Table A. 9**).

In section **1.5.1.1.3** it was also shown that the surface tension can be correlated with the total solubility parameter (**eqn. 27** and from **eqn. 29** to **eqn. 32**). By testing such semi-empirical correlations γ_L-δ_T for the set of organic solvents, it was found that the Jarray′ approach (**eqn. 31**[XIV]), is the closest to the experimental values .

Table 12: Comparison between the experimental and calculated δT parameter of organic compounds and their relative deviation percentage.

NADES	γ (mN/m) [a]	δ_T (Exp) [38]	δ_T(SEM)					δ_T(EM)				
			eqn. 27	eqn. 29	eqn. 30	eqn. 31	eqn. 32	StP	HK	HKF	Ymt	Hoy
Water	72.8	47.81	40.32	44.19	54.11	58.15	43.12	N/D	N/D	N/D	N/D	N/D
MeOH	22.7	29.61	19.69	21.58	28.38	24.96	21.05	22.46	29.83	28.31	14.69	29.94
EtOH	22.1	26.52	18.28	20.03	26.54	22.86	19.54	22.13	25.56	25.18	15.2	26.19
1-prOH	23.0	24.60	17.89	19.61	26.04	22.29	19.13	21.81	23.61	23.38	15.5	24.24
2-prOH	23.0	24.6	17.83	19.54	25.95	22.19	19.06	21.32	22.84	22.97	14.97	22.00
EG	47.7	33.11	25.87	28.35	36.28	34.43	27.66	28.74	34.21	35.89	17.08	35.08
Gly	64.0	36.16	31.33	34.33	43.11	43.17	33.50	35.12	35.41	36.39	17.72	35.45
CHx	24.9	16.8	16.96	18.58	24.81	20.92	18.13	18.79	15	16.77	16.83	18.01
Hx	18.4	14.9	15.06	16.51	22.3	18.20	16.11	16.10	14.59	14.61	14.88	16.60
AARD%			**19.15**	**15.65**	**17.21**	**15.59**	**16.63**	**12.61**	**3.85**	**4.20**	**33.19**	**4.89**

[a] Data collected from the ***"Table of organic solvents"*** created by **professor Murov** [107].

[XI] $\delta_D^2 + k(\delta_P^2 + \delta_H^2) = 17\left(\gamma_L/V_m^{\frac{1}{3}}\right)$

[XII] $\delta_D^2 + 0.632\,\delta_P^2 + 0.632\,\delta_H^2 = 13.9\left(\gamma_L/V_m^{\frac{1}{3}}\right)$

[XIII] $\delta_D^2 + 0.7152(\delta_P^2 + \delta_H^2) = 13.9\left(\gamma_L/V_m^{\frac{1}{3}}\right)$

[XIV] $\delta_T\,(\mathrm{cal.\,cm^{-3}})^{1/2} = 4.0\left(\gamma_L/V_m^{\frac{1}{3}}\right)^{0.59}$

Even so, as can be seen, the difference between the SEM is very little. However, still all the five EM evaluated (StP, HK, HKF, Ymt and Hoy) have shown to be in better agreement with the experimental one than the SEM. Once more, the HK model, with its lowest AARD%, proved to be the best choice to estimate δ_H or δ_T of the organic solvents. Therefore, it was then suggested to use it again as a reference to evaluate the δ_T and consequently the δ_H parameters of NADES obtained from the different approaches in studied and presented in **Table 13**.

Table 13: Surface tension (in mN/m) and calculation of NADES´s δ_H, through the referenced δ_T-γ_L correlative equations (**eqn. 27** and **eqn. 29** - **eqn. 32**), and EM (StP, HK, HKF, Ymt and Hoy). Values are presented in MPa$^{1/2}$.

NADES	**γ_L (mN/m)**	**eqn. 27**		**eqn. 29**		**eqn. 30**		**eqn. 31**		**eqn. 32**		**δ_T (EM)**				
		δ_T	**δ_H**	**δ_T**	**δ_H**	**δ_T**	**δ_H**	**δ_T**	**δ_H**	**δ_T**	**δ_H**	**StP**	**HK**	**HKF**	**Ymt**	**Hoy**
B1	41.04	25.22	N/D	**27.64**	N/D	35.47	N/D	33.43	N/D	26.97	N/D	29.74	**29.35**	25.37	18.52	37.70
B2	54.87	28.20	17.68	**30.91**	21.74	39.22	32.48	38.13	31.17	30.15	20.65	23.82	**31.18**	31.21	19.77	37.84
B3	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	32.03	**30.13**	29.44	19.25	40.68
B4	48.18	27.74	14.69	**30.40**	19.25	38.64	30.64	37.40	29.06	29.66	18.05	39.68	**29.98**	29.56	19.70	40.24
C1	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	25.07	**28.26**	27.62	17.36	29.98
C2	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	28.60	**29.48**	28.78	18.04	30.23
C3	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	24.58	**27.17**	28.02	18.32	29.08
F1	48.44	27.89	19.07	**30.56**	22.81	38.82	33.07	37.63	31.66	29.82	21.80	57.54	**40.09**	37.99	22.57	44.80
G1	45.24	27.42	10.87	**30.05**	16.41	38.23	28.78	36.89	26.96	29.32	15.03	37.49	**35.14**	32.95	21.98	41.13
G2	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	39.06	**37.12**	35.36	21.35	35.41
G3	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	48.48	**39.64**	37.58	22.23	41.68
G4	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	39.23	**36.77**	34.69	21.34	35.39
G5	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	48.46	**39.18**	36.41	22.19	41.65
G6	46.15	26.87	17.79	**29.45**	21.49	37.55	31.69	36.02	29.87	28.73	20.49	54.86	**38.13**	41.59	22.38	43.65
G7	49.34	27.72	20.68	**30.38**	24.13	38.62	33.92	37.37	32.49	29.64	23.19	54.81	**38.11**	42.71	22.34	43.63
P1	34.75	25.30	10.01	**27.73**	15.14	35.57	26.93	33.55	24.21	27.06	13.86	34.24	**38.74**	40.06	23.40	44.65
T1	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	56.82	**40.88**	42.29	22.86	45.36
T2	47.41	28.13	19.50	**30.83**	23.23	39.13	33.47	38.03	32.17	30.08	22.22	56.57	**40.36**	41.30	22.81	45.34
M1	30.37	19.11	9.26	**20.94**	12.62	27.63	22.00	24.09	17.35	20.43	11.75	20.38	**21.36**	21.40	16.43	19.15
M2	32.78	18.61	6.61	**20.40**	10.65	26.98	20.62	23.35	15.58	19.90	9.66	20.86	**21.47**	21.86	16.03	19.43
M3	31.77	18.12	6.39	**19.86**	10.34	26.33	20.15	22.62	14.98	19.37	9.38	19.19	**19.37**	19.71	16.42	18.82

NADES	γ_L (mN/m)	eqn. 27		eqn. 29		eqn. 30		eqn. 31		eqn. 32		δ_T (EM)				
		δ_T	δ_H	δ_T	δ_H	δ_T	δ_H	δ_T	δ_H	δ_T	δ_H	**StP**	**HK**	**HKF**	**Ymt**	**Hoy**
M4	31.30	18.03	5.88	**19.76**	10.00	26.21	19.92	22.49	14.67	19.27	9.01	19.59	**19.94**	20.34	16.26	19.00
M5	30.82	17.93	5.20	**19.65**	9.57	26.09	19.65	22.34	14.31	19.17	8.55	19.92	**20.42**	20.86	16.13	19.15
M6	32.02	18.27	6.43	**20.02**	10.42	26.53	20.29	22.85	15.15	19.53	9.44	19.86	**20.34**	20.78	16.15	19.13
M7	N/D*	N/D	N/D	**N/D**	N/D	N/D	N/D	N/D	N/D	N/D	N/D	19.49	**19.92**	20.38	16.21	19.06
M8	33.09	18.35	6.82	**20.11**	10.69	26.64	20.48	22.97	15.40	19.62	9.73	16.47	**19.30**	20.10	16.27	18.99
M9	32.75	18.38	6.62	**20.15**	10.58	26.68	20.44	23.01	15.35	19.66	9.61	19.78	**20.30**	20.78	16.13	19.17
M10	31.83	18.11	5.99	**19.85**	10.09	26.32	20.02	22.61	14.80	19.36	9.10	19.72	**20.22**	20.69	16.14	19.14
M11	33.12	18.51	7.05	**20.28**	10.89	26.84	20.68	23.20	15.66	19.79	9.94	19.86	**20.41**	20.89	16.10	19.19
M12	32.30	18.32	6.42	**20.07**	10.42	26.59	20.32	22.92	15.19	19.58	9.45	20.03	**20.63**	21.12	16.05	19.25
M13	33.49	18.46	7.33	**20.23**	11.06	26.78	20.74	23.13	15.74	19.74	10.13	19.00	**19.18**	19.56	16.42	18.81
M14	33.51	18.56	7.23	**20.34**	11.03	26.91	20.79	23.28	15.80	19.85	10.08	19.44	**19.79**	20.22	16.26	19.00
M15	31.54	18.89	7.59	**20.71**	11.38	27.35	21.18	23.77	16.30	20.20	10.43	20.24	**21.37**	21.52	16.51	18.97
M16	31.98	18.04	4.83	**19.78**	9.42	26.24	19.65	22.51	14.31	19.29	8.36	19.50	**19.99**	20.53	16.16	19.14
M17	32.62	18.34	6.36	**20.10**	10.40	26.63	20.32	22.96	15.20	19.61	9.41	19.89	**20.48**	21.01	16.06	19.24
M18	33.21	18.85	5.37	**20.66**	10.02	27.30	20.46	23.71	15.35	20.16	8.93	20.67	**21.33**	22.44	16.25	19.31
M19	32.30	18.54	5.29	**20.32**	9.86	26.88	20.18	23.24	14.99	19.82	8.79	20.59	**21.27**	22.18	16.14	19.33
M20	31.57	18.28	4.75	**20.03**	9.47	26.55	19.83	22.86	14.53	19.55	8.39	20.53	**21.23**	21.97	16.06	19.35
M21	31.38	18.19	5.23	**19.94**	9.69	26.43	19.87	22.73	14.60	19.45	8.65	20.49	**21.20**	21.84	16.01	19.36
AARD%*		**14.04**		**6.92**		**24.52**		**12.07**		**8.43**		-	-	-	-	-

N/D – not determined (equipment problems)

* AARD% between the δ_T from HK and those of the semi-empirical models.

Observing the results, it can be concluded that, in general, the investigated SEM , to some extent, in accordance with the HK. Unlike organic solvents where Jarray's equation was identified as the closest to the HK, for NADES the Hildebrand-Scott-Lee model (**eqn. 29**[XV]) stands out as the most similar to it.

3.3.3.1 Correlating δ_H with W%

Among the three HSPs, δ_H is undoubtedly the ideal parameter to better describe the changes that may occur in the solubility of systems due to their water content. Hence, traces of any relationship between the hydrogen-bond parameter and water content were investigated. All the models used previously to predict δ_H were analyzed and are find presented in **Figure 17**.

[XV] $\delta_T\,(\mathrm{cal.\,cm^{-3}})^{1/2} = 4.1\left(\gamma_L/V_m^{\frac{1}{3}}\right)^{0.43}$

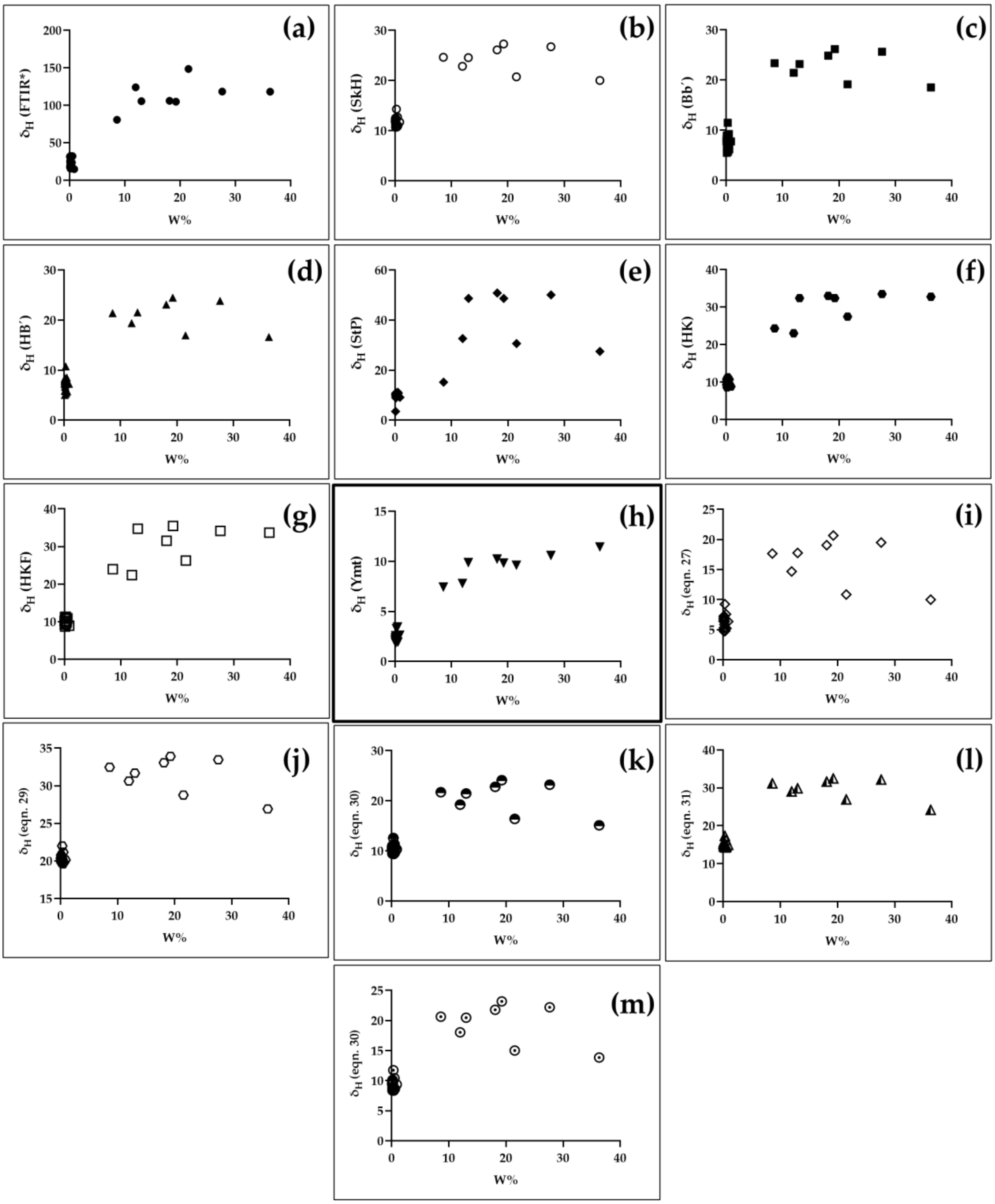

Figure 17: Correlation between the water content measured (W%, X axis) and the δ_H determined by the different methods studied (in $MPa^{1/2}$): **(a)** - Hansen FTIR* method modified in this work (see **Table A. 7**, appendix); (b) – Skaarup and Hansen (*SkH*, **eqn. 23**); **(c)** - Beerbower (*Bb´*, **eqn. 24**); **(d)** – Hansen-Beerbower (*HB´*, **eqn. 26**); **(e)** – Stefanis-Panayiotou (StP); **(f)** – Hoftyzer-Van Krevelen (HK); **(g)** – Hoftyzer-Van Krevelen-Fedors (HKF); **(h)** - Yamamoto; **(i)** – Beerbower (**eqn. 27**); **(j)** – Hildebrand-Scott-Lee (**eqn. 29**); **(k)** – Sheldon (**eqn. 30**); **(l)** – Jarray (**eqn. 31**); **(m)** – Gordon (**eqn. 32**).

As can be seen in the graphics, there is no linear relationship between δ_H and W%. Despite it been shown a large discrepancy from the experimental values, the best fit found was between δ_H from the Ymt model with W% (the graphic in the centre), when the δ_H showed a slight tendency to increase with the increase of W%.

3.4 Solvatochromic Parameters

3.4.1 Assessment of NADES´s Polarity

The solvatochromic parameters, polarity (E_{NR}) and Kamlet-Taft multiparameter (π^*, α and β), were used to characterize the solvent strength of NADES, i.e., their capacity to act as such. Through the study of polarity (E_{NR}), it was observed that, except for hexane (Hx) and cyclohexane (CHx), most NADES (blue) exhibit polarities quite similar to the conventional organic solvents (red) (**Figure 18**). This is certainly very interesting, as it may be a good indication to, once again, reinforce the concept of the potential of NADES as alternative green solvents and possibly even replace the commonly used harmful or toxic ones.

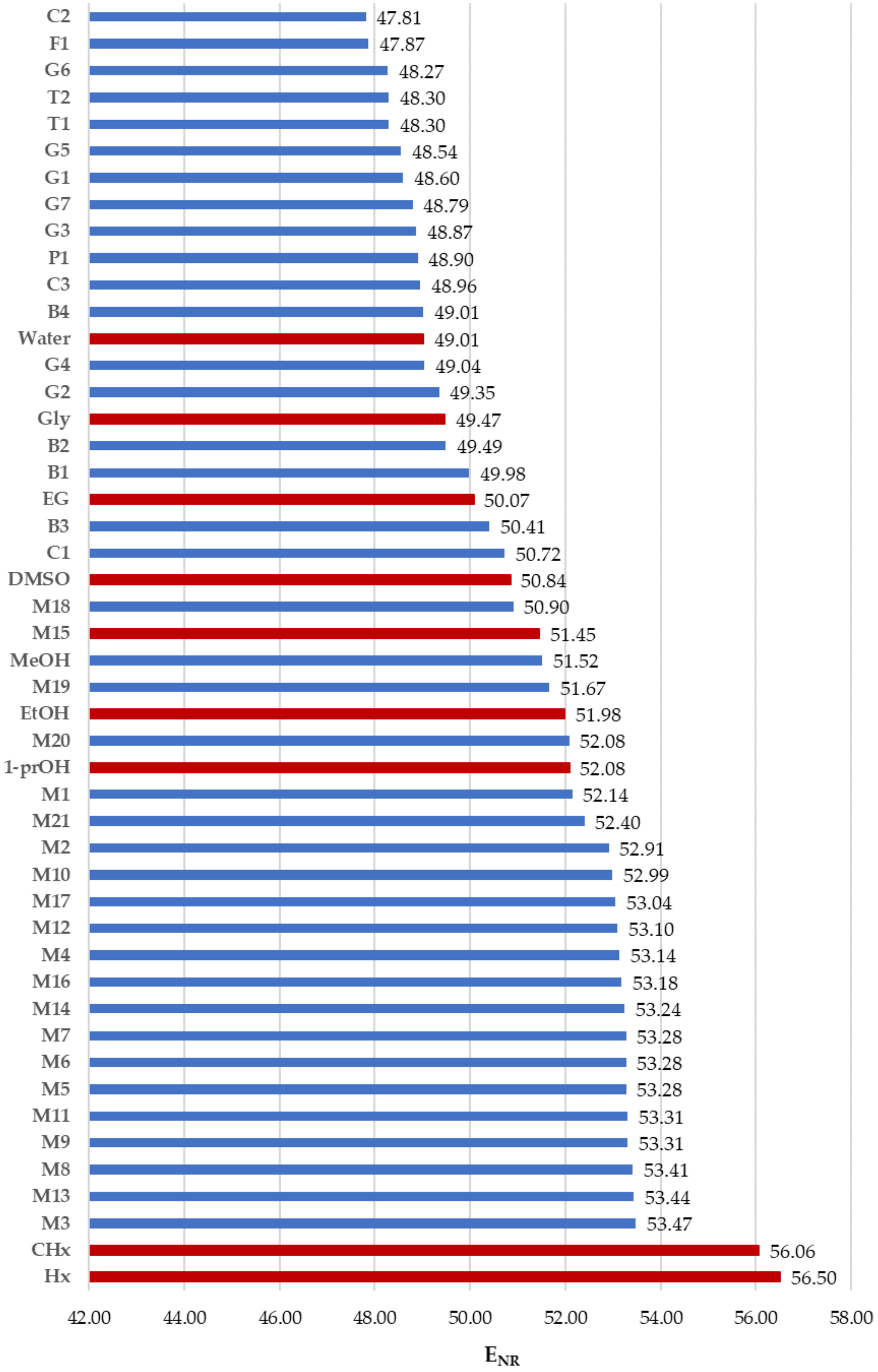

Figure 18: Polarity of the NADES (blue bars) and some organic solvents (red bars) organized in descending order (from top to bottom).

Using Nile red as dye means that the ground state is better stabilized by hydrophobic solvents, which means an increase in the energy difference between the two states (ΔE) and therefore a deviation of the dye´s absorption curve to a lower wavelength. Therefore, when **eqn.** 39[XVI] is used, the higher values of E_{NR} the lower is the polarity (e.g., CHx and Hx). In this perspective, according to **Figure 18**, **C2** (ChCl:Gly (1:2)) and **M3** (Men:DecA (1:1)) are, respectively, the most and less polar systems found in this work.

3.4.1.1 Correlation between E_{NR} and δ_P/ δ_H

Taking into account that both, E_{NR} and δ_P parameters, are descriptive measures of polarity it would make sense to assume a priori some kind of correlation between them. As it can be seen in **Figure 19**, such a relationship truly exists between E_{NR} and the semi-empirical δ_P (a) and is much better perceptible between E_{NR} and empirical δ_P (b).

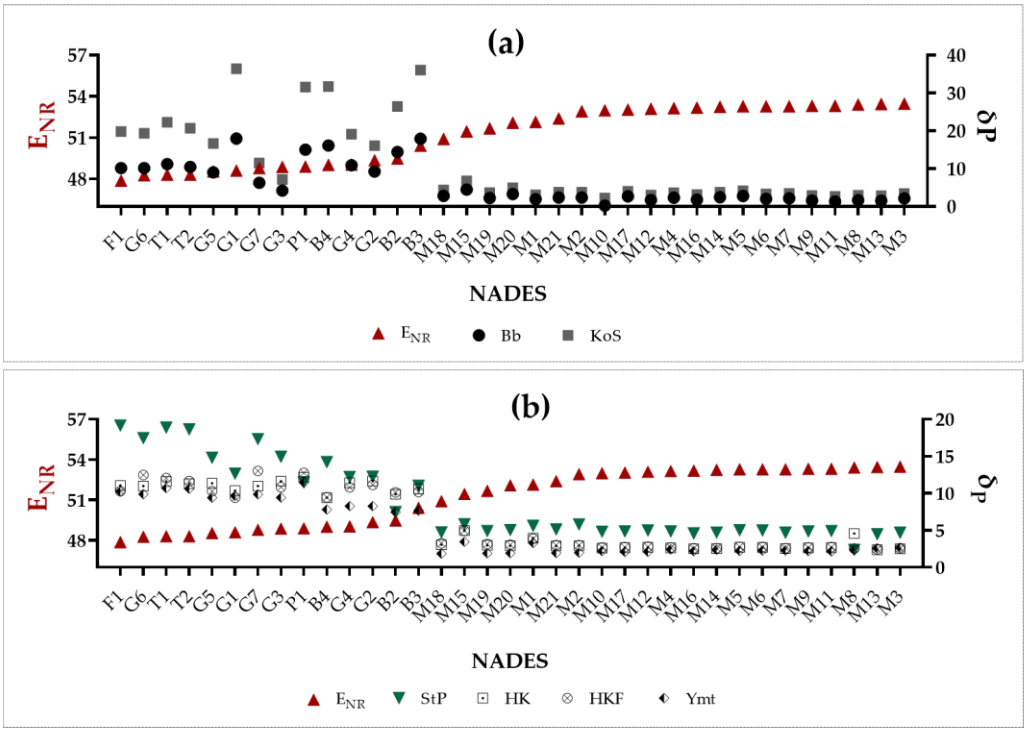

Figure 19: Relationship between E_{NR} and the δ_P estimated through the two studied methods, the SEM (a) and the EM (b).

[XVI] $E_{NR} = \frac{28591.5}{\lambda_{max}}$

The profile displayed in both graphs confirms that low polarity systems have a lower contribution of the polar parameter (δ_P) and vice versa. Furthermore, such behaviour was also detected when polarity was correlated with the hydrogen-bond parameter (δ_H) (**Figure 20**).

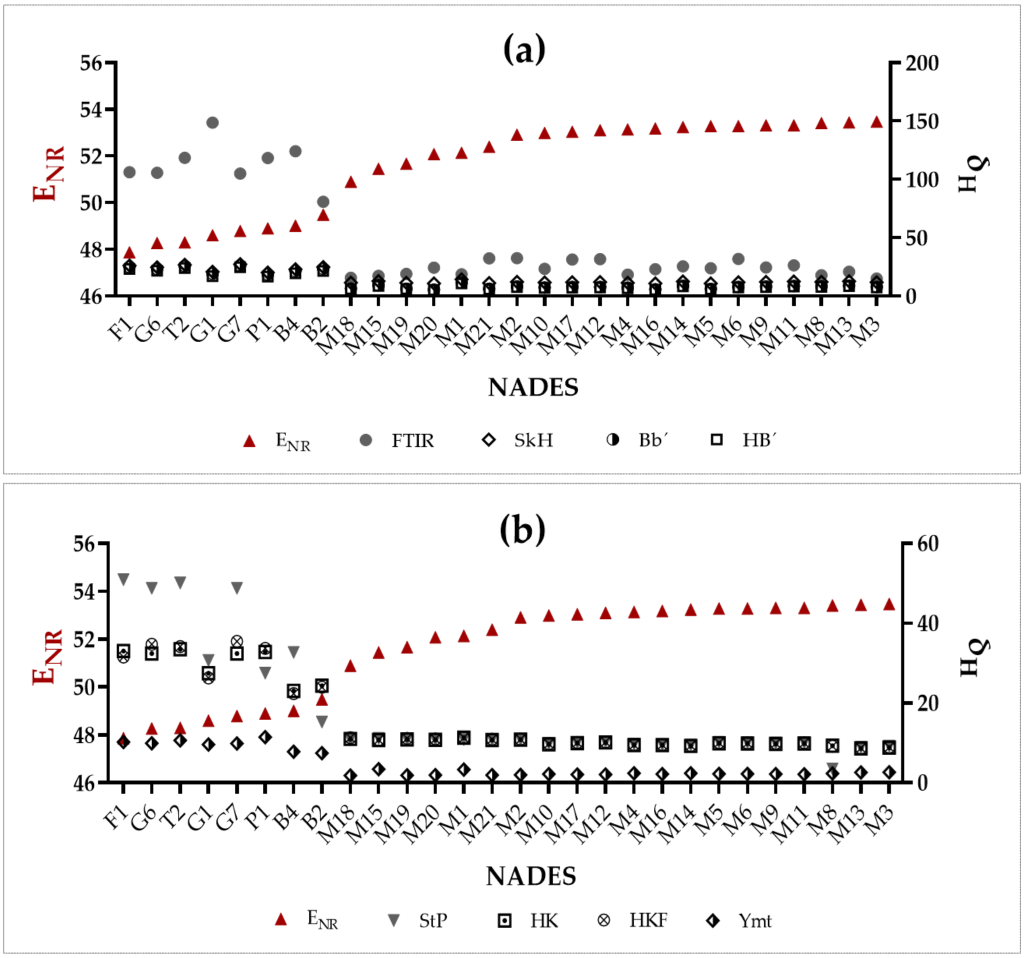

Figure 20: Relationship between E_{NR} and the δ_H estimated through the two studied methods, the SEM (a) and the EM (b).

Such information taken from **Figure 19** and **Figure 20** is extremely important as it means that new models can be developed through these correlations. Moreover, considering the facility of the E_{NR} measurement, the determination of δ_P or δ_H would be surely easier and faster.

3.4.1 Assessment of NADES´s KTPs

The three parameters of Kamlet-Taft not only allow to complement the polarity study, as well introduce parameters that provide a more comprehensive view of the solvent strength and behaviour. As shown before, Dwamena and co-works, introduced three equations, **eqn. 41**[XVII], **eqn. 48**[XVIII] and **eqn. 50**[XIX] (this set of equations was abbreviated to ***DE***, from "Dwamena equations"), describing them, in the same order, as a more simple and suitable approach to rewrite the **eqn**. **40**[XX], **eqn. 47**[XXI] and **eqn**. **49**[XXII] (set abbreviated to ***OE***, from "original equations"), to estimate, respectively, π^*, α and β of DES. In order to understand their differences, both approaches were evaluated, being that the solvent pair DMSO and hexane were used as a reference to calculate either to the π^*, using **eqn**. **40**, or β, though **eqn**. **49**. All the results are listed in **Table 14**. Here, it was also observed that the dipole moment calculated by the correlative models between π^*-μ (**eqn. 42**[XXIII], **eqn. 43**[XXIV] and **eqn**. **44**[XXV]), mainly from the **eqn. 42**, are very similar to those found in this work using Onsager and Salem methods (**Table 9**).

[XVII] $\pi^* = 0.314\,(27.52 - \varpi_{\mathrm{DM4A}})$

[XVIII] $\alpha = (19.967 - 1.024\pi^* - \varpi_{\mathrm{NR}})/1.6078$

[XIX] $\beta = (1.035\varpi_{\mathrm{DM4A}} + 2.64 - \varpi_{\mathrm{4NA}})/2.80$

[XX] $\pi^* = (\bar{\upsilon}_{\mathrm{solvent}} - \bar{\upsilon}_{\mathrm{cyclohexane}})/(\bar{\upsilon}_{\mathrm{DMSO}} - \bar{\upsilon}_{\mathrm{cyclohexane}})$

[XXI] $\alpha = 0.0649 * (\mathrm{E_T}(30)) - 0.72\pi^* - 2.03$

[XXII] $\beta = [0.76(\Delta\bar{\upsilon}_{\mathrm{solvent}} - \Delta\bar{\upsilon}_{\mathrm{hexane}})]/(\Delta\bar{\upsilon}_{\mathrm{DMSO}} - \Delta\bar{\upsilon}_{\mathrm{hexane}})$

[XXIII] $\pi^* = 0.03 + 0.23\mu$

[XXIV] $\pi^* = 0.03 + 0.23\mu$

[XXV] $\pi^* = 0.56 + 0.11\mu$

Table 14: Maximum absorption wavelength of the used probes obtained experimentally and used to calculate the solvatochromic parameters of organic solvents and NADES.

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π^*	α	β	μ^{+}
1	**Water**	583.3 ± 0.3	49.01	421.3 ± 0.6	380.0 ± 0.0	1.14 [a]	0.33 [a]	0.21 [a]	4.83; 2.49; 5.27
						1.19 [b]	1.00 [b]	0.32 [b]	5.04; 2.63; 5.73
		593.2 [80]	48.21[80]	N/A	N/A	1.09 [111]	1.17 [111]	0.18 [111]	4.61; 2.34; 4.82
		585.4 [92]	48.90 [92]	N/A	N/A	1.14 [112]	1.23 [112]	0.29 [112]	4.83; 2.49; 5.27
		584.5 [113]	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2	**MeOH**	555.0 ± 0.1	51.52	392.0 ± 0.0	371.3 ± 0.6	0.69 [a]	0.82 [a]	0.75 [a]	2.87; 1.2; 1.18
						0.63 [b]	0.81 [b]	0.75 [b]	2.61; 1.03; 0.64
		549.6 [80]	52.02 [80]	N/A	N/A	0.60[108]	0.93[108]	0.62[108]	2.48; 0.94; 0.36
		559.5 [92]	51.10 [92]	N/A	N/A	N/A	N/A	N/A	-0.13; -0.77; -5.09

Nº	Organic solvent	NR (λmax ± SD)	ENR (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ+
3	**EtOH**	550.0 ± 0.0	52.00	388.0 ± 0.0	372.0 ± 0.0	0.62 [a]	0.90 [a]	0.89 [a]	2.57; 1; 0.55
						0.55 [b]	0.74 [b]	0.87 [b]	2.26; 0.8; -0.09
		548.3[27]	52.15[27]	N/A	N/A	0.54 [112]	0.83 [112]	0.77 [112]	2.22; 0.77; -0.18
		552.3 [92]	51.76 [92]	N/A	N/A	N/A	N/A	N/A	-0.13; -0.77; -5.09
		539.8 [113]	N/A	N/A	N/A	N/A	N/A	N/A	-0.13; -0.77; -5.09
4	**1-prOH**	549.0 ± 0.1	52.08	387.7 ± 0.6	375.3 ± 1.2	0.62 [a]	0.91 [a]	1.01 [a]	2.57; 1; 0.55
						0.54 [b]	0.74 [b]	0.96 [b]	2.22; 0.77; -0.18
		545.6 [80]	52.40 [80]	N/A	N/A	0.53 [111]	0.84 [111]	0.85 [111]	2.17; 0.74; -0.27
		549.70 [92]	52.02 [92]	N/A	N/A	0.52 [112]	0.78 [112]	NA	2.13; 0.71; -0.36
5	**EG**	571.0 ± 0.1	50.07	406.0 ± 0.0	375.3 ± 2.3	0.91 [a]	0.56 [a]	0.47 [a]	3.83; 1.83; 3.18

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ^{+}
						0.91 ^{b}	0.95 ^{b}	0.53 ^{b}	3.83; 1.83; 3.18
		565.2	50.58	N/A	N/A	0.92[108]	0.90[64]	0.52[64]	3.87; 1.86; 3.27
		557.3 [113]	N/A	N/A	N/A	N/A	N/A	N/A	-0.13; -0.77; -5.09
6	**Gly**	578.0 ± 0.0	49.47	415.3 ± 0.6	386.7 ± 1.2	1.05 ^{a}	0.43 ^{a}	0.58 ^{a}	4.43; 2.23; 4.45
						1.08 ^{b}	0.97 ^{b}	0.61 ^{b}	4.57; 2.31; 4.73
		580.4 [111]	49.88 [111]	N/A	N/A	1.04 [111]	0.93 [111]	0.67 [111]	4.39; 2.2; 4.36
7	**DMSO**	562.3 ± 0.1	50.84	412.0 ± 0.0	389.7 ± 0.6	1.00 ^{a}	0.55 ^{a}	0.76 ^{a}	4.22; 2.09; 4
						1.02 ^{b}	0.71 ^{b}	0.75 ^{b}	4.3; 2.14; 4.18
		544.0 [113]	N/A	N/A	N/A	1.00 [112]	0.00 [112]	0.76 [112]	4.22; 2.09; 4
8	**CHx**	510.0 ± 0.0	56.06	358 ± 0	329.3 ± 1.2	0.08 ^{a}	1.55 ^{a}	0.28 ^{a}	0.22; -0.54; -4.36

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ^{+}
						-0.13 [b]	0.31 [b]	0.42 [b]	-0.7; -1.14; -6.27
		487.6 [80]	58.63 [80]	N/A	N/A	0.00 [112]	0.00 [112]	0.00 [112]	-0.13; -0.77; -5.09
		459.0 [113]	N/A	N/A	N/A	N/A	N/A	N/A	-0.13; -0.77; -5.09
9	**Hx**	506.0 ± 0.0	56.50	354.0 ± 0.0	319.7 ± 0.6	0.00 [a]	1.64 [a]	0.00 [a]	-0.13; -0.77; -5.09
						-0.23 [b]	0.27[b]	0.21 [b]	-1.13; -1.43; -7.18
		484.4 [80]	59.02 [80]	N/A	N/A	-0.08 [112]	0.00 [112]	0.00 [112]	-0.48; -1.00; -5.82
10	**Bet:Glc:W (5:2:10)**	572.0 ± 0.0	49.99	419 ± 1.4	388.0 ± 0.0	1.10 [a]	0.42 [a]	0.52 [a]	4.65; 2.37; 4.91
						1.15 [e]	0.81[e]	0.56 [e]	4.87; 2.51; 5.36
11	**Bet:Gly:Suc:W (2:3:1:5)**	577.7 ± 0.2	49.49	418.7 ± 1.2	390 ± 2	1.10 [a]	0.39 [a]	0.59 [a]	4.65; 2.37; 4.91
						1.14 [b]	0.92 [b]	0.61[b]	4.83; 2.49; 5.27

Nº	Organic solvent	NR (λmax ± SD)	ENR (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ^{+}
12	**Bet:sorb:W (3:1:10)**	567.2 ± 0.4	50.41	420 ± 0	389 ± 1.4	1.12 [a]	0.44 [a]	0.53 [a]	4.74; 2.43; 5.09
						1.17 [b]	0.71 [b]	0.56 [b]	4.96; 2.57; 5.55
13	**Bet:Suc:Pro:W (5:2:2:21)**	583.3 ± 0.3	49.01	419.7 ± 0.6	390.7 ± 1.2	1.11 [a]	0.35 [a]	0.59 [a]	4.7; 2.4; 5
						1.16 [b]	1.02 [b]	0.61 [b]	4.91; 2.54; 5.45
14	**ChCl:EG (1:2)**	563.7 ± 0.1	50.72	412.3 ± 0.6	387.3 ± 1.2	1.00 [a]	0.54 [a]	0.68 [a]	4.22; 2.09; 4
						1.03 [b]	0.73 [b]	0.69 [b]	4.35; 2.17; 4.27
						1.11[75]	0.89[75]	0.64[75]	4.7; 2.4; 5
15	**ChCl:Gly (1:2)**	598 ± 0	47.81	415.5 ± 0.7	386 ± 0	1.05 [a]	0.32 [a]	0.55 [a]	4.43; 2.23; 4.45
						1.08 [b]	1.33 [b]	0.59 [b]	4.57; 2.31; 4.73
						1.11[75]	1.49[75]	0.52[75]	4.7; 2.4; 5
16	**ChCl:Ure (1:2)**	584 ± 0	48.96	418 ± 0	388 ± 0	1.09 [a]	0.36 [a]	0.55 [a]	4.61; 2.34; 4.82
						1.13 [b]	1.05 [b]	0.58 [b]	4.78; 2.46;

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ[+]
									5.18
						1.14 [75]	1.42 [75]	0.50 [75]	4.83; 2.49; 5.27
17	**Fru:Glc:Suc:W (1:1:1:10)**	597.3 ± 0.1	47.87	425.3 ± 1.2	387.3 ± 1.2	1.19 [a]	0.22 [a]	0.34 [a]	5.04; 2.63; 5.73
						1.26 [b]	1.20 [b]	0.41 [b]	5.35; 2.83; 6.36
18	**Glc:Pro:Gly:W(3:5:3:20)**	588.3 ± 0.3	48.60	420.7 ± 0.6	388.7 ± 1.2	1.13 [a]	0.31 [a]	0.50 [a]	4.78; 2.46; 5.18
						1.18 [b]	1.10 [b]	0.54 [b]	5; 2.6; 5.64
19	**Gly:Fru (4:1)**	579.3 ± 0.7	49.35	415 ± 1.4	388 ± 0	1.04 [a]	0.42 [a]	0.63 [a]	4.39; 2.2; 4.36
						1.08 [b]	1.00 [b]	0.65 [b]	4.57; 2.31; 4.73
20	**Gly:Fru:Sorb:W (1:1:1:3)**	585 ± 0.1	48.87	421 ± 0	392 ± 0	1.13	0.33	0.59	4.78; 2.46; 5.18
						1.18 [b]	1.03 [b]	0.61 [b]	5; 2.6; 5.64
21	**Gly:Glc (4:1)**	583 ± 0.1	49.04	418 ± 2	387.3 ± 0.6	1.09 [b]	0.37 [b]	0.53 [b]	4.61; 2.34; 4.82
						1.13 [b]	1.03 [b]	0.57 [b]	4.78; 2.46;

Nº	**Organic solvent**	**NR (λmax ± SD)**	**ENR (Kcal/mol)**	**DM4N (λmax ± SD)**	**4NA (λmax ± SD)**	**π***	**α**	**β**	**μ^{+}**
									5.18
22	**Gly:Glc:Sorb:w (1:1:1:3)**	589 ± 0.1	48.54	425 ± 1.4	390 ± 0	1.19 [a]	0.27 [a]	0.43 [a]	5.04; 2.63; 5.73
						1.25 [b]	1.06 [b]	0.48 [b]	5.3; 2.8; 6.27
23	**Gly:Suc:Sorb:W (2:1:2:10)**	592.3 ± 0.2	48.27	424.3 ± 0.6	388 ± 0	1.18 [a]	0.25 [a]	0.38 [a]	5; 2.6; 5.64
						1.24 [b]	1.13 [b]	0.45 [b]	5.26; 2.77; 6.18
24	**Gly:Tre:Sorb:W (2:1:2:10)**	586.0 ± 0.0	48.79	424.5 ± 0.7	388 ± 0	1.18 [a]	0.29 [a]	0.38 [a]	5; 2.6; 5.64
						1.24 [b]	1.01 [b]	0.45 [b]	5.26; 2.77; 6.18
25	**Pro:Gly:Sorb:W (1:1:1:13)**	584.7 ± 0.1	48.90	424.3 ± 0.6	389.7 ± 0.6	1.18 [a]	0.30 [a]	0.43 [a]	5; 2.6; 5.64
						1.24 [b]	0.99 [b]	0.49 [b]	5.26; 2.77; 6.18
26	**Tre:Fru:W (1:2:13)**	592.0 ± 0.3	48.30	426 ± 0	390.5 ± 0.7	1.20 [a]	0.24 [a]	0.42 [a]	5.09; 2.66; 5.82
						1.27 [b]	1.10 [b]	0.47 [b]	5.39; 2.86; 6.45
27	**Tre:Glc:W (1:2:13)**	592.0 ± 0.3	48.30	428 ± 0	389.5 ± 0.7	1.23 [a]	0.22 [a]	0.34 [a]	5.22; 2.74; 6.09

Nº	Organic solvent	NR (λmax ± SD)	ENR (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ[+]
						1.30 [b]	1.08 [b]	0.41 [b]	5.52; 2.94; 6.73
28	**Men:AcetA (1:1)**	548.3 ± 0.1	52.14	386 ± 0	364 ± 2	0.59 [a]	0.93 [a]	0.68 [a]	2.43; 0.91; 0.27
						0.51 [b]	0.75 [b]	0.71 [b]	2.09; 0.69; -0.45
						0.53 [114]	1.64 [114]	0.60 [114]	2.17; 0.74; -0.27
29	**Men:Bor (7:2)**	540.3 ± 0.1 [92]	52.91	382 ± 0	367.3 ± 1.2	0.52 [a]	1.03 [a]	0.92 [a]	2.13; 0.71; -0.36
						0.42 [b]	0.64 [b]	0.90 [b]	1.7; 0.43; -1.27
30	**Men:DecA (1:1)**	534.7 ± 0.1	53.48	377 ± 1.4	354.5 ± 0.7	0.43 [a]	1.13 [a]	0.62 [a]	1.74; 0.46; -1.18
						0.31 [b]	0.59 [b]	0.67 [b]	1.22; 0.11; -2.27
31	**Men:DecA (2:1)**	538 ± 0.0 [92]	53.14	376 ± 0	360 ± 0	0.42 [a]	1.12 [a]	0.86 [a]	1.7; 0.43; -1.27
						0.29 [b]	0.67 [b]	0.85	1.13; 0.06; -2.45

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ^{+}
32	**Men:DecA (4:1)**	536.7 ± 0.1	53.28	378.5 ± 0.7	359 ± 1.4	0.46[a]	1.10[a]	0.74[a]	1.87; 0.54; -0.91
						0.35[b]	0.61[b]	0.76[b]	1.39; 0.23; -1.91
33	**Men:DecA (7:2)**	536.7 ± 0.1 [92]	53.28	377 ± 1.4	363 ± 1.4	0.43[a]	1.12[a]	0.93[a]	1.74; 0.46; -1.18
						0.31	0.63	0.91	1.22; 0.11; -2.27
34	**Men:LauA (2.7:1)**	536.7 ± 0.1	53.28	378 ± 0	360 ± 0	0.45[a]	1.10[a]	0.79[a]	1.83; 0.51; -1
						0.33	0.62	0.80	1.3; 0.17; -2.09
35	**Men:LauA (2:1)**	535.3 ± 0.1	53.41	378.0 ± 0.0	359.3 ± 0.6	0.45[a]	1.11[a]	0.77[a]	1.83; 0.51; -1
						0.33[b]	0.59[b]	0.78[b]	1.3; 0.17; -2.09
36	**Men:LauA (4.5:1)**	536.3 ± 0.1	53.31	378.5 ± 0.7	361.0 ± 1.4	0.46[a]	1.10[a]	0.81[a]	1.87; 0.54; -0.91
						0.35	0.60	0.82	1.39; 0.23; -1.91

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ^{+}
37	**Men:LauA (4:1)**	539.6 ± 0.1	52.99	379.0 ± 1.0	364.0 ± 0	0.47[a]	1.07[a]	0.90[a]	1.91; 0.57; -0.82
						0.36	0.66	0.88	1.43; 0.26; -1.82
38	**Men:LauA (5.3:1)**	536.3 ± 0.2	53.31	378.0 ± 0.0	362.5 ± 0.7	0.45[a]	1.10[a]	0.88[a]	1.83; 0.51; -1
						0.33[b]	0.61[b]	0.87[b]	1.3; 0.17; -2.09
39	**Men:LauA (8:1)**	538.4 ± 0.1 [92]	53.10	380.0 ± 0.0	366 ± 0	0.49[a]	1.07[a]	0.94[a]	2; 0.63; -0.64
						0.38	0.63	0.91	1.52; 0.31; -1.64
40	**Men:LauA:DecA (2:1:1)**	535.0 ± 0.1 [92]	53.44	376.3 ± 0.6	353.3 ± 0.6	0.42[a]	1.13[a]	0.60[a]	1.7; 0.43; -1.27
						0.30	0.60	0.66	1.17; 0.09; -2.36
41	**Men:LauA:DecA (4:1:1)**	537.0 ± 0.1 [92]	53.24	378.3 ± 0.6	358.3 ± 0.6	0.46[a]	1.10[a]	0.72[a]	1.87; 0.54; -0.91
						0.34[b]	0.62[b]	0.75[b]	1.35; 0.2; -2
42	**Men:LevA (1:1)**	555.7 ± 0.1	51.45	392.0 ± 0.0	368.0 ± 0.0	0.69[a]	0.81[a]	0.63[a]	2.87; 1.2;

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π*	α	β	μ^{+}
									1.18
						0.63[b]	0.82[b]	0.67[b]	2.61; 1.03; 0.64
						0.66 [114]	1.56 [114]	0.58 [114]	2.74; 1.11; 0.91
43	**Men:MyrA (4:1)**	537.7 ± 0.1 [92]	53.18	379.0 ± 1.0	360.0 ± 2.0	0.47[a]	1.08[a]	0.76[a]	1.91; 0.57; -0.82
						0.36[b]	0.62[b]	0.78[b]	1.43; 0.26; -1.82
44	**Men:MyrA (8:1)**	539 ± 0.1	53.05	379.5 ± 0.7	368.0 ± 0.0	0.48[a]	1.07[a]	1.02[a]	1.96; 0.6; -0.73
						0.37[b]	0.64[b]	0.98[b]	1.48; 0.29; -1.73
45	**Men:Thy (1:1)**	561.7 ± 0.1 [92]	50.90	400.0 ± 0.0	369.5 ± 0.7	0.82[a]	0.69[a]	0.45[a]	3.43; 1.57; 2.36
						0.79[b]	0.84[b]	0.52[b]	3.3; 1.49; 2.09
46	**Men:Thy (2:1)**	553.3 ± 0.1 [92]	51.67	395.5 ± 0.7	368.0 ± 0.0	0.75[a]	0.79[a]	0.53[a]	3.13; 1.37; 1.73
						0.70[b]	0.73[b]	0.58[b]	2.91; 1.23;

Nº	Organic solvent	NR (λmax ± SD)	E_{NR} (Kcal/mol)	DM4N (λmax ± SD)	4NA (λmax ± SD)	π^*	α	β	μ[+]
									1.27
47	**Men:Thy (4:1)**	549.0 ± 0.1 [92]	52.08	390.5 ± 0.7	369.0 ± 1.4	0.66 [a]	0.87 [a]	0.71 [a]	2.74; 1.11; 0.91
						0.60 [b]	0.71 [b]	0.73 [b]	2.48; 0.94; 0.36
48	**Men:Thy (8:1)**	545.7 ± 0.1 [92]	52.40	386.5 ± 0.7	366.5 ± 0.7	0.60 [a]	0.94 [a]	0.75 [a]	2.48; 0.94; 0.36
						0.52 [b]	0.69 [b]	0.76 [b]	2.13; 0.71; -0.36

[a] π^*, α, and β that were calculated using OE (**eqn. 40**, **eqn. 47** and **eqn. 49**).

[b] π^*, α, and β that were calculated using DE (**eqn. 41**, **eqn. 48** and **eqn. 50**).

[+] Dipole moments calculated using equations **eqn. 42**, **eqn. 43** and **eqn. 44**, respectively.

Here it is possible to confirm that most of the hydrophilic systems are more susceptible to polarization than water, which in turn, is superior to the hydrophobic ones. Furthermore, both π^* as well β, calculated by the two approaches referred above, show values very similar. However, regarding to α, significant differences were found between the values obtained from **eqn. 47** and **eqn. 48**, especially the order of acidity. This is because according to **eqn. 47**, hydrophilic systems are tendentially more acidic than hydrophobic ones and therefore have a greater tendency to donate protons. However, the Dwamena equation (**eqn. 48**), shows exactly the opposite situation. Taking into account the acidic nature of the majority of hydrophobic HBD's, it would make sense to consider **eqn. 47** as the most appropriate to be used, but given the fact that hydrophilic systems components are also constituted by several hydrogen donor groups (OH), the values from **eqn. 48** should perhaps not be considered incorrect. As shown in **Figure 21**, both approaches were also used to evaluate the variation of KTPs with the increase of carbon chain lengths of hydrophobic NADES. For a better analysis, systems with equal molar ratios were compared (colourless graphic bars).

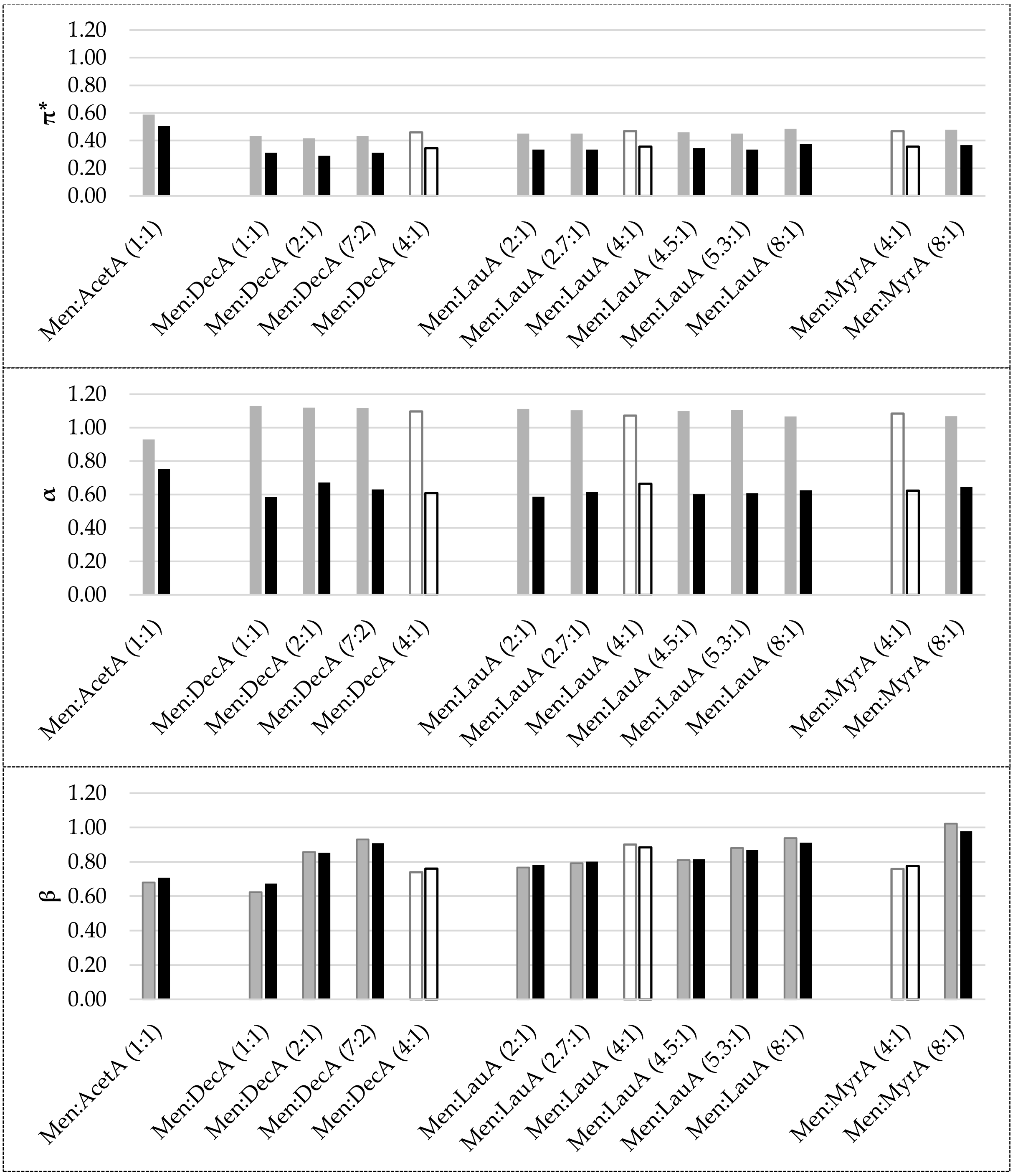

Figure 21: Variation of the three KTPs with the increase of the carboxylic chain (from left to right). The grey graphic bars represent the values calculated using the **OE** (**eqn. 40, eqn. 47** and **eqn. 49**), and the black ones are the values obtained when the **DE** (**eqn. 41**, **eqn. 48** and **eqn. 50**) are used.

According to the graphs above, KTPs vary independently from system to system and are not correlated with either the molar ratio of the system or the size of the fatty acid chain. Factors such as structure, types of interaction and hydrogen-bond network can be pointed as some of the reasons for the this behaviour. Also, when the type of relationship existent between the KTPs and related properties was investigated, a very good correlation with parameters such as π^*-E_{NR}, π^*-δ_P and π^*-δ_H was found (**Figure 22**):

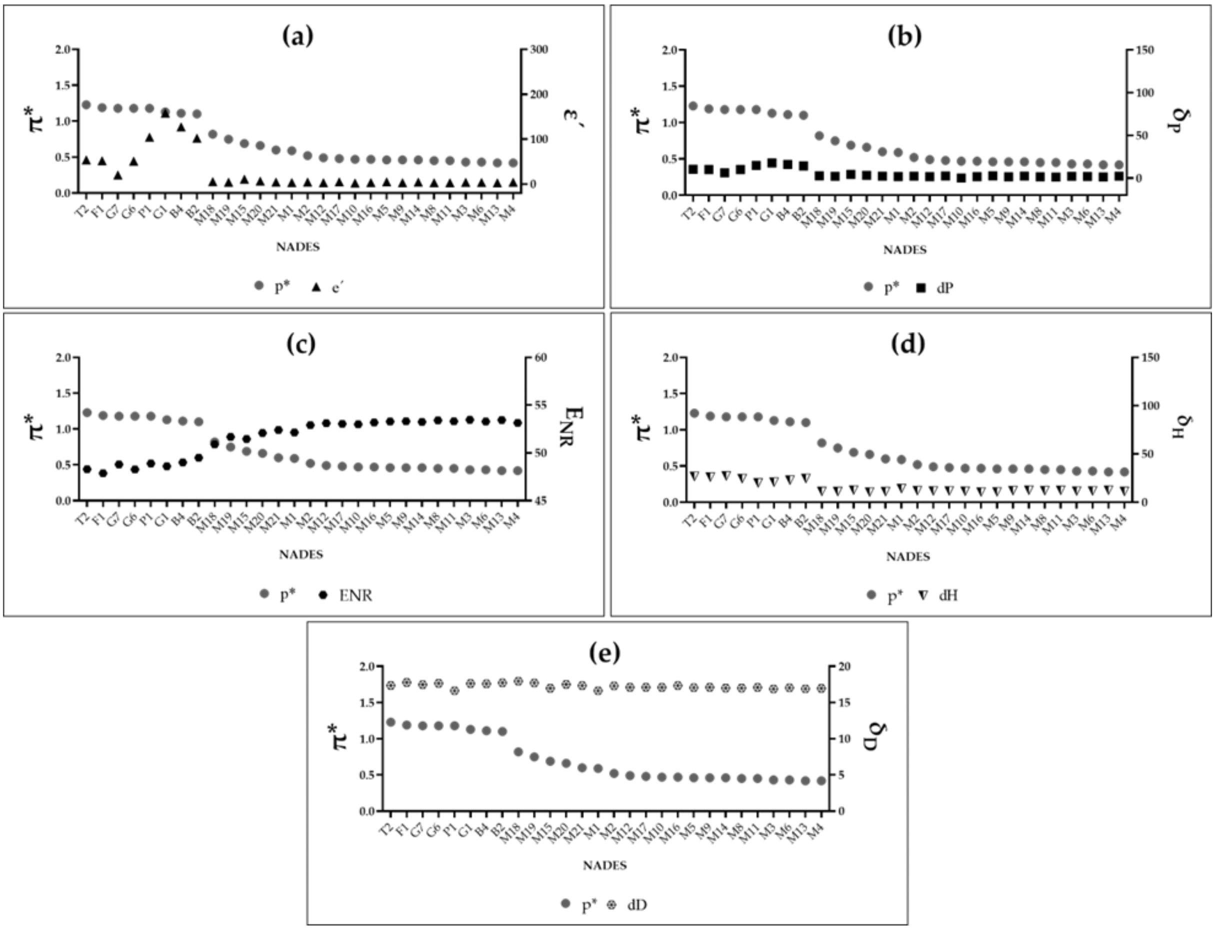

Figure 22: Correlation of polarizability of Kamlet-Taft (π^*) with dielectric constant (a), polar parameter of HSPs (b), polarity (c), hydrogen bond (d) and disper-sion parameters (e). For this correlation, the values of δ_D, δ_P and δ_H parameters used were those obtained using the models of YAH, Bb and SkH, respectively.

On the other hand, as it known, the acidity or basicity of a compound is affected by its water content, which in turn, may influence in the hydrogen-bond formation. Therefore, the acidity (α) and basicity (β) parameters of Kamlet-Taft were correlated with water content and hydrogen-bond parameter (**Figure 23**).

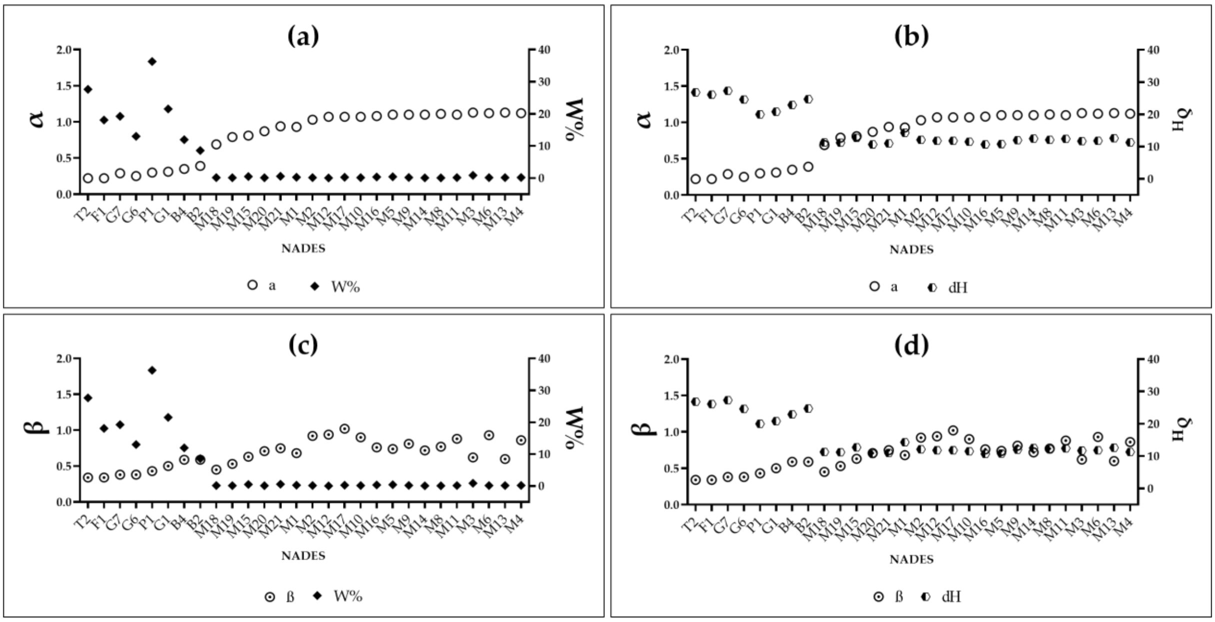

Figure 23: Correlation between acidity (α) and basicity (β) parameters of Kamlet-Taft with water content ((a) and (c), respectively) and hydrogen bond parameter ((b) and (d), respectively).

As it can be confirmed, except for a slight tendency observed between α- δ_H , no significant relationship was found between α-W%, β-W%, or β- δ_H.

3.4.1.1 Replacement of Solvents Using KTPs

One of the most recent investigations suggests the implementation of KTPs to map organic solvents commonly used in pharmaceutical industries and find potential candidates to replace the hazardous solvents, mainly the dipolar aprotic ones such as DMFO, DMSO ACN (acetonitrile) [90], [115]. On the other side, solvents such as water, ethanol, methanol, etc, are often recommended, however, due to their characteristics in the solubilization of active pharmaceutical ingredients (API), in some cases, it is necessary for an approach such as solvent-pair mixtures [90]. Therefore, in this perspective, NADES can be pointed to as a good object of study. This assessment was made through the ternary plots of the KTPs, demonstrated in **Figure 24.** Yet, it is important to mention that the values shown in the plot correspond to the fraction of each parameter.

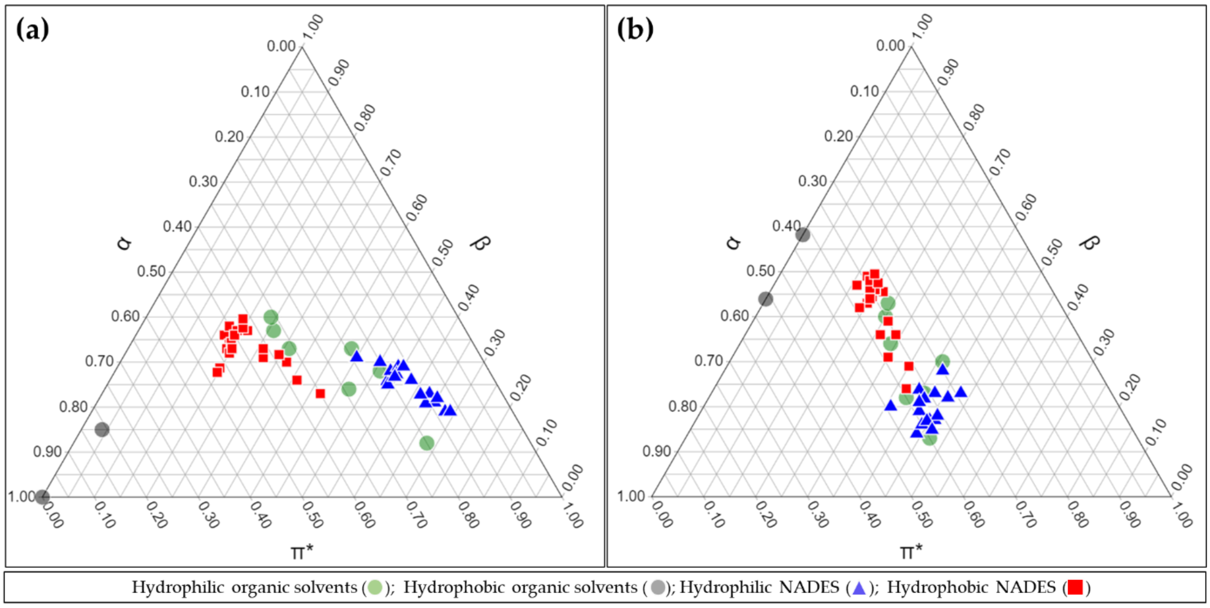

Figure 24: Ternary plots of KTPs (π*, α and β). The values were obtained by using **OE** (**eqn. 40, eqn. 47** and **eqn. 49**), **(a)**, and **DE** (**eqn. 41**, **eqn. 48** and **eqn. 50**), **(b)**. The values are written in fractional form.

As can be noted in **Figure 24**, the KTPs of both hydrophobic as well hydrophilic NADES exhibit an activity very similar to the conventional organic solvents such as water, methanol, ethanol, etc (green circles), reasserting that NADES can be certainly a good alternative to these solvents. Moreover, given the high value of the acidity (α) found for these systems, it can be also good indicative of their potential in replacing hazardous solvents, as, contrarily to NADES, one feature that is said to be characteristic of these solvents is their considerable impassioned ability to donate hydrogen bonds and establish stronger bonds [115].

3.5 Solubility Evaluation

As the main goal of this work is to evaluate the ability of NADES to act as a solvent, it was then investigated the affinity degree that may guide the explanation of the solubilization of a drug, such as ibuprofen, in these systems. Thus, different methods were used in order to understand their performance in NADES solubility study. Unlike EM, where the ibuprofen HSPs were estimated using the group contribution method (GCM) of each model, for the evaluation with the values obtained from the SEM, as well as the experimental ones (in the case of organic solvents), the ibuprofen HSPs used were taken from the HSPiP software [116].

To simplify the next steps of this work, a brief description of the models utilized, as well which parameter was used in this chapter is shown in **Figure 25**.

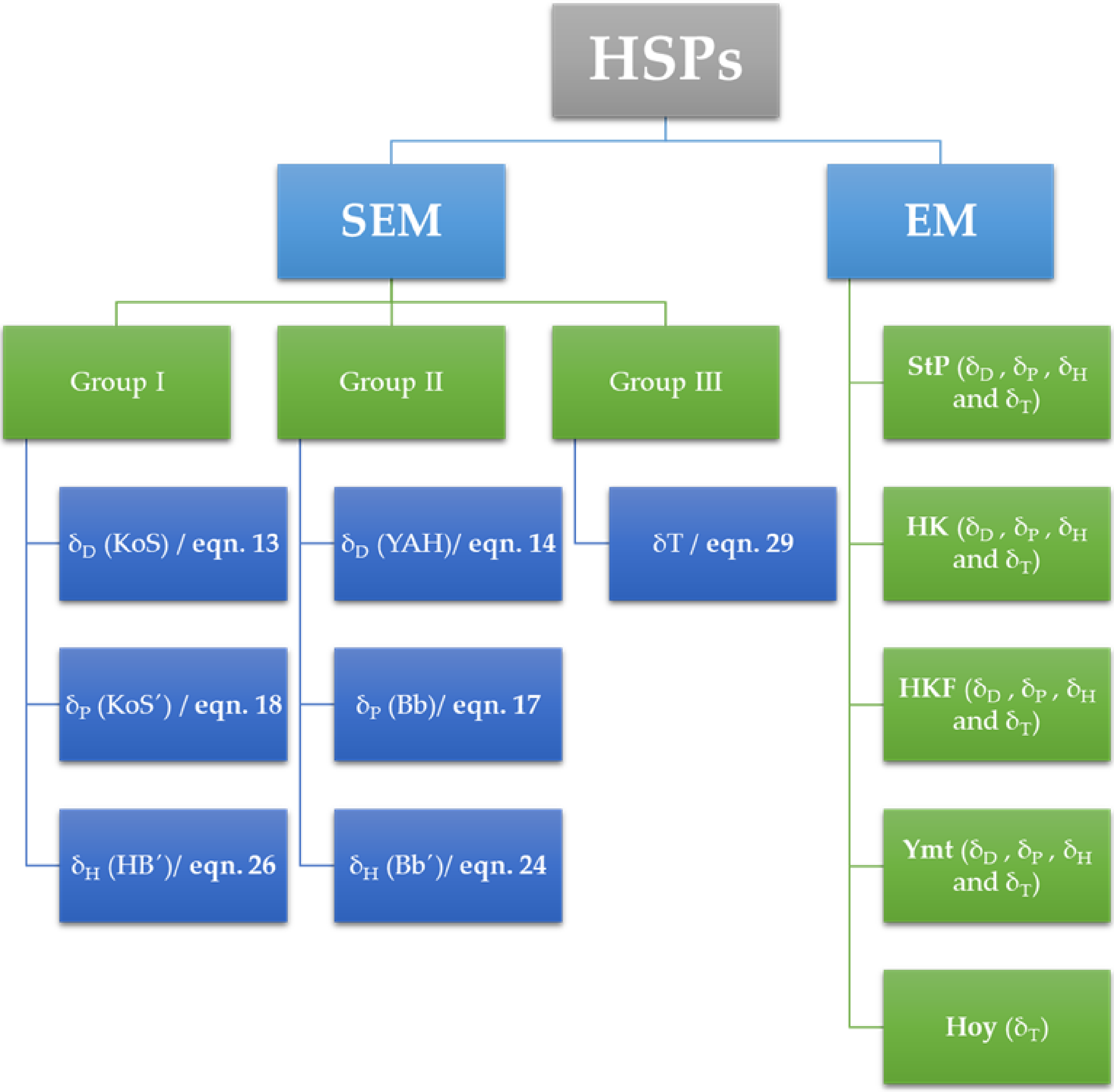

Figure 25: Description of the models used in the validation.

As can be observed in **Figure 25**, the HSPs estimated from the SEM were organized into three groups (Group I, II and III) and used for the evaluation. The solubility assessment was performed through studies in 1D, 2D, and 3D.

3.5.1 One-dimensional

Starting with a 1D analysis, both methods, HK and Greenhalgh, were assessed. By employing the HK methodology (**eqn. 37**[XXVI]), the set of graphics shown in **Figure 26** were acquired.

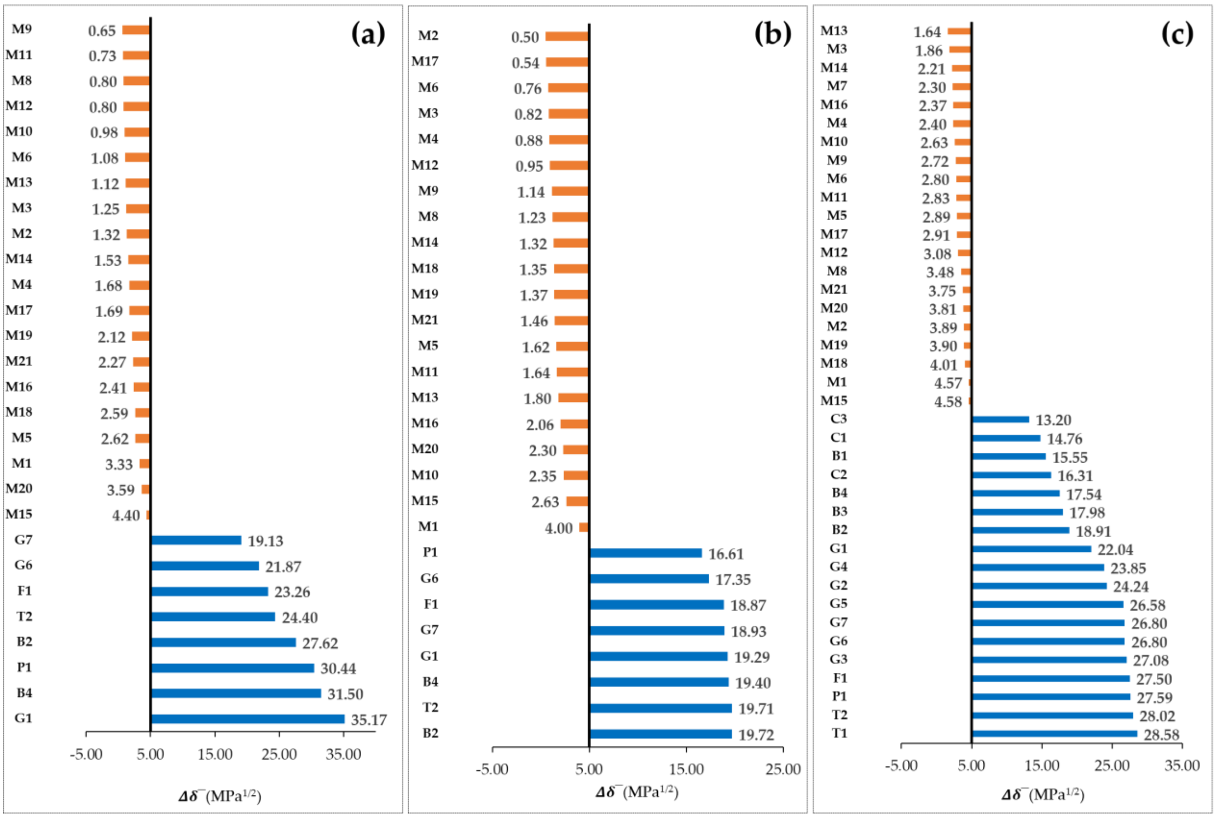

Figure 26: HK´s 1D solubility charts of ibuprofen in NADES, estimated from the semi-empirical models (group I (a) and group II (b)) and the empirical model, HK (c). To achieve these results, it was used **Table A. 10** presented in the appendix.

On the other hand, using the Greenhalgh method (**eqn. 38**[XXVII]) it was possible to obtain the four-following graphics (**Figure 27**).

[XXVI] $\Delta\bar{\delta} = \sqrt{(\delta_D^{S1} - \delta_D^{S2})^2 + (\delta_P^{S1} - \delta_P^{S2})^2 + (\delta_H^{S1} - \delta_H^{S2})^2} \leq 5\ \mathrm{MPa}^{1/2}$

[XXVII] $\Delta\delta_T = \left|\delta_T^{S1} - \delta_T^{S2}\right| \leq 7\ \mathrm{MPa}^{1/2}$

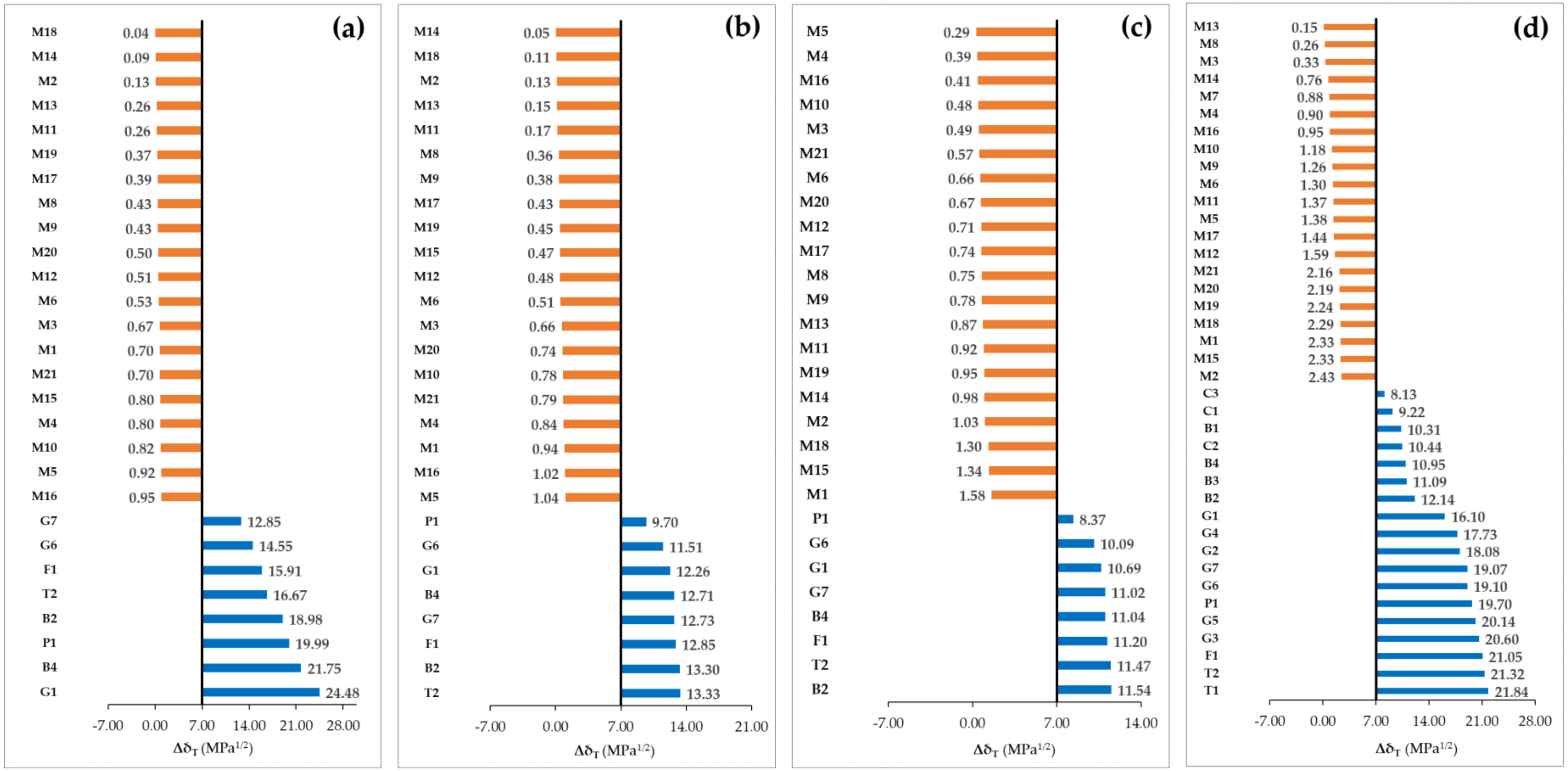

Figure 27: Greenhalgh´s 1D solubility charts of ibuprofen in NADES, estimated from the semi-empirical models (group I **(a)**, group II **(b)** and **eqn. 29** (c)) and the empirical model HK (d).

In both cases (**Figure 26** and **Figure 27**), according to the author's assumptions, the closer to zero the value (orange bars), the greater the affinity of the solvent with ibuprofen and therefore it is mostly likely to it be soluble in NADES. Likewise, systems with values above the established threshold (blue bars) indicate low affinity between ibuprofen-NADES, which consequently indicates a low chance of ibuprofen being solubilized in these systems. The HK approach is in fact quite similar to Hansen´s, contrarily to the Greenhalgh hypothesis, which is exclusively based on the Hildebrand solubility parameter. As can be seen, the classification order from the most (top) and less (bottom) soluble varies from method to method and none of them match with the reference model HK.

3.5.1 Two-dimensional

The ibuprofen solubility in NADES was also evaluated using the 2D-chart of Badgley presented in **Figure 28**.

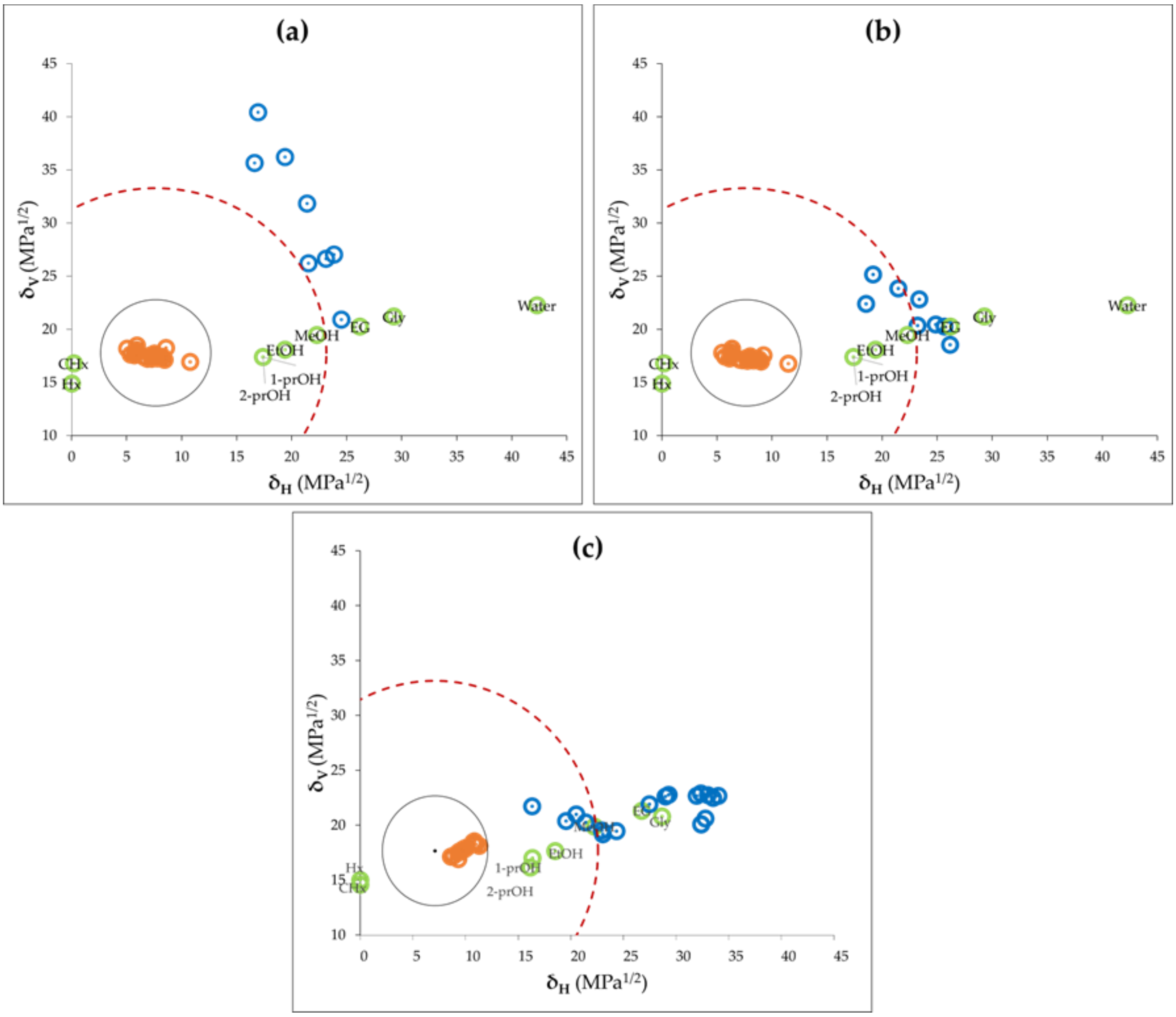

Figure 28: Bagley's 2D solubility charts, predicted using the semi-empirical models (group I **(a)** and group II **(b)**) and the empirical model, HK **(c)**. The green, blue, and orange circles represent the organic solvents, the hydrophilic and hydrophobic NADES, respectively (see more information in **Table A. 10** and **Figure A. 6**).

The 2D graphs presented above confirm once again the high solubility of ibuprofen in hydrophobic NADES in contrast to its low hydrophilic systems and solubility in organic solvents. Considering the water position in the two charts (a) and (b), what can be presumed is that the solubility of ibuprofen in hydrophilic NADES is relatively higher than in water. Furthermore, it is also well-known that ibuprofen has a high solubility in solvents such as methanol, ethanol, and propanol [117], however, these solvents are not covered by the Bagley interaction radius (solid black line circumference, R_0 = 5 MPa$^{1/2}$). Thus, adjusting the R_0 to have these solvents within the solubility circle, it was found that a radius value of about 15.5 MPa$^{1/2}$ would be most suitable (dashed red line circumference).

3.5.1 Three-dimensional

If the found value of R_0 is assumed to be the Hansen sphere, it is still possible to make an assessment of the solubility of the results shown in **Figure 28** through the 3D charts demonstrated in **Figure 29**.

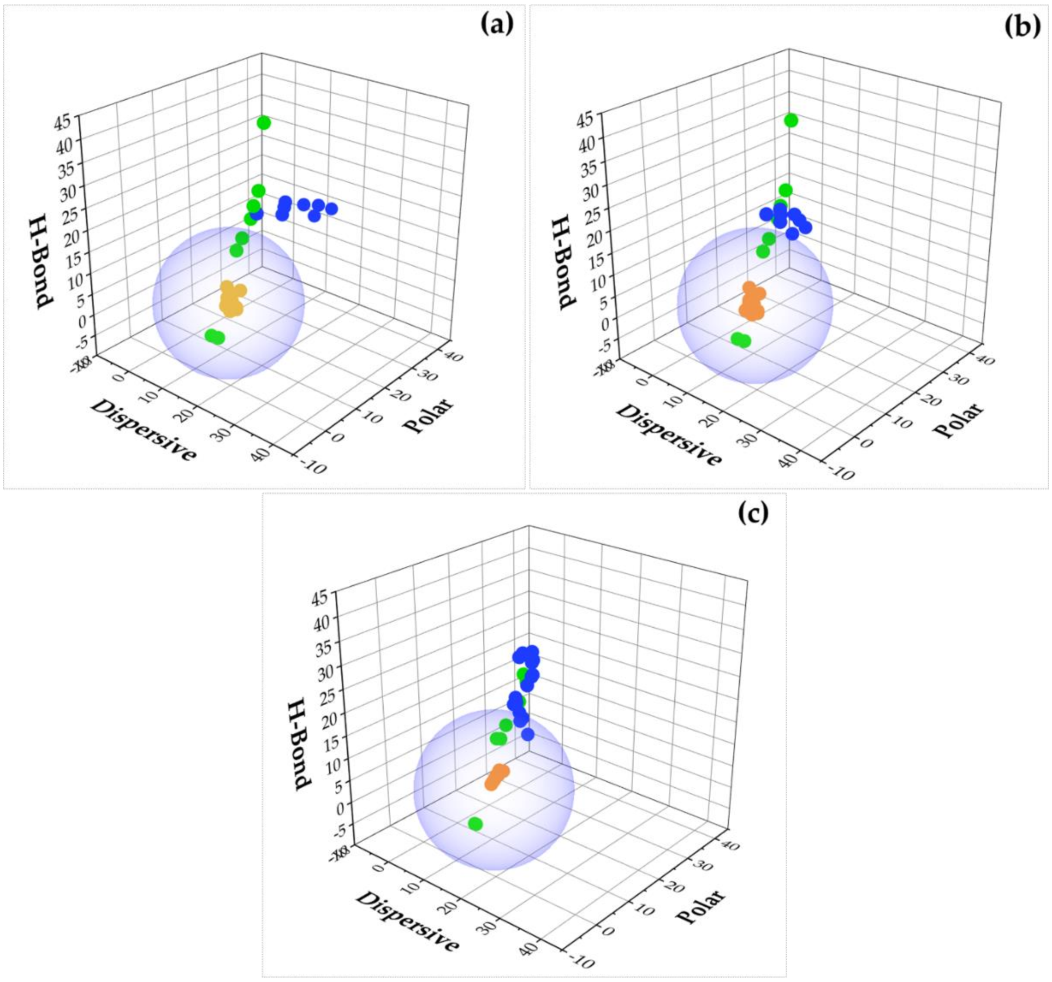

Figure 29: 3D representation of HSPs estimated from group I (a), group II (b) and HK (c).

Such representation is often used in HSPs studies and as can be seen, it allows for a better elucidation of the NADES position relatively to the ibuprofen sphere and thus identify and screen potential solvents for this solute.

3.6 Validation of the models

In general, the HSPs only provide information about the affinity/miscibility extension between two or more materials and not the solubility. Hence, in practice, this tool only works for qualitative analysis. But since the solubility is directly proportional to the affinity degree, a more reasonable validation would be comparing these two properties. Thus, considering first the experimental solubility values of ibuprofen in hydrophilic systems, it was found that in descendent order of solubility (from top to bottom), B4 > B1 > T2 >> water >>> G3 and although it was not possible to find the solubility of ibuprofen in the systems studied in the literature, it was observed that the values obtained were in the same range, as can be confirmed in **Table 15**.

Table 15: Experimental solubility of ibuprofen in the investigated NADES, obtained by HPLC, at room temperature.

NADES	ID	Solubility ± SD (mg/mL)	From Literature (mg/mL)
Bet:Glc:W (5:2:10)	B1	0.341 ± 9.11E-04	N/A
Bet:Gly:Suc:W (2:3:1:5)	B2	0.204 ± 6.65E-05	N/A
Bet:sorb:W (3:1:10)	B3	N/D	N/A
Bet:Suc:Pro:W (5:2:2:21)	B4	0.343 ± 3.49E-04	N/A
ChCl:EG (1:2)	C1	N/D	24.29 ± 0.18 [36]
ChCl:Gly (1:2)	C2	N/D	3.82 ± 0.03 [36]; 4.5 ± 0.8 [118][a]
ChCl:Ure (1:2)	C3	N/D	4.50 ± 0.01 [36]; 9 ± 2 [118][a]
Fru:Glc:Suc:W (1:1:1:10)	F1	0.041 ± 5.59E-04	N/A
Glc:Pro:Gly:W(3:5:3:20)	G1	N/D	N/A
Gly:Fru (4:1)	G2	0.114 ± 2.49E-04	N/A

NADES	ID	Solubility ± SD (mg/mL)	From Literature (mg/mL)
Gly:Fru:Sorb:W (1:1:1:3)	G3	0.022 ± 1.67E-04	N/A
Gly:Glc (4:1)	G4	0.130 ± 9.18E-04	N/A
Gly:Glc:Sorb:w (1:1:1:3)	G5	0.050 ± 2.43E-03	N/A
Gly:Suc:Sorb:W (2:1:2:10)	G6	0.028 ± 1.24E-04	N/A
Gly:Tre:Sorb:W (2:1:2:10)	G7	0.047 ± 5.47E-04	N/A
Pro:Gly:Sorb:W (1:1:1:13)	P1	0.167 ± 1.01E-03	N/A
Tre:Fru:W (1:2:13)	T1	0.050 ± 9.89E-04	N/A
Tre:Glc:W (1:2:13)	T2	0.209 ± 7.53E-02	N/A
Water	W0	0.059 ± 1.31E-03	0.070 ± 0.00 [36]; 0.055 ± 0.004 [118][a]
Men:AcetA (1:1)	M1	298.053 ± 5.94E-02	N/A
Men:Bor (7:2)	M2	170.851 ± 2.29E-02	N/A
Men:DecA (1:1)	M3	159.463 ± 1.11E-02	N/A
Men:DecA (2:1)	M4	210.908 ± 3.99E-03	N/A
Men:DecA (4:1)	M5*	211.169 ± 1.03E-03	N/A
Men:DecA (7:2)	M6*	147.425 ± 2.11E-03	N/A
Men:LauA (2.7:1)	M7	222.924 ± 9.99E-03	N/A
Men:LauA (2:1)	M8*	162.045 ± 1.65E-03	N/A
Men:LauA (4.5:1)	M9	224.197 ± 2.63E-03	N/A
Men:LauA (4:1)	M10*	204.668 ± 1.17E-02	N/A
Men:LauA (5.3:1)	M11*	138.97 ± 3.86E-04	N/A
Men:LauA (8:1)	M12*	131.41 ± 9.84E-04	N/A
Men:LauA:DecA (2:1:1)	M13	152.31 ± 4.20E-02	N/A
Men:LauA:DecA (4:1:1)	M14*	161.872 ± 4.96E-03	N/A
Men:LevA (1:1)	M15*	198.055 ± 1.09E-02	N/A
Men:MyrA (4:1)	M16*	204.218 ± 5.76E-03	N/A
Men:MyrA (8:1)	M17*	207.86 ± 4.67E-03	N/A
Men:Thy (1:1)	M18*	128.949 ± 2.41E-02	N/A
Men:Thy (2:1)	M19*	181.355 ± 3.30E-04	N/A
Men:Thy (4:1)	M20*	170.731 ± 5.09E-03	N/A
Men:Thy (8:1)	M21*	171.261 ± 1.13E-02	N/A
Other from literature (continuation)			

NADES	ID	Solubility ± SD (mg/mL)	From Literature (mg/mL)
System	**Solubility ± SD**	**Units**	**Ref**
Bet:Gly:W (1:2:1)	4.9 ± 0.2	mg/g	[118]
Ethanol (EtOH)	467 ± 18		
Glycerol (Gly)	2.3 ± 0.1		
Men:Camp (1:1)[b]	282.11 ± 6.67	mg/mL	[119]

[a] Solubility values in mg/g.
[b] Camp = Camphor
* Original samples that contained precipitate in the vial.

When comparing these solubility data with the Ibuprofen-NADES affinity, estimated through the studied semi-empirical models (SEM), the results presented in **Table 16** were obtained.

Table 16: Comparison of ibuprofen solubility and affinity for the listed hydrophilic systems. The affinity values presented correspond to those calculated from the semi-empirical models (SEM) shown in **Figure 26** ((**a**) and (**b**)) and **Figure 27** ((**a**) and (**b**)), respectively.

NADES	Solubility (mg/mL)	SEM					
		$\Delta\bar{\delta}$ (MPa$^{1/2}$)		$\Delta\delta_T$ (MPa$^{1/2}$)			
		Group I	Group II	Group I	Group II	Eqn. 27	Eqn. 29
Bet:Suc:Pro:W (5:2:2:21)	**B4** (0.343)	**G7** 19.13	**P1** 16.59	**G7** (14.83)	**P1** (10.57)	**P1** (5.94)	**P1** (8.37)
Tre:Glc:W (1:2:13)	**T2** (0.209)	**G6** 21.87	**G6** 17.36	**B2** (18.98)	**G6** (11.39)	**G6** (7.51)	**G7** (11.02)
Bet:Gly:Suc:W (2:3:1:5)	**B2** (0.204)	**F1** 23.26	**F1** 18.87	**G6** (19.68)	**T2** (12.00)	**G7** (8.36)	**G7** (11.02)
Pro:Gly:Sorb:W (1:1:1:13)	**P1** (0.167)	**T2** 24.40	**G7** 18.94	**F1** (21.10)	**G7** (12.37)	**B4** (8.37)	**B4** (11.04)
Water	**W0** (0.059)	**B2** 27.62	**B4** 19.40	**T2** (22.19)	**B4** (12.63)	**F1** (8.52)	**F1** (11.20)
Gly:Tre:Sorb:W (2:1:2:10)	**G7** (0.047)	**P1** 30.44	**B2** 19.73	**W0** (28.44)	**F1** (12.73)	**T2** (8.77)	**T2** (11.47)
Fru:Glc:Suc:W (1:1:1:10)	**F1** (0.041)	**B4** 31.50	**T2** 19.93	**P1** (31.06)	**B2** (12.99)	**B2** (8.84)	**B2** (11.54)
Gly:Suc:Sorb:W (2:1:2:10)	**G6** (0.028)	**W0** 37.27	**W0** 37.27	**B4** (32.54)	**W0** (28.44)	**W0** (20.96)	**W0** (24.83)

Being both, solubility and affinity, organized in descending order, i.e., from the systems with higher solubility and affinity to those with lowest, it can be inferred that none of the investigated SEM followed truly the sequence identified in solubility order. According to the experimental data, ibuprofen has a high solubility in betaine-based NADES, mainly (**B4**), and low solubility in sugars-based ones such as **G6**. Therefore, it would be expected that these two systems (**B4** and **G6**) would have, respectively, the lowest and highest values of $\Delta\bar{\delta}$ and $\Delta\delta_T$. In other words, these two NADES were supposed to be the ones with the highest and the lowest affinity. However, as can be seen in **Table 16**, the results revealed to be very different from this assumption. For instance, most of the models indicated that by the affinity calculated using the HSPs, the solubility of ibuprofen should be higher in **P1** and lower in **W0** (Water).

The experimental solubility data was also used to validate the sequence of affinity of ibuprofen in hydrophilic NADES estimated through the empirical models. The results presented in **Table 17**.

Table 17: Comparison of ibuprofen solubility and affinity for the listed hydrophilic systems. The affinity values were obtained from the evaluation of the empirical models (**EM**), using the methods of HK (**eqn. 37**) and Greenhalgh (**eqn. 38**). Points that coincide solubility with affinity are highlighted in green.

Solubility (mg/mL)	**EM**								
	$\Delta\bar{\delta}$ (MPa$^{1/2}$)				$\Delta\delta_T$ (MPa$^{1/2}$)				
	StP	**HK**	**HKF**	**Ymt**	**StP**	**HK**	**HKF**	**Hoy**	**Ymt**
B4 (0.343)	**B2** (9.35)	**B1** (15.55)	**B1** (13.46)	**B1** (4.61)	**B2** (4.68)	**B1** (10.31)	**B1** (6.01)	**G4** (17.32)	**B1** (0.99)
B1* (0.341)	**B1** (17.19)	**B4** (17.54)	**B4** (16.91)	**B2** (5.65)	**B1** (10.60)	**B4** (10.95)	**B4** (10.20)	**G2** (17.34)	**B4** (2.17)
T2 (0.209)	**P1** (22.21)	**B2** (18.91)	**B2** (18.59)	**B4** (6.17)	**P1** (15.10)	**B2** (12.14)	**B2** (11.85)	**B1** (19.63)	**B2** (2.24)
B2 (0.204)	**G2** (27.32)	**G4** (23.85)	**G4** (22.42)	**G4** (6.87)	**G2** (19.92)	**G4** (17.73)	**G4** (15.33)	**B2** (19.77)	**G4** (3.81)
P1 (0.167)	**G4** (27.52)	**G2** (24.24)	**G2** (23.00)	**G2** (6.88)	**G4** (20.10)	**G2** (18.08)	**G2** (16.00)	**B4** (22.16)	**G2** (3.81)
G4* (0.130)	**B4** (28.03)	**G5** (26.58)	**G5** (24.29)	**G5** (8.40)	**B4** (20.54)	**G7** (19.07)	**G5** (17.05)	**G5** (23.58)	**G5** (4.66)
G2* (0.114)	**G5** (37.53)	**G7** (26.80)	**G3** (25.34)	**G3** (8.44)	**W0** (28.67)	**G6** (19.10)	**G3** (18.22)	**G3** (23.61)	**G3** (4.69)
W0 (0.059)	**G3** (37.56)	**G6** (26.80)	**F1** (25.71)	**G7** (8.98)	**G5** (29.32)	**P1** (19.70)	**F1** (18.63)	**G7** (25.56)	**G7** (4.81)
T1* (0.050)	**W0** (37.71)	**G3** (27.08)	**P1** (28.58)	**G6** (9.05)	**G3** (29.35)	**G5** (20.14)	**P1** (20.70)	**G6** (25.58)	**G6** (4.85)
G5* (0.050)	**G7** (44.18)	**F1** (27.50)	**T2** (28.70)	**F1** (9.51)	**G7** (35.67)	**G3** (20.60)	**T2** (21.94)	**P1** (26.58)	**F1** (5.04)
G7 (0.047)	**G6** (44.22)	**P1** (27.59)	**G6** (29.46)	**T2** (10.02)	**G6** (35.72)	**F1** (21.05)	**G6** (22.23)	**F1** (26.73)	**T2** (5.28)
F1* (0.041)	**T2** (45.90)	**T2** (28.02)	**T1** (29.60)	**T1** (10.12)	**T2** (37.43)	**T2** (21.32)	**T1** (22.93)	**T2** (27.27)	**T1** (5.33)
G6 (0.028)	**T1** (46.15)	**T1** (28.58)	**G7** (30.38)	**P1** (11.19)	**T1** (37.69)	**T1** (21.84)	**G7** (23.35)	**T1** (27.29)	**P1** (5.86)
G3* (0.022)	**F1** (46.82)	**W0** (37.88)	**W0** (37.83)	**W0** (39.79)	**F1** (38.41)	**W0** (28.77)	**W0** (28.45)	**W0** (29.74)	**W0** (30.27)

* **B1** = Bet:Glc:W (5:2:10); **G2** = Gly:Fru (4:1); **G3** = Gly:Fru:Sorb:W (1:1:1:3); **G4** = Gly:Glc (4:1); **G5** = Gly:Glc:Sorb:w (1:1:1:3); **T1** = Tre:Fru:W (1:2:13).

As it can be confirmed, there is no correlation between solubility and HSPs (affinity). Yet, it was still possible to see that in the case of empirical models HK and HKF, the position, in affinity (painted green), of systems such as **B4**, **B3** and **P1** (in HKF) matches their position in the solubility range.

The same methodology was followed for the validation of both semi and empirical models, regarding the hydrophobic NADES. Starting with the evaluation of the semi-empirical models (SEM), once again, no direct relationship was observed to exist, and as can be seen in **Table 18**, the affinity of **M1**, calculated with the δ_T parameter from **eqn. 27**, was the only point found that interlace affinity with solubility. Similarly, to what has also been seen in the study of water content, density, viscosity, Kamlet-Taft parameter, etc, the solubility of NADES is not entirely dependent on the molar fraction of menthol ($X_{Men}/X_{(Men+LauA)}$). Using for example the system Men:LauA, it was found that the solubility of **M5** > **M4** > **M3** > **M6**, however, when expressed in a molar fraction the following other is **M5** > **M6** > **M4** > **M3** (equal to 0.8, 0.78, 0.67 and 0.50 mols of menthol, respectively).

Table 18: Comparison of ibuprofen solubility and affinity for the listed hydrophobic systems. The affinity values presented correspond to those calculated from the semi-empirical models (SEM) shown in **Figure 26** (**(a)** and **(b)**) and **Figure 27** (**(a)** and **(b)**), respectively, as well as the two models presented in **eqn. 27** and **eqn. 29**. The point that coincides with solubility with affinity is highlighted in green.

NADES	**Solubility (mg/mL)**	**SEM**					
		$\Delta\bar{\delta}$ (MPa$^{1/2}$)		$\Delta\delta_T$ (MPa$^{1/2}$)			
		Group I	**Group II**	**Group I**	**Group II**	**Eqn. 27**	**Eqn. 29**
Men:AcetA (1:1)	**M1** (298.05)	**M9** (0.65)	**M17** (0.26)	**M18** (0.04)	**M13** (0.00)	**M1** (0.26)	**M5** (0.29)
Men:LauA (4,5:1)	**M9** (224.20)	**M11** (0.73)	**M3** (0.69)	**M14** (0.09)	**M14** (0.01)	**M15** (0.47)	**M4** (0.39)
Men:DecA (4:1)	**M5** (211.17)	**M8** (0.80)	**M6** (0.70)	**M2** (0.13)	**M11** (0.11)	**M18** (0.51)	**M16** (0.41)
Men:DecA (2:1)	**M4** (210.91)	**M12** (0.80)	**M2** (0.75)	**M13** (0.26)	**M17** (0.21)	**M2** (0.75)	**M10** (0.48)
Men:MyrA (8:1)	**M17** (207.86)	**M10** (0.98)	**M4** (0.77)	**M11** (0.26)	**M8** (0.22)	**M14** (0.80)	**M3** (0.49)
Men:LauA (4:1)	**M10** (204.67)	**M6** (1.08)	**M12** (1.01)	**M19** (0.37)	**M9** (0.35)	**M19** (0.82)	**M21** (0.57)
Men:MyrA (4:1)	**M16** (204.22)	**M13** (1.12)	**M9** (1.12)	**M17** (0.39)	**M2** (0.43)	**M11** (0.86)	**M6** (0.66)
Men:LevA (1:1)	**M15** (198.05)	**M3** (1.25)	**M8** (1.16)	**M8** (0.43)	**M18** (0.43)	**M13** (0.90)	**M20** (0.67)
Men:Thy (2:1)	**M19** (181.35)	**M2** (1.32)	**M14** (1.30)	**M9** (0.43)	**M6** (0.44)	**M9** (0.98)	**M12** (0.71)
Men:Thy (8:1)	**M21** (171.26)	**M14** (1.53)	**M18** (1.31	**M20** (0.50)	**M3** (0.52)	**M8** (1.01)	**M17** (0.74)
Men:Bor (7:2)	**M2** (170.85)	**M4** (1.68)	**M19** (1.37	**M12** (0.51)	**M12** (0.57)	**M17** (1.02)	**M8** (0.75)
Men:Thy (4:1)	**M20** (170.73)	**M17** (1.69)	**M5** (1.60	**M6** (0.53)	**M19** (0.67)	**M12** (1.05)	**M9** (0.78)
Men:LauA (2:1)	**M8** (162.04)	**M19** (2.12)	**M11** (1.62	**M3** (0.67)	**M15** (0.68)	**M20** (1.08)	**M13** (0.87)
Men:LauA:DecA (4:1:1)	**M14** (161.87)	**M21** (2.27)	**M21** (1.65	**M1** (0.70)	**M4** (0.70)	**M6** (1.09)	**M11** (0.92)
Men:DecA (1:1)	**M3** (159.46)	**M16** (2.41)	**M13** (1.74	**M21** (0.70)	**M10** (0.73)	**M21** (1.17)	**M19** (0.95)
Men:LauA:DecA (2:1:1)	**M13** (152.31)	**M18** (2.59)	**M16** (2.10	**M15** (0.80)	**M20** (0.89)	**M3** (1.25)	**M14** (0.98)
Men:DecA (7:2)	**M6** (147.43)	**M5** (2.62)	**M20** (2.32)	**M4** (0.80)	**M5** (0.98)	**M10** (1.25)	**M2** (1.03)
Men:LauA (5,3:1)	**M11** (138.97)	**M1** (3.33)	**M10** (2.34)	**M10** (0.82)	**M16** (1.19)	**M16** (1.32)	**M18** (1.30)
Men:LauA (8:1)	**M12** (131.41)	**M20** (3.59)	**M15** (2.58)	**M5** (0.92)	**M21** (1.29)	**M4** (1.34)	**M15** (1.34)
Men:Thy (1:1)	**M18** (128.95)	**M15** (4.40)	**M1** (3.89)	**M16** (0.95)	**M1** (1.50)	**M5** (1.43)	**M1** (1.58)

As expected, the solubility of ibuprofen in hydrophobic systems is considerably higher than in hydrophilic ones. Moreover, the results indicated that ibuprofen has relatively a greater solubilization in the system Men:AcetA (1:1), **(M1),** than in Men:Thy (1:1), **(M18)**. On the other hand, while assessing the effectiveness of empirical models (EM), it was once again very evident that the predicted affinities are not in agreement, as shown in **Table 19**, but it was still possible to identify a few more points where these two parameters crossed.

Table 19: Comparison of ibuprofen solubility and affinity for the listed hydrophobic systems. The affinity values were obtained from the evaluation of the empirical models (**EM**), using the methods of HK (**eqn. 37**) and Greenhalgh (**eqn. 38**). Points that coincide solubility with affinity are highlighted in green.

Solubility (mg/mL)	**EM**								
	$\Delta\bar{\delta}$ (MPa$^{1/2}$)				$\Delta\delta_T$ (MPa$^{1/2}$)				
	StP	**HK**	**HKF**	**Ymt**	**StP**	**HK**	**HKF**	**Hoy**	**Ymt**
M1 (298.05)	**M13** (2.70)	**M13** (1.64)	**M13** (1.65)	**M15** (2.04)	**M3** (0.05)	**M13** (0.15)	**M13** (0.21)	**M13** (0.74)	**M15** (1.02)
M9 (224.20)	**M3** (3.01)	**M3** (1.86)	**M3** (1.88)	**M1** (2.10)	**M13** (0.14)	**M8** (0.26)	**M3** (0.35)	**M3** (0.75)	**M1** (1.11)
M7 (222.92)	**M16** (3.20)	**M14** (2.21)	**M8** (2.07)	**M3** (2.42)	**M14** (0.30)	**M3** (0.33)	**M8** (0.74)	**M15** (0.90)	**M13** (1.12)
M5 (211.17)	**M14** (3.23)	**M7** (2.30)	**M14** (2.25)	**M13** (2.46)	**M7** (0.36)	**M14** (0.76)	**M14** (0.86)	**M8** (0.92)	**M3** (1.12)
M4 (210.91)	**M7** (3.26)	**M16** (2.37)	**M7** (2.36)	**M4** (2.64)	**M16** (0.36)	**M7** (0.88)	**M4** (0.98)	**M14** (0.93)	**M8** (1.26)
M17 (207.86)	**M4** (3.47)	**M4** (2.40)	**M4** (2.44)	**M14** (2.66)	**M4** (0.45)	**M4** (0.90)	**M7** (1.02)	**M4** (0.93)	**M14** (1.27)
M10 (204.67)	**M10** (3.56)	**M10** (2.63)	**M16** (2.45)	**M8** (2.68)	**M10** (0.58)	**M16** (0.95)	**M16** (1.17)	**M7** (0.99)	**M4** (1.27)
M16 (204.22)	**M9** (3.64)	**M9** (2.72)	**M10** (2.70)	**M7** (2.76)	**M9** (0.65)	**M10** (1.18)	**M10** (1.34)	**M6** (1.06)	**M18** (1.28)
M15 (198.05)	**M11** (3.75)	**M6** (2.80)	**M9** (2.80)	**M6** (2.80)	**M11** (0.72)	**M9** (1.26)	**M6** (1.42)	**M16** (1.07)	**M7** (1.32)
M19 (181.35)	**M17** (3.75)	**M11** (2.83)	**M6** (2.87)	**M5** (2.84)	**M6** (0.73)	**M6** (1.30)	**M9** (1.42)	**M10** (1.07)	**M16** (1.38)
M21 (171.26)	**M6** (3.80)	**M5** (2.89)	**M11** (2.92)	**M10** (2.86)	**M17** (0.75)	**M11** (1.37)	**M5** (1.50)	**M5** (1.08)	**M6** (1.38)
M2 (170.85)	**M8** (3.83)	**M17** (2.91)	**M5** (2.96)	**M16** (2.88)	**M5** (0.78)	**M5** (1.38)	**M11** (1.53)	**M1** (1.08)	**M19** (1.39)
M20 (170.73)	**M5** (3.87)	**M12** (3.08)	**M17** (3.01)	**M9** (2.88)	**M12** (0.89)	**M17** (1.44)	**M17** (1.65)	**M9** (1.09)	**M10** (1.39)
M8 (162.04)	**M12** (3.97)	**M8** (3.48)	**M12** (3.17)	**M11** (2.92)	**M15** (1.11)	**M12** (1.59)	**M12** (1.76)	**M11** (1.12)	**M5** (1.40)
M14 (161.87)	**M18** (4.29)	**M21** (3.75)	**M21** (3.94)	**M12** (2.99)	**M1** (1.24)	**M21** (2.16)	**M1** (2.04)	**M17** (1.17)	**M9** (1.41)
M3 (159.46)	**M19** (4.36)	**M20** (3.81)	**M2** (3.95)	**M17** (2.99)	**M21** (1.35)	**M20** (2.19)	**M15** (2.16)	**M12** (1.17)	**M11** (1.43)
M13 (152.31)	**M20** (4.42)	**M2** (3.89)	**M20** (4.05)	**M2** (3.10)	**M20** (1.39)	**M19** (2.24)	**M21** (2.48)	**M18** (1.24)	**M17** (1.47)
M6 (147.43)	**M21** (4.46)	**M19** (3.90)	**M19** (4.22)	**M21** (3.16)	**M19** (1.45)	**M18** (2.29)	**M2** (2.50)	**M19** (1.26)	**M20** (1.47)
M11 (138.97)	**M1** (4.71)	**M18** (4.01)	**M18** (4.45)	**M20** (3.17)	**M18** (1.53)	**M1** (2.33)	**M20** (2.61)	**M20** (1.28)	**M12** (1.48)
M12 (131.41)	**M2** (4.78)	**M1** (4.57)	**M1** (4.45)	**M19** (3.18)	**M2** (1.73)	**M15** (2.33)	**M19** (2.82)	**M21** (1.29)	**M2** (1.51)
M18 (128.95)	**M15** (5.23)	**M15** (4.58)	**M15** (4.52)	**M18** (3.20)	**M8** (2.66)	**M2** (2.43)	**M18** (3.08)	**M2** (1.36)	**M21** (1.53)

It is common knowledge that variables like temperature, pressure, hydrophilic/hydrophobic nature, and surface area have a significant impact on the dissolution rate of a solid solute in a liquid solvent. But it is also true that other properties such as volume molar (V_m), water content (W%), polarity (E_{NR}), dielectric constant (ε'), etc., may play a very important role in this process. Therefore, in an attempt to understand if any of these parameters could have affected the solubility, it was then established the following correlations shown in **Figure 30**.

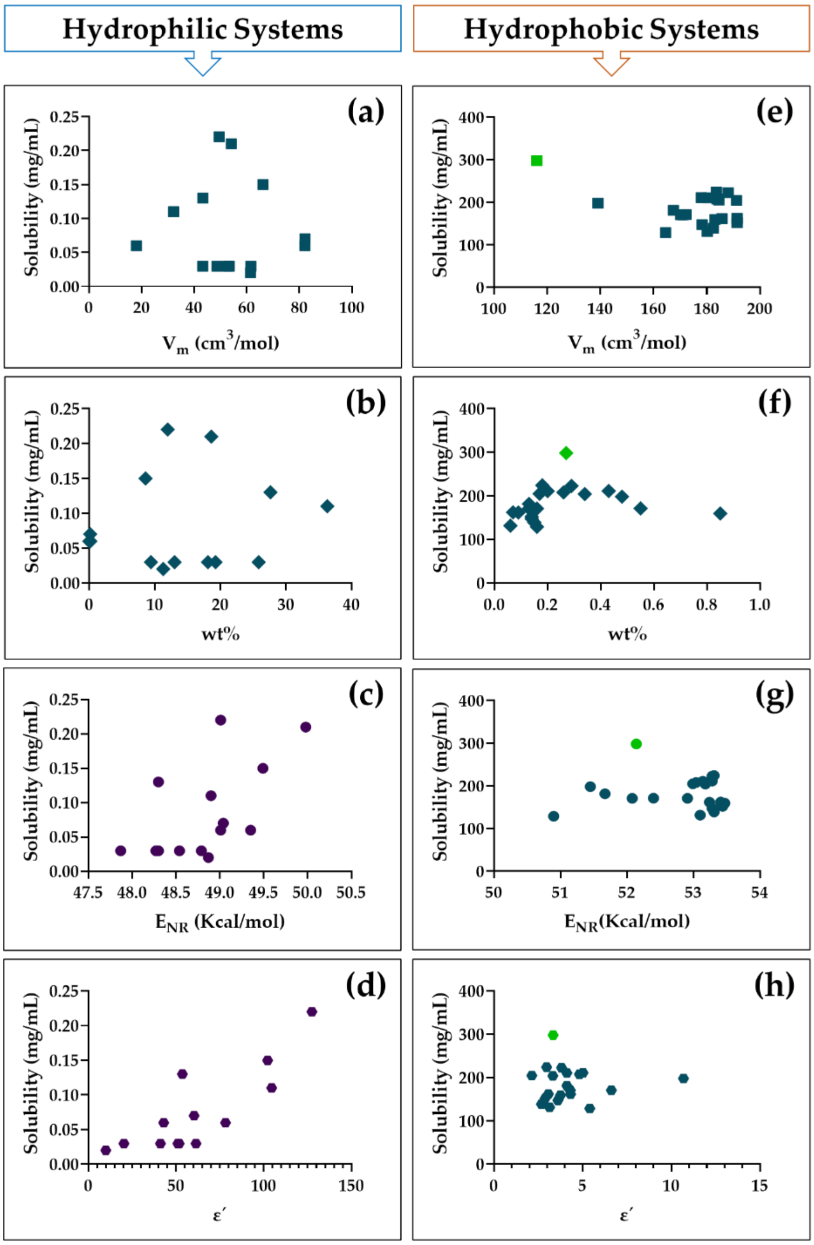

Figure 30: Correlations between the volume molar (V_m), water content (W%), polarity (E_{NR}) and dielectric constant (ε´) of hydrophilic (from (a) to (d)) and hydrophobic systems (from (e) to (h)), and their respective solubilities. The green points represent the M1 system.

Theoretically, there are some conditions that could explain the solubility values obtained, as for example the fact smaller molecules tend to provide better packing because of surface contact, it would be expected that, for both hydrophilic and hydrophobic systems, the solubility would increase with decreasing molar volume (V_m). This is in fact the case for the system **M1**, as highlighted in **Figure 30 (e)**. Besides, in general, the relationship between ibuprofen and water is known to be very conditioned due to their nature (hydrophobic vs hydrophilic), therefore, it would be expected that the lower the water content (W%) of a eutectic system, the greater its solubility. However, such a relationship was also not observed particularly in the hydrophilic systems where the differences between the W% are more evident (**Figure 30 (b)**). Moreover, as was discussed, E_{NR} and ε′are two parameters that can be used to evaluate the polarity of solvents, therefore it would be expected that solubility increases with the increase of E_{NR} (↑ E_{NR} = ↓ polarity = ↑ solubility of ibuprofen) and with a decrease of ε′ (↓ ε′ = ↓ polarity = ↑ solubility of ibuprofen), but once more, it was not the case **Figure 30** ((**c**)/(**d**) and (**g**)/(**h**)). In general, what was concluded from **Figure 30** is that none of these parameters (V_m, W%, E_{NR} or ε′) had a significantly influence on the solubility values. Furthermore, despite having identified a slight tendency of proportional increase between ε′ and solubility in graph **(d)**, it totally deviates from the hypothesis assumed here.

Although the solubility data contradicts the results of the theoretical models, it is also true that one of the major problems of working with NADES is the lack of adequate and reliable analytical instruments. For example, due to technical limitations or to avoid equipment damage, the quantification of an analyte in NADES by HPLC or UV-vis is always supported by a co-solvent. Thus, hypothetically, even if mild, the presence of a new compound in the mixture can lead to an increase or decrease in the solubility of the analyte and this will certainly depend on the affinity established between the three compounds: NADES + analyte + co-solvent. There has also been another experimental error that might have contributed to such results. Precipitates were detected before the HPLC injection in some of the hydrophobic samples (identified in **Table 15**), which may have affected the solubility values, causing the order found (from most to least soluble) to diverge from that predicted by the models. Nevertheless, as these results were obtained for only one compound, a more comprehensive study may be needed to validate such observations.

Another approach that would be very interesting to explore is the solubility assessment using the COSMO-RS software, as this is frequently used by the scientific community due to the reliable values provided. Furthermore, with such a powerful tool it would also be possible to evaluate other parameters studied in this work such as polarity, Kamlet-Taft parameters and even the HSPs would certainly contribute a lot to this investigation.

As shown throughout the discussion of this work, most of the physical properties determined experimentally are in agreement with the theoretical models used to assess the HSPs of NADES as well the affinity between them and ibuprofen. Therefore, using the group contribution tables presented in the appendix (**Table A. 11** to **Table A. 14**), it was also possible to estimate the HSPs of various components of NADES and then provide the large list presented in **Table A. 15** (in appendix), which may ultimately be helpful to many researchers in the future works.

4

CONCLUSIONS

During this thesis, several simple methods that can be used to estimate HSPs were presented, from solely empirical models based on the group contribution method (EM) to those that were classified as semi-empirical models (SEM) due to the correlation between solubility parameters and other physical properties. EM are widely used by the scientific community due to some of their notable advantages such as satisfactory results, and mainly their applicability in different types of compounds. On the other hand, most of the SEM are often strictly recommended for regular solvents, which make them dubious in the case of unconventional formulations such as NADES. Furthermore, due to the lack of NADES experimental physicochemical data, the development of the most suitable semi-empirical models is still limited. Regarding those existing models both EM and SEM, not much is really known about their performance in the NADES field. Therefore, the main objective of this work was to explore a set of these famous models and evaluate if they could be used to unravel NADES properties. In other words, the idea was to correlate the affinity estimated from the HSPs with solubility data.

By solely examining its physical properties it was confirmed that the behaviour of NADES is very unpredictable and cannot be explained by some related properties. parameters such as water content, viscosity, density, dielectric constant, dipole moment, polarity, etc., have shown, in most cases, that they are not dependent on the type, length of chain, or molar fraction of each component.

By employing some of these experimental values in the semi-empirical correlative models studied, it was possible to estimate the three Hansen solubility parameters, as well as the total solubility parameter/Hildebrand. In other to ensure the efficiency of these models, a set of organic solvents, with experimental HSPs known, were used. We can henceconclude that the empirical model of Hoftyzer and Van-Krevelen (HK) is the most suitable one, and therefore, a potential alternative to the experimental determination of HSPs, due to its very low relative deviation. On the other hand, when correlating properties such as water content, and polarity with the HSPs, good linearity was observed with the HSPs predicted by the empirical model proposed by Yamamoto, Abbott, and Hansen (Ymt), although, compared to other models, showed greater deviations.

The evaluation of the solubility was carried out using 1D, 2D, and 3D graphics. This allowed us to identify the systems for which ibuprofen has the greatest affinity. Furthermore, it was even possible to introduce a new approach to determine the Hansen sphere, which is usually very difficult to achieve.

Finally, although most of the investigated models showed a certain consistency with the results of the other physical properties, it was concluded by the experimental values of solubility, that none of them justified why the solubility of ibuprofen is higher in some systems than in others. Therefore, as future perspective it is suggested a complementary solubility study using the COSMO-RS software; a more comprehensive investigation of solubility with other APIs; the use of molecular dynamics to illustrate the interactions established between ibuprofen and NADES and fundament the results obtained; and finally, analyze the temperature effect in the investigated properties.

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A

AN APPENDIX

This chapter contains information that complement this investigation. The first part (**A.1**) reports the acquired experimental data and their use to calculate the semi-empirical models (SEM). On the other hand, the second part (**A.2**), focuses the empirical models (EM), tables with groups contribution for each model, and finally an extensive list containing the HSPs of some of the most known DES components, estimated using the studied EM.

A. 1 Physical characterization of NADES and estimation of their HSPs using semi-empirical models (SEM)

Table A. 1: Experimental data of viscosity, density at different temperatures and molar volume (at 298.15 K) water content, refractive index, and surface tension of hydrophilic NADES at room temperature.

NADES	T (K)	η (mPa.s)	SD*	ρ (g/cm^3)	SD*	V_m (cm^3/mol)	W%[a]	n_D	γ_L (mN/m)
B1	293.15	1032.05	9.55E+00	1.2268	4.81E-04	54.13	18.6 ± 0.84	1.4762 ± 0.001	41.04 ± 3.95
	298.15	679.90	4.85E+00	1.2239	4.17E-04				
	303.15	459.68	2.64E+00	1.2211	5.52E-04				
	308.15	319.89	1.68E+00	1.2184	6.15E-04				
	313.15	228.37	1.05E+00	1.2156	7.00E-04				
B2	293.15	6486.25	4.67E+01	1.2979	3.75E-04	66.21	8.58 ± 1.32	1.4865 ± 0.002	54.87 ± 1.01
	298.15	3936.65	2.57E+01	1.2947	2.26E-04				
	303.15	2457.90	3.82E+00	1.2915	3.46E-04				
	308.15	1578.45	1.48E+00	1.2885	3.68E-04				
	313.15	1044.30	1.70E+00	1.2855	3.11E-04				
B3	293.15	123.27	7.44E+00	1.1881	2.33E-03	43.03	12.96 ± 1.11	1.4598 ± 0.000	ND
	298.15	90.87	5.07E+00	1.1848	2.57E-03				
	303.15	68.21	3.61E+00	1.1820	2.97E-03				
	308.15	52.24	2.64E+00	1.1790	3.16E-03				
	313.15	40.76	1.99E+00	1.1761	3.06E-03				
	318.15	32.34	1.55E+00	1.1731	3.19E-03				
	323.15	26.06	1.22E+00	1.1700	3.55E-03				
	328.15	21.31	9.72E-01	1.1671	3.42E-03				

	333.15	17.65	7.85E-01	1.1640	3.59E-03				
	338.15	14.79	6.41E-01	1.1610	3.73E-03				
	343.15	12.53	5.22E-01	1.1578	3.93E-03				
B4[b]	293.15	508.54	2.51E+02	1.2620	3.84E-03	49.50	11.97 ± 0.46	1.4824 ± 0.005	48.18 ± 3.79
	303.15	386.64	2.44E+02	1.2590	3.84E-03				
	313.15	197.50	1.10E+02	1.2534	5.26E-03				
	323.15	109.87	5.37E+01	1.2477	5.42E-03				
	333.15	66.19	2.86E+01	1.2419	5.49E-03				
	343.15	49.89	1.37E+01	1.2389	5.57E-03				
C1[c]	293.15	40.07	3.10E-02	1.1207	5.77E-06	78.71	0.19 ± 0.04	1.4764 ± 0.003	N/D
	303.15	26.95	2.84E-02	1.1143	5.77E-06				
	313.15	18.98	2.87E-02	1.1086	1.00E-05				
	323.15	13.88	4.18E-02	1.1030	1.53E-05				
	333.15	10.51	4.36E-02	1.0974	1.53E-05				
C2[c]	293.15	472.97	N/A	1.1943	N/A	90.61	1.18 ± 0.3	1.4677 ± 0.011	N/D
	303.15	246.79	N/A	1.1854	N/A				
	313.15	133.37	N/A	1.1827	N/A				
	323.15	81.59	N/A	1.1770	N/A				
	333.15	53.81	N/A	1.1713	N/A				
	343.15	36.74	N/A	1.1648	N/A				
	353.15	26.33	N/A	1.1575	N/A				
C3[c]	298.15	748.09	N/A	1.1433	N/A	72.27	2.15 ± 0.02	1.4779 ± 0.019	N/D
	303.15	511.61	N/A	1.1410	N/A				

	308.15	351.46	N/A	1.1387	N/A				
	313.15	243.04	N/A	1.1363	N/A				
	318.15	169.57	N/A	1.1340	N/A				
	323.15	119.81	N/A	1.1317	N/A				
	328.15	86.09	N/A	1.1294	N/A				
F1	293.15	3842.00	5.98E+02	1.3962	2.02E-03	48.71	18.09 ± 3.65	1.4849 ± 0.001	48.44 ± 0.3
	298.15	2395.55	2.56E+02	1.3940	8.91E-04				
	303.15	1347.67	1.76E+02	1.3898	2.02E-03				
	308.15	887.59	8.19E+01	1.3877	9.33E-04				
	313.15	546.47	5.36E+01	1.3835	2.05E-03				
G1	293.15	478.77	2.21E+00	1.2900	5.66E-05	43.93	21.53 ± 2.74	1.4799 ± 0.001	45.24 ± 1.34
	298.15	322.55	1.66E+00	1.2869	8.49E-05				
	303.15	223.05	1.17E+00	1.2841	2.83E-05				
	308.15	158.54	8.49E-01	1.2810	8.49E-05				
	313.15	115.69	5.79E-01	1.2781	8.49E-05				
G2	293.15	15709.5	8.27E+01	1.3402	5.66E-05	82.08	0.17 ± 0.09	1.4911 ± 0.001	ND
	303.15	5431.6	1.41E+01	1.3336	1.84E-04				
	313.15	2061.55	1.06E+00	1.3267	5.66E-05				
	323.15	863.38	1.06E+00	1.3200	2.83E-05				
	333.15	395.31	9.48E-01	1.3127	1.13E-04				
G3	293.15	13013.00	2.52E+02	1.3833	6.51E-04	61.41	11.27 ± 0.53	1.4924 ± 0.004	ND
	303.15	4078.60	7.38E+01	1.3765	8.56E-04				
	313.15	1446.05	1.29E+01	1.3695	6.22E-04				

	323.15	584.56	4.13E+00	1.3625	5.30E-04				
	333.15	268.14	1.56E+00	1.3552	5.44E-04				
G4	293.15	17974.00	1.74E+02	1.3375	7.21E-04	82.16	0.14 ± 0.08	1.4913 ± 0.000	ND
	303.15	6230.25	2.16E+01	1.3310	7.07E-04				
	313.15	2395.95	1.46E+01	1.3246	7.71E-04				
	323.15	1022.65	3.04E+00	1.3182	8.63E-04				
	333.15	481.74	1.61E+00	1.3119	1.14E-03				
G5	293.15	14695.50	2.62E+01	1.3790	5.02E-04	61.56	9.4 ± 0.31	1.4923 ± 0.004	ND
	303.15	4554.05	7.69E+01	1.3725	2.90E-04				
	313.15	1648.85	2.13E+01	1.3660	3.96E-04				
	323.15	684.90	8.35E+00	1.3599	3.18E-04				
	333.15	318.84	3.01E+00	1.3537	5.23E-04				
G6	293.15	3522.80	7.85E+01	1.3617	8.34E-04	52.60	13.01 ± 0.55	1.4849 ± 0.002	46.15 ± 2.1
	303.15	1251.65	7.28E+00	1.3550	1.08E-03				
	313.15	515.10	5.42E+00	1.3487	9.76E-04				
	323.15	239.84	3.08E+00	1.3422	9.83E-04				
	333.15	123.70	1.40E+00	1.3355	9.83E-04				
G7	293.15	1469.60	9.48E+01	1.3407	2.83E-05	53.36	19.25 ± 2.08	1.4776 ± 0.003	49.34 ± 2.41
	303.15	590.19	3.36E+01	1.3347	9.19E-05				
	313.15	268.01	1.38E+01	1.3287	5.66E-05				
	323.15	135.74	5.73E+00	1.3225	1.13E-04				
	333.15	75.22	3.07E+00	1.3161	6.36E-05				
P1	293.15	25.74	3.25E-02	1.2134	2.55E-04	32.19	36.31 ± 1.2	1.4413 ± 0.000	34.75 ± 1.65

	298.15	20.17	3.54E-03	1.2105	3.18E-04				
	303.15	16.06	1.84E-02	1.2074	3.11E-04				
	308.15	12.99	2.83E-02	1.2046	4.67E-04				
	313.15	10.67	2.96E-02	1.2017	1.48E-04				
T1	293.15	553.06	5.30E+00	1.3576	6.15E-04	43.25	25.84 ± 1.11	1.4735 ± 0.006	ND
	298.15	238.57	3.10E+00	1.3517	6.29E-04				
	303.15	115.09	1.52E+00	1.3451	7.92E-04				
	308.15	61.83	7.21E-01	1.3381	7.71E-04				
	313.15	36.33	3.67E-01	1.3312	7.57E-04				
T2	293.15	669.86	3.14E+01	1.3557	1.36E-03	43.30	27.64 ± 0.25	1.4742 ± 0.003	47.41 ± 1.21
	303.15	289.39	1.23E+01	1.3502	1.58E-03				
	313.15	141.01	5.12E+00	1.3447	1.58E-03				
	323.15	76.29	2.67E+00	1.3389	1.51E-03				
	333.15	44.83	1.43E+00	1.3329	1.54E-03				

[a] The mean of water content ± standard deviation (SD*)
[b] Data of viscosity and density retrieved from reference [120]
[c] The data of viscosities and density were retrieved from reference [121]
N/A – Not available
N/D – Not determined (equipment problems)

Table A. 2: Experimental data of viscosity, density, molar volume (at 298.15 K), water content, refractive index and surface tension hydrophobic NADES.

NADES	T (K)	η (mPa.s)	SD	ρ (g/cm³)	SD	V_m (cm³/mol)	W%	n_D	γ_L (mN/m)
M1	293.15	11.44	1.48E-02	0.9347	6.36E-05	116.14	0.27 ± 0.04	1.4407 ± 0.001	30.37 ± 0.35
	303.15	7.07	1.87E-02	0.9264	2.12E-05				
	313.15	4.69	1.36E-02	0.9181	2.83E-05				
	323.15	3.30	5.09E-03	0.9099	9.19E-05				
	333.15	2.43	3.96E-03	0.9015	2.12E-05				
M2	293.15	150.69	3.30E-01	0.9131	3.40E-05	171.11	0.16 ± 0.03	1.4667 ± 0.001	32.78 ± 0.47
	303.15	56.22	1.57E-01	0.9058	9.63E-05				
	313.15	25.22	9.43E-02	0.8985	1.77E-04				
	323.15	12.94	5.78E-02	0.8910	2.73E-04				
	333.15	7.44	3.51E-02	0.8833	3.60E-04				
M3	293.15	20.23	2.47E-02	0.9000	2.12E-05	183.07	0.85 ± 0.04	1.4497 ± 0.001	31.77 ± 1.45
	303.15	12.79	8.49E-03	0.8926	1.41E-05				
	313.15	8.55	1.03E-02	0.8852	2.12E-05				
	323.15	6.01	9.40E-03	0.8779	4.24E-05				
	333.15	4.41	8.70E-03	0.8704	1.41E-05				
M4	293.15	28.08	7.07E-03	0.8993	4.67E-04	180.46	0.20 ± 0.02	1.4533 ± 0.000	31.3 ± 1.48
	303.15	16.19	1.63E-02	0.8913	1.41E-03				
	313.15	10.07	1.63E-02	0.8825	3.56E-03				
	323.15	6.69	1.16E-02	0.8719	8.08E-03				

NADES	T (K)	η (mPa.s)	SD	ρ (g/cm^3)	SD	V_m (cm^3/mol)	W%	n_D	γ_L (mN/m)
	333.15	4.69	8.63E-03	0.8594	1.52E-02				
M5	293.15	39.34	5.16E-02	0.8991	2.12E-05	177.91	0.43 ± 0.03	1.4569 ± 0.001	30.82 ± 0.51
	303.15	20.48	7.07E-04	0.8917	5.66E-05				
	313.15	11.79	7.07E-04	0.8845	8.49E-05				
	323.15	7.38	7.85E-03	0.8771	7.07E-05				
	333.15	4.93	6.29E-03	0.8696	1.06E-04				
M6	293.15	36.46	5.80E-02	0.8993	2.12E-05	178.27	0.14 ± 0.01	1.4561 ± 0.001	32.02 ± 0.55
	303.15	19.43	1.06E-02	0.8919	4.24E-05				
	313.15	11.39	3.54E-03	0.8846	2.12E-05				
	323.15	7.23	9.55E-03	0.8773	1.41E-05				
	333.15	4.89	9.76E-03	0.8698	7.07E-06				
M7	293.15	35.20	3.22E-01	0.8970	7.07E-05	188.09	0.29 ± 0.0	1.4564 ± 0.001	ND
	303.15	19.51	9.69E-02	0.8898	5.66E-05				
	313.15	11.74	1.77E-02	0.8825	4.24E-05				
	323.15	7.59	1.41E-03	0.8752	4.95E-05				
	333.15	5.21	7.50E-03	0.8678	3.54E-05				
M8	293.15	32.03	1.70E-01	0.8960	1.00E-03	191.43	0.07 ± 0.01	1.4550 ± 0.001	33.09 ± 0.22
	303.15	18.47	3.20E-02	0.8890	1.10E-03				
	313.15	11.42	2.50E-02	0.8810	1.10E-03				
	323.15	7.54	1.90E-02	0.8740	1.10E-03				

NADES	T (K)	η (mPa.s)	SD	ρ (g/cm³)	SD	V_m (cm³/mol)	W%	n_D	γ_L (mN/m)
	333.15	5.25	1.60E-02	0.8670	1.20E-03				
M9	293.15	44.00	1.56E-02	0.8974	2.12E-05	183.63	0.18 ± 0.01	1.4585 ± 0.001	32.75 ± 0.63
	303.15	22.63	8.49E-03	0.8902	2.83E-05				
	313.15	12.88	3.54E-03	0.8829	2.12E-05				
	323.15	7.97	2.19E-03	0.8756	7.07E-06				
	333.15	5.29	2.12E-04	0.8682	1.41E-05				
M10	293.15	42.50	6.16E-02	0.8973	6.65E-05	184.57	0.17 ± 0.02	1.4593 ± 0.001	31.83 ± 0.86
	303.15	22.22	3.09E-03	0.8901	5.91E-05				
	313.15	12.87	3.68E-03	0.8828	6.18E-05				
	323.15	8.03	3.32E-03	0.8755	5.91E-05				
	333.15	5.36	3.45E-03	0.8681	6.18E-05				
M11	293.15	46.47	3.54E-03	0.8975	1.41E-05	182.47	0.15 ± 0.01	1.4583 ± 0.001	33.12 ± 0.03
	303.15	23.48	9.05E-02	0.8903	6.36E-05				
	313.15	13.19	9.19E-03	0.8830	2.12E-05				
	323.15	8.09	8.49E-04	0.8757	2.12E-05				
	333.15	5.32	2.40E-03	0.8682	3.54E-05				
M12	293.15	55.27	3.18E-02	0.8971	5.23E-04	180.19	0.06 ± 0.02	1.4591 ± 0.001	32.3 ± 0.17
	303.15	26.42	1.63E-02	0.8897	6.29E-04				
	313.15	14.23	5.66E-03	0.8824	7.07E-04				
	323.15	8.45	7.78E-03	0.8750	8.27E-04				

NADES	T (K)	η (mPa.s)	SD	ρ (g/cm^3)	SD	V_m (cm^3/mol)	W%	n_D	γ_L (mN/m)
	333.15	5.41	2.62E-03	0.8676	8.34E-04				
M13	293.15	23.24	3.95E-02	0.8976	5.73E-05	191.44	0.14 ± 0.02	1.4513 ± 0.001	33.49 ± 0.04
	303.15	14.53	7.72E-03	0.8902	7.41E-05				
	313.15	9.66	7.72E-03	0.8831	4.90E-05				
	323.15	6.71	4.87E-03	0.8758	4.11E-05				
	333.15	4.88	1.24E-03	0.8684	2.87E-05				
M14	293.15	30.11	6.64E-02	0.8981	5.79E-05	185.74	0.09 ± 0.01	1.4547 ± 0.001	33.51 ± 1.08
	303.15	17.36	3.40E-03	0.8907	6.94E-05				
	313.15	10.83	4.50E-03	0.8836	5.35E-05				
	323.15	7.15	5.50E-03	0.8763	4.55E-05				
	333.15	5.00	5.38E-03	0.8689	4.55E-05				
M15	293.15	39.87	8.20E-02	0.9831	7.07E-06	139.14	0.48 ± 0.03	1.4538 ± 0.001	31.54 ± 0.87
	303.15	21.48	3.54E-02	0.9752	5.66E-05				
	313.15	12.82	1.98E-02	0.9673	7.07E-05				
	323.15	8.28	2.50E-02	0.9595	7.07E-05				
	333.15	5.70	1.91E-02	0.9516	7.07E-06				
M16	293.15	46.32	3.61E-01	0.8957	6.36E-05	191.20	0.34 ± 0.07	1.4608 ± 0.006	31.98 ± 0.68
	303.15	24.25	1.97E-01	0.8885	5.66E-05				
	313.15	13.96	1.10E-01	0.8814	6.36E-05				
	323.15	8.71	5.69E-02	0.8741	9.90E-05				

NADES	T (K)	η (mPa.s)	SD	ρ (g/cm^3)	SD	V_m (cm^3/mol)	W%	n_D	$γ_L$ (mN/m)
	333.15	5.82	3.74E-02	0.8668	9.90E-05				
M17	293.15	57.58	4.00E-01	0.8962	1.91E-04	183.86	0.26 ± 0.02	1.4604 ± 0.001	32.62 ± 0.23
	303.15	27.70	1.98E-01	0.8884	7.14E-04				
	313.15	14.99	1.27E-01	0.8799	1.99E-03				
	323.15	8.94	1.18E-01	0.8713	3.17E-03				
	333.15	5.72	5.30E-02	0.8623	4.65E-03				
M18	293.15	53.95	5.94E-02	0.9364	1.56E-04	164.51	0.16 ± 0.01	1.4923 ± 0.001	33.21 ± 0.33
	303.15	24.47	5.09E-02	0.9289	1.56E-04				
	313.15	12.94	5.94E-02	0.9214	1.13E-04				
	323.15	7.67	3.87E-02	0.9138	1.13E-04				
	333.15	4.95	1.58E-02	0.9061	1.63E-04				
M19	293.15	68.94	1.56E-01	0.9236	6.34E-05	167.46	0.13 ± 0.02	1.4818 ± 0.001	32.3 ± 0.18
	303.15	29.77	4.79E-02	0.9162	7.13E-05				
	313.15	15.16	1.69E-02	0.9088	4.78E-05				
	323.15	8.64	8.07E-03	0.9013	2.05E-05				
	333.15	5.42	4.39E-03	0.8937	1.25E-05				
M20	293.15	79.69	1.80E-01	0.9137	4.24E-05	170.19	0.13 ± 0.01	1.474 ± 0.001	31.57 ± 0.46
	303.15	33.34	1.10E-02	0.9063	4.32E-05				
	313.15	16.47	4.55E-03	0.8990	3.74E-05				
	323.15	9.15	4.50E-03	0.8915	2.87E-05				

NADES	T (K)	η (mPa.s)	SD	ρ (g/cm^3)	SD	V_m (cm^3/mol)	W%	n_D	γ_L (mN/m)
	333.15	5.60	5.54E-03	0.8839	2.05E-05				
M21	293.15	86.31	1.43E-01	0.9064	1.84E-04	172.17	0.55 ± 0.02	1.4682 ± 0.001	31.38 ± 0.77
	303.15	35.31	2.05E-02	0.8991	2.05E-04				
	313.15	17.08	7.07E-03	0.8918	2.55E-04				
	323.15	9.36	3.89E-03	0.8844	1.63E-04				
	333.15	5.66	1.77E-03	0.8769	7.78E-05				

Table A. 3: Dielectric constants of Organic solvents obtained at room temperature and in a frequency (freq.) range of 10^{-1}-10^{6} Hz. The points used for the calculation are highlighted in gray.

Freq. [Hz]	**ε´**								
	Organic Solvents								
	Water	**MeOH**	**EtOH**	**1-PrOH**	**2-PrOH**	**EG**	**Gly**	**Hx**	**CHx**
1.00E+06	443.00	34.10	34.60	21.10	19.60	38.80	45.70	2.00	2.19
9.08E+05	456.00	34.30	34.50	21.00	19.50	38.60	45.50	1.99	2.19
6.10E+05	78.10	34.30	34.30	20.90	19.40	38.30	45.00	1.98	2.19
4.09E+05	**78.20**	**34.60**	**34.50**	**20.90**	**19.40**	**38.20**	**44.80**	**1.96**	**2.18**
2.75E+05	79.40	35.10	34.80	20.90	19.40	38.10	44.70	1.96	2.18
1.85E+05	80.80	36.30	35.40	20.90	19.40	38.10	44.60	1.95	2.18
1.24E+05	83.60	39.30	36.80	20.90	19.40	38.20	44.60	1.94	2.18
1.00E+05	86.30	41.90	38.00	21.00	19.40	38.20	44.60	1.93	2.18
8.32E+04	89.70	45.10	39.60	21.00	19.40	38.20	44.60	1.92	2.18
5.58E+04	102.00	57.40	46.00	21.20	19.50	38.30	44.60	1.91	2.18
3.75E+04	129.00	83.50	58.50	21.60	19.70	38.40	44.60	1.90	2.18
2.52E+04	187.00	138.00	84.90	22.40	20.00	38.50	44.70	1.89	2.18
1.69E+04	307.00	252.00	140.00	24.10	20.80	38.80	44.70	1.88	2.18
1.13E+04	558.00	483.00	250.00	27.60	22.10	39.30	44.70	1.87	2.18
1.00E+04	686.00	596.00	304.00	29.40	22.90	39.30	44.70	1.86	2.18

Freq. [Hz]	**ε´**								
	Organic Solvents								
	Water	**MeOH**	**EtOH**	**1-PrOH**	**2-PrOH**	**EG**	**Gly**	**Hx**	**CHx**
7.62E+03	1080.00	934.00	464.00	35.00	25.10	40.10	44.70	1.85	2.18
5.12E+03	2110.00	1760.00	860.00	50.40	31.30	42.10	44.80	1.84	2.18
3.44E+03	4060.00	3170.00	1550.00	82.00	43.80	46.20	44.80	1.83	2.18
2.31E+03	7450.00	5330.00	2650.00	147.00	69.40	54.50	44.90	1.83	2.18
1.55E+03	12700.00	8320.00	4290.00	278.00	121.00	71.40	45.10	1.82	2.18
1.00E+03	20800.00	12400.00	6780.00	574.00	240.00	111.00	45.50	1.81	2.18
6.98E+02	29500.00	16200.00	9400.00	1040.00	432.00	177.00	45.90	1.80	2.17
4.69E+02	42200.00	20500.00	12600.00	1980.00	830.00	320.00	47.30	1.80	2.17
3.15E+02	60200.00	24500.00	16700.00	3630.00	1580.00	607.00	50.10	1.79	2.17
2.11E+02	86600.00	28900.00	21200.00	6370.00	2940.00	1170.00	55.80	1.78	2.17
1.42E+02	127000.00	33700.00	26300.00	10600.00	5290.00	2210.00	67.60	1.77	2.17
1.00E+02	179000.00	38300.00	31300.00	15800.00	8540.00	3700.00	88.20	1.77	2.17
9.52E+01	193000.00	39100.00	32000.00	16400.00	9040.00	3900.00	92.20	1.76	2.17
6.39E+01	285000.00	45100.00	38600.00	24000.00	14700.00	6530.00	143.00	1.75	2.17
4.29E+01	419000.00	52500.00	46100.00	33600.00	22200.00	10200.00	247.00	1.74	2.17
2.88E+01	632000.00	61400.00	55200.00	44900.00	31100.00	15300.00	461.00	1.74	2.17
1.94E+01	893000.00	72700.00	66400.00	58200.00	41300.00	22700.00	891.00	1.74	2.17
1.30E+01	1220000.00	87500.00	81300.00	74100.00	53900.00	33500.00	1730.00	1.73	2.18
1.00E+01	1480000.00	98300.00	92800.00	87000.00	63500.00	43200.00	2630.00	1.73	2.17
8.72E+00	1650000.00	105000.00	100000.00	94300.00	69100.00	48700.00	3250.00	1.72	2.17
5.86E+00	2140000.00	126000.00	123000.00	121000.00	88600.00	73300.00	5850.00	1.73	2.15
3.93E+00	2660000.00	153000.00	157000.00	155000.00	114000.00	109000.00	9840.00	1.72	2.11
2.64E+00	3200000.00	185000.00	197000.00	200000.00	147000.00	162000.00	15900.00	1.74	2.08

Freq. [Hz]	ε´								
	Organic Solvents								
	Water	**MeOH**	**EtOH**	**1-PrOH**	**2-PrOH**	**EG**	**Gly**	**Hx**	**CHx**
1.77E+00	3770000.00	222000.00	251000.00	259000.00	192000.00	241000.00	24600.00	1.79	2.09
1.00E+00	4720000.00	285000.00	357000.00	374000.00	283000.00	431000.00	44900.00	1.98	2.12
7.99E-01	5280000.00	321000.00	438000.00	431000.00	328000.00	557000.00	56400.00	2.11	2.08
5.37E-01	6810000.00	374000.00	562000.00	552000.00	424000.00	885000.00	85700.00	2.58	2.10
3.60E-01	8990000.00	447000.00	729000.00	686000.00	536000.00	1430000.00	130000.00	3.43	1.97
2.42E-01	12600000.00	540000.00	977000.00	826000.00	664000.00	2210000.00	199000.00	4.58	1.75
1.62E-01	19100000.00	684000.00	1250000.00	982000.00	803000.00	3060000.00	304000.00	5.71	1.43
1.00E-01	31800000.00	1010000.00	1720000.00	1240000.00	1020000.00	3820000.00	506000.00	5.25	1.28

Table A. 4: Dielectric constant of **NADES** obtained at room temperature and in a frequency (freq.) range of 10^{-1}-10^{6} Hz. The points used for the calculation are highlighted in gray.

Freq. [Hz]	**ε′**											
	NADES											
	B2	**B3**	**B4**	**F1**	**G1**	**G2**	**G3**	**G4**	**G5**	**G6**	**G7**	**P1**
1.00E+06	103.00	163.00	129.00	51.50	871.00	42.60	9.91	59.00	39.80	51.50	20.40	109.00
9.08E+05	102.00	161.00	128.00	51.40	165.00	42.60	9.92	59.10	39.90	51.40	20.40	108.00
6.10E+05	102.00	156.00	127.00	51.50	160.00	42.70	9.93	59.80	40.60	51.10	20.30	106.00
4.09E+05	**102.00**	**153.00**	**127.00**	**51.80**	**158.00**	**43.00**	**9.97**	**60.30**	**41.10**	**51.00**	**20.30**	**105.00**
2.75E+05	102.00	152.00	128.00	52.00	157.00	43.20	10.00	60.60	41.50	51.00	20.20	104.00
1.85E+05	103.00	152.00	128.00	52.20	157.00	43.40	10.10	60.90	41.80	51.00	20.20	104.00
1.24E+05	103.00	152.00	128.00	52.40	156.00	43.50	10.20	61.10	42.00	51.10	20.20	104.00
1.00E+05	103.00	152.00	128.00	52.40	156.00	43.50	10.30	61.10	42.10	51.10	20.20	104.00
8.32E+04	103.00	152.00	128.00	52.50	156.00	43.50	10.30	61.20	42.20	51.10	20.20	104.00
5.58E+04	103.00	152.00	128.00	52.50	156.00	43.60	10.50	61.30	42.20	51.10	20.20	106.00
3.75E+04	103.00	152.00	128.00	52.60	156.00	43.60	10.70	61.30	42.30	51.10	20.20	107.00
2.52E+04	103.00	152.00	128.00	52.60	156.00	43.60	10.90	61.40	42.30	51.10	20.30	110.00
1.69E+04	103.00	152.00	128.00	52.60	156.00	43.60	11.30	61.40	42.30	51.20	20.30	114.00
1.13E+04	103.00	153.00	128.00	52.70	156.00	43.60	11.60	61.40	42.30	51.30	20.30	124.00
1.00E+04	103.00	153.00	128.00	52.70	157.00	43.60	11.80	61.40	42.40	51.30	20.30	129.00
7.62E+03	103.00	154.00	128.00	52.70	157.00	43.60	12.10	61.40	42.40	51.40	20.30	145.00
5.12E+03	103.00	157.00	128.00	52.80	158.00	43.70	12.70	61.50	42.40	51.60	20.40	189.00
3.44E+03	103.00	163.00	128.00	52.90	161.00	43.70	13.30	61.50	42.40	51.80	20.40	284.00

Freq. [Hz]	**ε′**											
	NADES											
	B2	**B3**	**B4**	**F1**	**G1**	**G2**	**G3**	**G4**	**G5**	**G6**	**G7**	**P1**
2.31E+03	103.00	176.00	128.00	53.10	166.00	43.80	14.00	61.60	42.50	52.00	20.50	486.00
1.55E+03	103.00	204.00	129.00	53.30	178.00	44.10	14.70	61.80	42.50	52.30	20.50	907.00
1.00E+03	104.00	273.00	129.00	53.80	207.00	44.50	15.80	62.10	42.60	52.50	20.70	1900.00
6.98E+02	104.00	391.00	130.00	54.70	257.00	45.00	16.90	62.40	42.70	53.10	21.00	3480.00
4.69E+02	105.00	653.00	132.00	56.60	372.00	45.70	18.70	62.80	42.90	54.40	21.50	6600.00
3.15E+02	106.00	1180.00	137.00	60.60	614.00	46.30	21.50	63.40	43.10	57.00	22.70	11800.00
2.11E+02	109.00	2220.00	146.00	68.70	1120.00	46.90	25.40	64.20	43.40	62.50	25.00	19500.00
1.42E+02	115.00	4130.00	165.00	85.50	2150.00	47.30	30.90	65.60	43.60	74.20	29.80	30500.00
1.00E+02	126.00	6880.00	198.00	114.00	3830.00	47.70	37.00	67.90	43.80	94.80	37.90	43500.00
9.52E+01	128.00	7350.00	204.00	120.00	4130.00	47.70	38.70	68.30	43.90	99.00	39.50	45500.00
6.39E+01	154.00	12400.00	286.00	188.00	7710.00	48.30	47.70	73.80	44.30	152.00	59.00	67800.00
4.29E+01	208.00	19700.00	455.00	323.00	13500.00	49.40	58.80	84.90	45.00	263.00	98.00	103000.00
2.88E+01	315.00	30600.00	799.00	575.00	22300.00	51.60	75.20	107.00	46.50	495.00	175.00	158000.00
1.94E+01	528.00	47000.00	1480.00	1020.00	35100.00	56.20	93.10	148.00	49.50	977.00	322.00	243000.00
1.30E+01	938.00	72700.00	2800.00	1770.00	54100.00	65.60	116.00	223.00	55.50	1950.00	596.00	365000.00
1.00E+01	1380.00	97400.00	4240.00	2520.00	72400.00	76.90	135.00	302.00	62.50	3040.00	882.00	470000.00
8.72E+00	1690.00	114000.00	5220.00	3010.00	84900.00	85.30	148.00	357.00	67.60	3800.00	1070.00	535000.00
5.86E+00	3020.00	177000.00	9370.00	5010.00	135000.00	125.00	182.00	589.00	91.80	7160.00	1870.00	723000.00
3.93E+00	5120.00	277000.00	16100.00	8020.00	212000.00	209.00	221.00	972.00	140.00	12600.00	3130.00	945000.00
2.64E+00	8340.00	432000.00	26600.00	12700.00	322000.00	382.00	268.00	1570.00	233.00	21200.00	5150.00	1170000.00
1.77E+00	13000.00	669000.00	42300.00	19800.00	465000.00	723.00	330.00	2440.00	407.00	33200.00	8150.00	1430000.00
1.00E+00	23600.00	1200000.00	79800.00	36400.00	718000.00	1870.00	471.00	4330.00	891.00	61000.00	15300.00	1850000.00
7.99E-01	29400.00	1510000.00	105000.00	46600.00	845000.00	2660.00	541.00	5330.00	1200.00	76400.00	19700.00	2050000.00

Freq. [Hz]	**ε´**											
	NADES											
	B2	**B3**	**B4**	**F1**	**G1**	**G2**	**G3**	**G4**	**G5**	**G6**	**G7**	**P1**
5.37E-01	44800.00	2040000.00	169000.00	72600.00	1070000.00	4930.00	704.00	7660.00	1980.00	115000.00	30500.00	2450000.00
3.60E-01	67700.00	2600000.00	279000.00	116000.00	1310000.00	8530.00	904.00	11000.00	3160.00	179000.00	47600.00	2990000.00
2.42E-01	104000.00	3200000.00	456000.00	187000.00	1580000.00	13900.00	1160.00	15900.00	4930.00	293000.00	73900.00	3800000.00
1.62E-01	164000.00	3860000.00	694000.00	310000.00	1900000.00	21700.00	1460.00	23300.00	7600.00	467000.00	115000.00	4970000.00
1.00E-01	288000.00	4850000.00	1040000.00	578000.00	2420000.00	35900.00	194.00	37400.00	12800.00	697000.00	195000.00	6950000.00

Table A. 5: Dielectric constant of **NADES** obtained at room temperature and in a frequency (freq.) range of 10^{-1}-10^{6} Hz (continuation). The points used for the calculation are highlighted in gray.

Freq. [Hz]	ε´											
	NADES											
	T1	**T2**	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**	**M9**	**M10**
1.00E+06	62.90	54.70	3.35	4.31	3.77	4.13	5.05	3.60	3.82	3.08	2.98	2.15
9.08E+05	62.60	54.50	3.35	4.31	3.76	4.13	5.05	3.60	3.82	3.08	2.98	2.15
6.10E+05	61.70	53.90	3.34	4.30	3.76	4.12	5.03	3.60	3.81	3.07	2.97	2.14
4.09E+05	**61.40**	**53.60**	**3.34**	**4.30**	**3.75**	**4.11**	**5.02**	**3.60**	**3.81**	**3.07**	**2.97**	**2.14**
2.75E+05	61.20	53.50	3.34	4.30	3.74	4.11	5.02	3.61	3.80	3.07	2.97	2.14
1.85E+05	61.20	53.50	3.34	4.30	3.74	4.11	5.02	3.61	3.80	3.07	2.97	2.14
1.24E+05	61.20	53.40	3.34	4.30	3.74	4.11	5.01	3.61	3.80	3.07	2.97	2.14
1.00E+05	61.20	53.40	3.34	4.29	3.74	4.11	5.01	3.61	3.80	3.07	2.97	2.14
8.32E+04	61.20	53.40	3.34	4.29	3.74	4.11	5.01	3.62	3.80	3.07	2.97	2.14
5.58E+04	61.30	53.50	3.34	4.29	3.74	4.11	5.01	3.62	3.80	3.07	2.97	2.14
3.75E+04	61.40	53.50	3.34	4.29	3.74	4.11	5.01	3.62	3.80	3.07	2.97	2.14
2.52E+04	61.50	53.50	3.34	4.29	3.74	4.11	5.01	3.62	3.80	3.07	2.97	2.13
1.69E+04	61.60	53.60	3.34	4.29	3.74	4.11	5.01	3.62	3.80	3.07	2.97	2.13
1.13E+04	61.90	53.60	3.34	4.29	3.74	4.11	5.00	3.63	3.80	3.07	2.97	2.13
1.00E+04	61.90	53.70	3.34	4.29	3.74	4.11	5.00	3.63	3.80	3.07	2.97	2.13
7.62E+03	62.20	53.80	3.34	4.29	3.74	4.11	5.00	3.63	3.80	3.07	2.97	2.13
5.12E+03	63.20	53.90	3.34	4.29	3.74	4.11	5.00	3.63	3.80	3.07	2.97	2.13
3.44E+03	65.20	54.00	3.35	4.29	3.74	4.11	5.00	3.63	3.80	3.07	2.97	2.13
2.31E+03	69.40	54.30	3.35	4.29	3.74	4.11	5.00	3.63	3.80	3.07	2.97	2.13
1.55E+03	78.40	55.00	3.36	4.29	3.74	4.11	5.00	3.63	3.80	3.07	2.97	2.13
1.00E+03	100.00	56.40	3.36	4.29	3.74	4.11	5.00	3.64	3.80	3.07	2.97	2.13

Freq. [Hz]	ε′											
	NADES											
	T1	**T2**	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**	**M9**	**M10**
6.98E+02	137.00	58.70	3.36	4.29	3.74	4.11	5.00	3.64	3.80	3.07	2.97	2.13
4.69E+02	219.00	64.00	3.36	4.29	3.74	4.11	5.00	3.65	3.80	3.07	2.97	2.13
3.15E+02	386.00	74.80	3.37	4.30	3.74	4.11	5.00	3.66	3.80	3.07	2.97	2.13
2.11E+02	723.00	96.50	3.38	4.30	3.74	4.11	5.00	3.67	3.80	3.07	2.97	2.13
1.42E+02	1380.00	140.00	3.40	4.30	3.74	4.11	5.00	3.71	3.80	3.07	2.97	2.13
1.00E+02	2440.00	213.00	3.45	4.30	3.74	4.11	5.00	3.77	3.80	3.07	2.97	2.14
9.52E+01	2640.00	227.00	3.46	4.30	3.74	4.11	5.00	3.78	3.80	3.07	2.97	2.14
6.39E+01	4930.00	396.00	3.57	4.30	3.74	4.12	5.00	3.88	3.80	3.07	2.97	2.14
4.29E+01	8930.00	721.00	3.73	4.30	3.74	4.12	5.00	4.00	3.81	3.08	2.97	2.15
2.88E+01	15500.00	1330.00	4.07	4.30	3.74	4.12	5.00	4.11	3.81	3.08	2.97	2.16
1.94E+01	25900.00	2430.00	4.69	4.30	3.75	4.13	5.01	4.18	3.81	3.08	2.98	2.17
1.30E+01	41400.00	4360.00	5.75	4.30	3.75	4.14	5.01	4.23	3.81	3.09	2.98	2.18
1.00E+01	55500.00	6270.00	6.92	4.31	3.75	4.14	5.02	4.25	3.82	3.09	2.98	2.19
8.72E+00	64800.00	7520.00	7.74	4.31	3.75	4.15	5.02	4.26	3.82	3.10	2.99	2.20
5.86E+00	101000.00	12600.00	11.10	4.33	3.76	4.16	5.03	4.28	3.82	3.10	2.99	2.22
3.93E+00	161000.00	20300.00	17.10	4.35	3.77	4.17	5.04	4.30	3.83	3.11	3.00	2.24
2.64E+00	258000.00	32500.00	27.10	4.38	3.77	4.18	5.05	4.31	3.83	3.12	3.01	2.26
1.77E+00	421000.00	51000.00	43.60	4.42	3.79	4.19	5.06	4.32	3.84	3.13	3.02	2.29
1.00E+00	826000.00	97500.00	86.30	4.49	3.79	4.20	5.08	4.34	3.86	3.14	3.04	2.33
7.99E-01	1110000.00	131000.00	113.00	4.51	3.80	4.20	5.08	4.35	3.86	3.15	3.04	2.36
5.37E-01	1670000.00	214000.00	174.00	4.54	3.81	4.23	5.11	4.39	3.87	3.16	3.05	2.39
3.60E-01	2370000.00	376000.00	269.00	4.56	3.83	4.26	5.17	4.44	3.88	3.21	3.06	2.44
2.42E-01	3190000.00	681000.00	403.00	4.56	3.86	4.33	5.29	4.53	3.90	3.27	3.07	2.53

Freq. **[Hz]**	ε′											
	NADES											
	T1	**T2**	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**	**M9**	**M10**
1.62E-01	4110000.00	1240000.00	597.00	4.56	3.93	4.45	5.51	4.71	3.93	3.37	3.10	2.63
1.00E-01	5430000.00	2280000.00	959.00	4.57	4.08	4.76	6.07	5.13	3.99	4.27	3.17	2.82

Table A. 6: Dielectric constant of **NADES** obtained at room temperature and in a frequency (freq.) range of 10^{-1}-10^{6} Hz (continuation). The points used for the calculation are highlighted in gray.

Freq. [Hz]	ε′										
	NADES (continuation)										
	M11	**M12**	**M13**	**M14**	**M15**	**M16**	**M17**	**M18**	**M19**	**M20**	**M21**
1.00E+06	2.69	3.15	2.90	4.34	10.80	3.33	4.82	5.42	4.12	6.65	4.30
9.08E+05	2.69	3.15	2.90	4.33	10.70	3.33	4.82	5.42	4.12	6.65	4.30
6.10E+05	2.68	3.15	2.90	4.32	10.70	3.33	4.82	5.41	4.11	6.63	4.29
4.09E+05	**2.68**	**3.14**	**2.89**	**4.32**	**10.70**	**3.32**	**4.82**	**5.40**	**4.11**	**6.62**	**4.29**
2.75E+05	2.68	3.14	2.89	4.32	10.70	3.32	4.83	5.40	4.10	6.62	4.29
1.85E+05	2.68	3.14	2.89	4.32	10.70	3.32	4.83	5.40	4.10	6.62	4.30
1.24E+05	2.68	3.14	2.89	4.32	10.70	3.32	4.85	5.39	4.10	6.62	4.30
1.00E+05	2.68	3.14	2.89	4.32	10.70	3.32	4.86	5.39	4.10	6.62	4.30
8.32E+04	2.68	3.14	2.89	4.32	10.70	3.32	4.86	5.39	4.10	6.62	4.30
5.58E+04	2.68	3.14	2.89	4.32	10.70	3.32	4.88	5.39	4.10	6.62	4.30
3.75E+04	2.68	3.14	2.89	4.32	10.70	3.32	4.91	5.39	4.10	6.62	4.31
2.52E+04	2.68	3.14	2.89	4.32	10.70	3.32	4.95	5.39	4.10	6.62	4.31
1.69E+04	2.68	3.14	2.89	4.32	10.70	3.32	4.99	5.39	4.10	6.62	4.31
1.13E+04	2.68	3.14	2.89	4.32	10.70	3.32	5.04	5.39	4.10	6.62	4.31
1.00E+04	2.68	3.14	2.89	4.32	10.70	3.32	5.05	5.39	4.10	6.62	4.31
7.62E+03	2.68	3.14	2.89	4.32	10.70	3.32	5.09	5.39	4.10	6.62	4.32
5.12E+03	2.68	3.14	2.89	4.32	10.70	3.32	5.14	5.39	4.10	6.62	4.32

Freq. [Hz]	ε′										
	NADES (continuation)										
	M11	**M12**	**M13**	**M14**	**M15**	**M16**	**M17**	**M18**	**M19**	**M20**	**M21**
3.44E+03	2.68	3.14	2.89	4.32	10.70	3.32	5.21	5.39	4.10	6.62	4.32
2.31E+03	2.68	3.14	2.89	4.32	10.70	3.32	5.30	5.39	4.10	6.62	4.32
1.55E+03	2.68	3.14	2.89	4.32	10.70	3.32	5.39	5.39	4.10	6.62	4.33
1.00E+03	2.68	3.14	2.89	4.32	10.80	3.32	5.52	5.40	4.10	6.62	4.33
6.98E+02	2.68	3.14	2.89	4.32	10.80	3.32	5.65	5.40	4.10	6.62	4.34
4.69E+02	2.68	3.14	2.89	4.32	10.80	3.32	5.81	5.40	4.10	6.62	4.35
3.15E+02	2.68	3.14	2.89	4.32	10.90	3.32	6.04	5.40	4.10	6.62	4.36
2.11E+02	2.68	3.14	2.89	4.32	11.20	3.32	6.31	5.40	4.10	6.62	4.37
1.42E+02	2.68	3.14	2.89	4.32	11.60	3.32	6.68	5.40	4.10	6.62	4.39
1.00E+02	2.68	3.14	2.89	4.32	12.40	3.32	7.04	5.40	4.11	6.62	4.41
9.52E+01	2.68	3.14	2.89	4.32	12.60	3.32	7.12	5.40	4.11	6.62	4.42
6.39E+01	2.68	3.15	2.90	4.32	14.50	3.33	7.69	5.40	4.11	6.63	4.45
4.29E+01	2.69	3.15	2.90	4.32	18.50	3.34	8.25	5.40	4.12	6.63	4.50
2.88E+01	2.69	3.15	2.90	4.32	26.70	3.35	9.21	5.41	4.13	6.65	4.56
1.94E+01	2.70	3.15	2.90	4.33	43.40	3.37	10.40	5.41	4.15	6.68	4.64
1.30E+01	2.70	3.15	2.90	4.33	77.10	3.40	11.80	5.42	4.18	6.72	4.75
1.00E+01	2.71	3.16	2.90	4.34	116.00	3.43	13.00	5.43	4.20	6.74	4.84
8.72E+00	2.71	3.16	2.91	4.34	144.00	3.45	13.80	5.44	4.21	6.75	4.89
5.86E+00	2.73	3.17	2.91	4.35	276.00	3.53	16.30	5.45	4.25	6.79	5.05
3.93E+00	2.74	3.18	2.91	4.35	535.00	3.65	N/A	5.46	4.27	6.83	5.25
2.64E+00	2.76	3.20	2.92	4.36	1040.00	3.87	N/A	5.48	4.29	6.87	5.48

Freq. [Hz]	ε′										
	NADES (continuation)										
	M11	**M12**	**M13**	**M14**	**M15**	**M16**	**M17**	**M18**	**M19**	**M20**	**M21**
1.77E+00	2.78	3.21	2.92	4.37	1970.00	4.18	N/A	5.51	4.32	6.93	5.72
1.00E+00	2.80	3.24	2.92	4.38	4830.00	4.89	N/A	5.61	4.39	7.09	6.16
7.99E-01	2.81	3.24	2.93	4.38	6670.00	5.26	N/A	5.68	4.43	7.21	6.37
5.37E-01	2.82	3.26	2.93	4.38	11300.00	6.01	N/A	5.88	4.57	7.55	6.77
3.60E-01	2.84	3.28	2.94	4.40	17800.00	6.91	N/A	6.25	4.81	8.16	7.26
2.42E-01	2.87	3.32	2.96	4.42	26100.00	7.94	N/A	8.42	5.28	10.90	7.90
1.62E-01	2.93	3.40	2.98	4.47	36400.00	9.18	N/A	9.84	7.40	13.30	8.77
1.00E-01	3.05	3.60	3.08	4.58	53300.00	10.90	N/A	12.80	9.58	18.80	10.20

Table A. 7: δ_H parameter of hydrophilic NADES estimated through different models.

NADES	V_m(cm^3/mol)	$\bar{\upsilon}$(cm^{-1})	λ(nm)	E_{vap}(cal/mol)	$E_{vap/2}$	n	δ_H (SEM)		RD%	δ_H (EM)			
							This thesis*	From **eqn. 21**		StP	HK	HKF	Ymt
B1	54.13	3251.12	3075.86	9298.20	4649.10	20	84.78	87.92	3.57	22.44	20.51	18.73	6.61
B2	66.21	3280.10	3048.69	9381.09	4690.54	22	80.75	83.38	3.14	15.23	24.35	23.97	7.44
B3	43.03	3280.26	3048.54	9381.54	4690.77	16	85.43	88.20	3.14	25.42	22.95	22.91	7.65
B4	49.50	3262.16	3065.45	9329.78	4664.89	39	124.00	128.38	3.41	32.69	23.05	22.40	7.81
C1	78.71	3306.44	3024.40	9456.42	4728.21	4	31.71	32.61	2.76	17.28	19.55	19.45	5.28
C2	90.61	3306.71	3024.15	9457.19	4728.60	6	36.20	37.22	2.75	21.51	21.41	21.25	5.65
C3	72.27	3255.80[a]	3071.45	9311.57	4655.79	4	32.83	34.03	3.50	13.99	16.32	16.67	6.31
F1	48.71	3272.10	3056.14	9358.21	4679.10	28	106.09	109.66	3.26	50.89	33.02	31.56	10.24
G1	43.93	3244.00	3082.61	9277.84	4638.92	50	148.63	154.30	3.68	30.67	27.47	26.28	9.63
G2	82.08	3293.49	3036.29	9419.38	4709.69	17	63.89	65.83	2.95	32.67	29.30	28.36	8.26
G3	61.41	3293.12	3036.63	9418.32	4709.16	17	73.86	76.10	2.95	42.56	32.37	30.99	9.43
G4	82.16	3293.12	3036.63	9418.32	4709.16	17	63.85	65.79	2.95	32.90	28.99	27.87	8.26
G5	61.56	3272.12	3056.12	9358.26	4679.13	17	73.53	76.01	3.26	42.57	31.95	30.07	9.40
G6	52.60	3271.96	3056.27	9357.81	4678.90	30	105.66	109.23	3.26	48.74	32.40	34.74	9.89
G7	53.36	3271.96	3056.27	9357.81	4678.90	30	104.92	108.46	3.26	48.74	32.40	35.48	9.85
P1	32.19	3271.96	3056.27	9357.81	4678.90	23	118.26	122.25	3.26	27.50	32.80	33.72	11.46
T1	43.25	3271.35	3056.84	9356.06	4678.03	31	118.45	122.46	3.27	50.29	34.01	34.94	10.68
T2	43.30	3271.12	3057.06	9355.40	4677.70	31	118.38	122.39	3.28	50.10	33.52	34.18	10.61
AARD%									**3.20**				

[a] Calculated by averaging the wavenumbers of the NH bands.

* Using the obtained energy ($E_{vap/2}$) instead of using the 5000 cal/mol established by Hansen.

Table A. 8: δ_H parameter of hydrophobic NADES estimated through different models.

NADES	**V_m(cm^3/mol)**	**$\bar{\upsilon}$(cm^{-1})**	**λ(nm)**	**E_{vap}(cal/mol)**	**$E_{vap/2}$**	**n**	**δ_H (SEM)**		**RD%**	**δ_H (EM)**			
							This thesis*	From **eqn. 21**		StP	HK	HKF	Ymt
M1	116.14	3378.70	2959.72	9663.08	4831.54	2	18.66	18.98	1.70	10.83	11.30	11.28	3.30
M2	171.11	3337.50	2996.25	9545.25	4772.63	9	32.41	33.17	2.30	10.91	10.83	10.94	1.99
M3	183.07	3432.20	2913.58	9816.09	4908.05	2	14.98	15.12	0.92	9.19	8.85	8.95	2.63
M4	180.46	3355.97	2979.76	9598.07	4799.04	3	18.27	18.65	2.03	9.72	9.44	9.55	2.41
M5	177.91	3345.51	2989.08	9568.16	4784.08	5	23.72	24.25	2.18	10.16	9.92	10.05	2.23
M6	178.27	3337.50	2996.25	9545.25	4772.63	9	31.75	32.50	2.30	10.08	9.84	9.97	2.26
M7	188.09	3333.34	2999.99	9533.35	4766.68	4	19.81	20.29	2.36	9.56	9.36	9.48	2.29
M8	191.43	3333.34	2999.99	9533.35	4766.68	3	17.68	18.11	2.36	3.50	9.30	9.20	2.36
M9	183.63	3325.74	3006.85	9511.62	4755.81	6	24.41	25.03	2.47	9.96	9.77	9.90	2.19
M10	184.57	3338.73	2995.15	9548.77	4774.38	5	23.26	23.81	2.28	9.88	9.68	9.81	2.21
M11	182.47	3317.24	3014.55	9487.31	4743.65	6	26.18	26.88	2.60	10.07	9.88	10.01	2.16
M12	180.19	3339.12	2994.80	9549.88	4774.94	9	31.59	32.33	2.28	10.29	10.11	10.25	2.10
M13	191.44	3427.30	2917.75	9802.08	4901.04	4	20.70	20.91	0.99	8.90	8.61	8.71	2.58
M14	185.74	3356.08	2979.67	9598.39	4799.19	6	25.47	26.00	2.03	9.50	9.26	9.37	2.38
M15	139.14	3437.30	2909.26	9830.68	4915.34	2	17.19	17.34	0.85	11.16	10.73	10.77	3.45
M16	191.20	3349.20	2985.79	9578.71	4789.36	5	22.89	23.39	2.13	9.55	9.43	9.57	2.18
M17	183.86	3338.66	2995.21	9548.57	4774.28	9	31.27	32.00	2.28	10.09	9.95	10.10	2.09
M18	164.51	3338.82	2995.07	9549.03	4774.51	2	15.58	15.95	2.28	10.84	10.97	11.30	1.85
M19	167.46	3328.10	3004.72	9518.37	4759.18	3	18.89	19.36	2.44	10.84	10.87	11.13	1.89
M20	170.19	3328.10	3004.72	9518.37	4759.18	5	24.19	24.79	2.44	10.84	10.79	11.00	1.92
M21	172.17	3337.93	2995.87	9546.48	4773.24	9	32.31	33.07	2.29	10.84	10.74	10.92	1.94
AARD%									**2.07**				

In the case of the ChCl:Ure (1:2) system (**C3**), the energy associated with the evaporation was calculated using the wavenumbers average of the two bands correspondent to the NH groups.

Although Hansen had attributed a fixed value of 5000 cal/mol to the OH energy, here, that energy was specifically determined for each system, using their experimental data. Meanwhile, as still can be observed in **Table A. 7**, The AARD% found between the two approaches to be inferior to 3%.

Correlation HSPs-γL: Example of calculation

Surface tension is indeed one of the most important physical properties correlated with C.E.D or HSPs. As an example, we can consider system **B2**. Using the equation proposed by Skaarup and Hansen (SkH), with a $k' = 0.80$, and the δ_D and δ_P calculated previously by the equations of Yamamoto-Abbott-Hansen (YAH) and Beerbower (Bb), respectively, we have:

$$\delta_{H\,(\mathbf{B2})} = \sqrt{\frac{17\gamma_L V_m^{-1/3} - \delta_D^2 - k\delta_P^2}{k}} = \sqrt{\frac{17 * 54.89 * (66.21^{-0.333}) - 8.67^2 - 0.8 * 7.07^2}{0.80}}$$

$$= \mathbf{12.06}\ (\mathrm{cal.cm^{-3}})^{\frac{1}{2}} \times 2.0455 = \mathbf{24.67}\ \mathrm{MPa}^{1/2}$$

This result, as it can be seen, is very similar to those from the EM, in particular HK and HKF. The two models of SkH (**eqn. 23**, when *k´*= 0.265) and **eqn. 25** are recommended by their authors as the most appropriate to be used in alcohols-based compounds, so, at first instance, these would be expected to be the most suitable for the studied systems. The results obtained using these two models can be found in **Table A. 9** and despite the fact that the results are very different from the ones in **Table 11**, up to this moment, no conclusion about the best one can be drawn. Taking into account the relatively good results obtained so far for the three empirical models StP, HK, and HKF, what can be pointed out is the fact that, according to the models of Skaarup and Hansen, NADES seem to be classified as homologous series, since the results are very similar.

Table A. 9: Determination of the δ_H parameter using SEM based on the HSPs-γ_L correlation.

NADES	**Vm (cm^3/mol)**	**γ (mN/m)**	**(in cal/cm^3)$^{1/2}$**		**δ_H (in MPa$^{1/2}$)**					**(in cal/cm^3)$^{1/2}$**		**δ_H (in MPa$^{1/2}$)**				
			δ_D (YAH)	**δ_P (Bb)**	**SkH (eqn. 23)***		**Bb´* (eqn. 24)**	**Bb´´ (eqn. 25)**	**HB´ (eqn. 26)**	**δ_D (KoS)**	**δ_P (KoS)**	**SkH (eqn. 23)***		**Bb´* (eqn. 24)**	**Bb´´ (eqn. 25)**	**HB´ (eqn. 26)**
					k´ = 0.80	**k´= 0.265**						**k´ = 0.80**	**k´= 0.265**			
B1	54.13	41.04	8.55	N/D	N/D	N/D	N/D	N/D	N/D	8.53	N/D	N/D	N/D	N/D	N/D	N/D
B2	66.21	54.87	8.67	7.02	24.67	47.47	23.38	67.02	21.42	8.63	12.91	11.01	42.12	7.75	-	-
B3	43.03	N/D	8.36	8.75	N/D	N/D	N/D	N/D	N/D	8.39	17.61	N/D	N/D	N/D	N/D	N/D
B4	49.50	48.18	8.60	7.86	22.87	45.83	21.47	57.19	19.42	8.57	15.49	-	36.91	-	-	-
C1	78.71	N/D	8.53	N/D	N/D	N/D	N/D	N/D	N/D	8.52	N/D	N/D	N/D	N/D	N/D	N/D
C2	90.61	N/D	8.63	N/D	N/D	N/D	N/D	N/D	N/D	8.59	N/D	N/D	N/D	N/D	N/D	N/D
C3	72.27	N/D	8.86	N/D	N/D	N/D	N/D	N/D	N/D	8.78	N/D	N/D	N/D	N/D	N/D	N/D
F1	48.71	48.44	8.69	4.95	26.13	47.63	24.88	76.77	23.14	8.65	9.69	19.93	44.63	18.29	33.40	15.81
G1	43.93	45.24	8.62	8.77	20.76	44.17	19.17	43.59	16.96	8.59	17.79	-	30.94	-	-	-
G2	82.08	N/D	8.75	4.50	N/D	N/D	N/D	N/D	N/D	8.69	7.83	N/D	N/D	N/D	N/D	N/D
G3	61.41	N/D	8.70	2.05	N/D	N/D	N/D	N/D	N/D	8.65	3.48	N/D	N/D	N/D	N/D	N/D
G4	82.16	N/D	8.76	5.31	N/D	N/D	N/D	N/D	N/D	8.70	9.34	N/D	N/D	N/D	N/D	N/D
G5	61.56	N/D	8.70	4.39	N/D	N/D	N/D	N/D	N/D	8.65	8.14	N/D	N/D	N/D	N/D	N/D
G6	52.60	46.15	8.63	4.95	24.58	45.07	23.22	71.07	21.55	8.60	9.46	18.32	42.06	16.47	23.74	14.01
G7	53.36	49.34	8.54	3.05	27.32	48.29	26.18	83.56	24.52	8.53	5.60	25.59	47.36	24.39	73.89	22.59
P1	32.19	34.75	8.14	7.32	20.03	40.80	18.53	47.33	16.65	8.22	15.41	-	29.58	-	-	-
T1	43.25	N/D	8.43	5.47	N/D	N/D	N/D	N/D	N/D	8.44	10.88	N/D	N/D	N/D	N/D	N/D
T2	43.30	47.41	8.48	5.11	26.77	48.82	25.67	79.18	23.86	8.48	10.12	19.93	45.44	18.42	30.80	15.82
M1	116.14	30.37	8.14	0.92	14.30	24.98	11.48	36.95	10.77	8.22	1.49	13.85	24.46	10.84	34.35	10.13

NADES	Vm (cm^3/mol)	γ (mN/m)	(in cal/cm^3)$^{1/2}$		δ_H (in MPa$^{1/2}$)					(in cal/cm^3)$^{1/2}$		δ_H (in MPa$^{1/2}$)				
			δ_D (YAH)	δ_P (Bb)	SkH (eqn. 23)*		Bb´* (eqn. 24)	Bb´´ (eqn. 25)	HB´ (eqn. 26)	δ_D (KoS)	δ_P (KoS)	SkH (eqn. 23)*		Bb´* (eqn. 24)	Bb´´ (eqn. 25)	HB´ (eqn. 26)
					k´ = 0.80	k´= 0.265						k´ = 0.80	k´= 0.265			
M2	171.11	32.78	8.46	1.16	12.07	21.23	8.02	25.37	7.50	8.47	1.83	11.69	21.00	7.45	22.31	6.88
M3	183.07	31.77	8.26	1.03	11.73	20.59	7.76	24.63	7.26	8.31	1.66	11.22	20.08	6.88	20.70	6.37
M4	180.46	31.30	8.29	1.13	11.33	19.96	7.08	22.25	6.61	8.34	1.77	10.81	19.47	6.12	17.72	5.62
M5	177.91	30.82	8.34	1.33	10.83	19.21	6.14	18.76	5.70	8.37	2.02	10.23	18.72	4.94	12.32	4.42
M6	178.27	32.02	8.33	0.98	11.82	20.74	7.81	24.86	7.31	8.37	1.62	11.39	20.35	7.09	21.49	6.57
M7	188.09	N/D	8.34	1.04	N/D	N/D	N/D	N/D	N/D	8.37	1.68	N/D	N/D	N/D	N/D	N/D
M8	191.43	33.09	8.31	0.81	12.14	21.22	8.32	26.69	7.80	8.35	1.44	11.75	20.83	7.68	23.82	7.15
M9	183.63	32.75	8.37	0.76	12.03	21.01	8.08	25.93	7.58	8.39	1.41	11.68	20.70	7.51	23.31	6.99
M10	184.57	31.83	8.35	0.10	11.53	20.03	7.30	23.68	6.86	8.38	1.07	11.20	19.72	6.73	21.15	6.28
M11	182.47	33.12	8.35	0.62	12.38	21.59	8.63	27.84	8.10	8.38	1.30	12.06	21.29	8.12	25.50	7.57
M12	180.19	32.30	8.37	0.82	11.85	20.73	7.81	24.99	7.32	8.39	1.47	11.49	20.41	7.20	22.15	6.69
M13	191.44	33.49	8.27	0.74	12.56	21.92	8.99	28.93	8.43	8.32	1.38	12.16	21.50	8.35	26.18	7.79
M14	185.74	33.51	8.32	1.18	12.47	21.94	8.81	27.98	8.24	8.35	1.83	12.01	21.52	8.09	24.56	7.49
M15	139.14	31.54	8.30	2.18	12.72	23.00	9.23	27.83	8.54	8.34	3.29	11.53	22.19	7.42	17.39	6.59
M16	191.20	31.98	8.48	0.88	10.74	18.83	5.71	18.00	5.33	8.48	1.53	10.42	18.64	5.10	14.62	4.67
M17	183.86	32.62	8.36	1.29	11.75	20.76	7.67	24.01	7.15	8.39	1.96	11.25	20.36	6.83	19.81	6.27
M18	164.51	33.21	8.78	1.35	11.35	20.11	6.36	19.48	5.91	8.71	2.13	11.12	20.29	6.08	16.52	5.52
M19	167.46	32.30	8.65	1.08	11.20	19.72	6.30	19.70	5.87	8.61	1.78	10.98	19.77	5.98	17.18	5.48
M20	170.19	31.57	8.55	1.59	10.68	19.12	5.48	15.84	5.03	8.54	2.41	10.09	18.88	4.27	6.61	3.65
M21	172.17	31.38	8.48	1.15	11.00	19.40	6.21	19.30	5.79	8.48	1.83	10.60	19.18	5.48	15.18	4.99

* Both, SkH (when k = 0.265) and Bb´´, are theoretical models proposed for being applied strictly for alcohol-based compounds.

Table A. 10: Parameters used in the evaluation 1D and 2D of ibuprofen solubility of the listed solvents.

ID	δ_D	δ_P	δ_H	δ_V	$Ra_{(V)}$	δ_T	$\Delta\bar{\delta}$	$\Delta\delta_T$
Ibu	17.62	2.47	7.64	17.79		19.36		
				Organic solvents				
Water	15.50	16.00	42.30	22.28	69.90	47.81	37.27	28.44
MeOH	15.10	12.30	22.30	19.48	29.51	29.61	17.83	10.24
EtOH	15.80	8.80	19.40	18.09	23.53	26.52	13.48	7.16
1-prOH	16.00	6.80	17.40	17.39	19.54	24.60	10.80	5.23
2-prOH	16.00	6.80	17.40	17.39	19.54	24.60	10.80	5.23
EG	17.00	11.00	26.2	20.25	37.44	33.11	20.44	13.75
Gly	17.40	12.10	29.3	21.19	43.85	36.16	23.71	16.80
CHx	16.80	0.00	0.20	16.80	15.01	16.80	7.88	2.56
Hx	14.90	0.00	0.00	14.90	16.34	14.90	8.48	4.46

ID	δ_D	δ_P	δ_H	δ_V	$Ra_{(V)}$	δ_T	$\Delta\bar{\delta}$	$\Delta\delta_T$
				Group I				
B2	17.73	26.41	21.42	31.81	39.31	38.35	27.62	18.98
B4	17.59	31.68	19.42	36.24	43.78	41.12	31.50	21.75
F1	17.78	19.82	23.14	26.63	35.67	35.27	23.26	15.91
G1	17.63	36.39	16.96	40.43	48.96	43.84	35.17	24.48
G6	17.66	19.34	21.55	26.19	32.50	33.92	21.87	14.55
G7	17.47	11.46	24.52	20.90	34.33	32.22	19.13	12.85
P1	16.65	31.53	16.65	35.65	40.01	39.35	30.44	19.99
T2	17.35	20.70	23.86	27.00	37.31	36.04	24.40	16.67
M1	16.65	3.05	10.77	16.93	6.49	20.06	3.33	0.70
M2	17.31	3.75	7.50	17.72	0.32	19.24	1.32	0.13
M3	16.89	3.40	7.26	17.23	1.37	18.69	1.25	0.67
M4	16.96	3.63	6.61	17.35	2.25	18.56	1.68	0.80
M5	17.05	4.13	5.70	17.54	3.91	18.45	2.62	0.92
M6	17.04	3.32	7.31	17.36	1.09	18.84	1.08	0.53
M8	17.00	2.95	7.80	17.25	1.12	18.94	0.80	0.43
M9	17.11	2.88	7.58	17.35	0.89	18.94	0.65	0.43
M10	17.09	2.19	6.86	17.23	1.93	18.54	0.98	0.82
M11	17.09	2.66	8.10	17.29	1.36	19.10	0.73	0.26
M12	17.11	3.00	7.32	17.38	1.06	18.85	0.80	0.51

ID	δ_D	δ_P	δ_H	δ_V	$Ra_{(V)}$	δ_T	$\Delta\bar{\delta}$	$\Delta\delta_T$
M13	16.91	2.82	8.43	17.15	2.05	19.11	1.12	0.26
M14	17.01	3.73	8.24	17.42	1.42	19.27	1.53	0.09
M15	16.97	6.73	8.54	18.26	2.03	20.16	4.40	0.80
M16	17.34	3.12	5.33	17.62	4.62	18.41	2.41	0.95
M17	17.11	4.01	7.15	17.57	1.07	18.97	1.69	0.39
M18	17.96	4.37	5.91	18.48	3.73	19.41	2.59	0.04
M19	17.70	3.64	5.87	18.07	3.58	19.00	2.12	0.37
M20	17.50	4.92	5.03	18.18	5.28	18.86	3.59	0.50
M21	17.34	3.74	5.79	17.74	3.71	18.66	2.27	0.70

ID	δ_D	δ_P	δ_H	δ_V	$Ra_{(V)}$	δ_T	$\Delta\bar{\delta}$	$\Delta\delta_T$
Group II								
B2	17.15	14.36	23.38	22.37	32.77	32.35	19.73	12.99
B4	17.45	16.07	21.47	23.72	30.09	31.99	19.40	12.63
F1	17.56	10.12	24.88	20.27	34.84	32.10	18.87	12.73
G1	17.77	17.94	19.17	25.25	27.47	31.70	19.29	12.34
G6	17.44	10.12	23.22	20.16	31.52	30.75	17.36	11.39
G7	16.80	6.25	26.18	17.93	37.09	31.73	18.94	12.37
P1	18.11	14.98	18.53	23.50	24.59	29.93	16.59	10.57
T2	14.68	10.44	25.67	18.02	36.05	31.36	19.93	12.00
M1	17.32	1.89	11.48	17.42	7.71	20.86	3.89	1.50
M2	16.99	2.36	8.02	17.15	1.49	18.94	0.75	0.43
M3	17.05	2.11	7.76	17.18	1.25	18.85	0.69	0.52
M4	17.11	2.31	7.08	17.27	1.54	18.66	0.77	0.70
M5	17.11	2.72	6.14	17.32	3.14	18.38	1.60	0.98
M6	17.12	2.01	7.81	17.24	1.16	18.93	0.70	0.44
M8	17.16	1.65	8.32	17.24	1.75	19.15	1.16	0.22
M9	17.14	1.55	8.08	17.21	1.45	19.02	1.12	0.35
M10	17.14	0.20	7.30	17.15	1.46	18.63	2.34	0.73
M11	17.16	1.28	8.63	17.21	2.30	19.26	1.62	0.11
M12	17.01	1.69	7.81	17.09	1.44	18.79	1.01	0.57
M13	17.09	1.51	8.99	17.15	2.98	19.36	1.74	0.00
M14	17.06	2.41	8.81	17.23	2.61	19.35	1.30	0.01
M15	17.22	4.46	9.23	17.79	3.17	20.04	2.58	0.68
M16	17.16	1.79	5.71	17.25	4.01	18.17	2.10	1.19
M17	17.82	2.63	7.67	18.01	0.44	19.57	0.26	0.21
M18	17.61	2.77	6.36	17.83	2.55	18.93	1.31	0.43
M19	17.46	2.22	6.30	17.60	2.71	18.69	1.37	0.67

ID	δ_D	δ_P	δ_H	δ_V	$Ra_{(V)}$	δ_T	$\Delta\bar{\delta}$	$\Delta\delta_T$
M20	17.34	3.26	5.48	17.64	4.33	18.47	2.32	0.89
M21	16.80	2.36	6.21	16.97	3.29	18.07	1.65	1.29

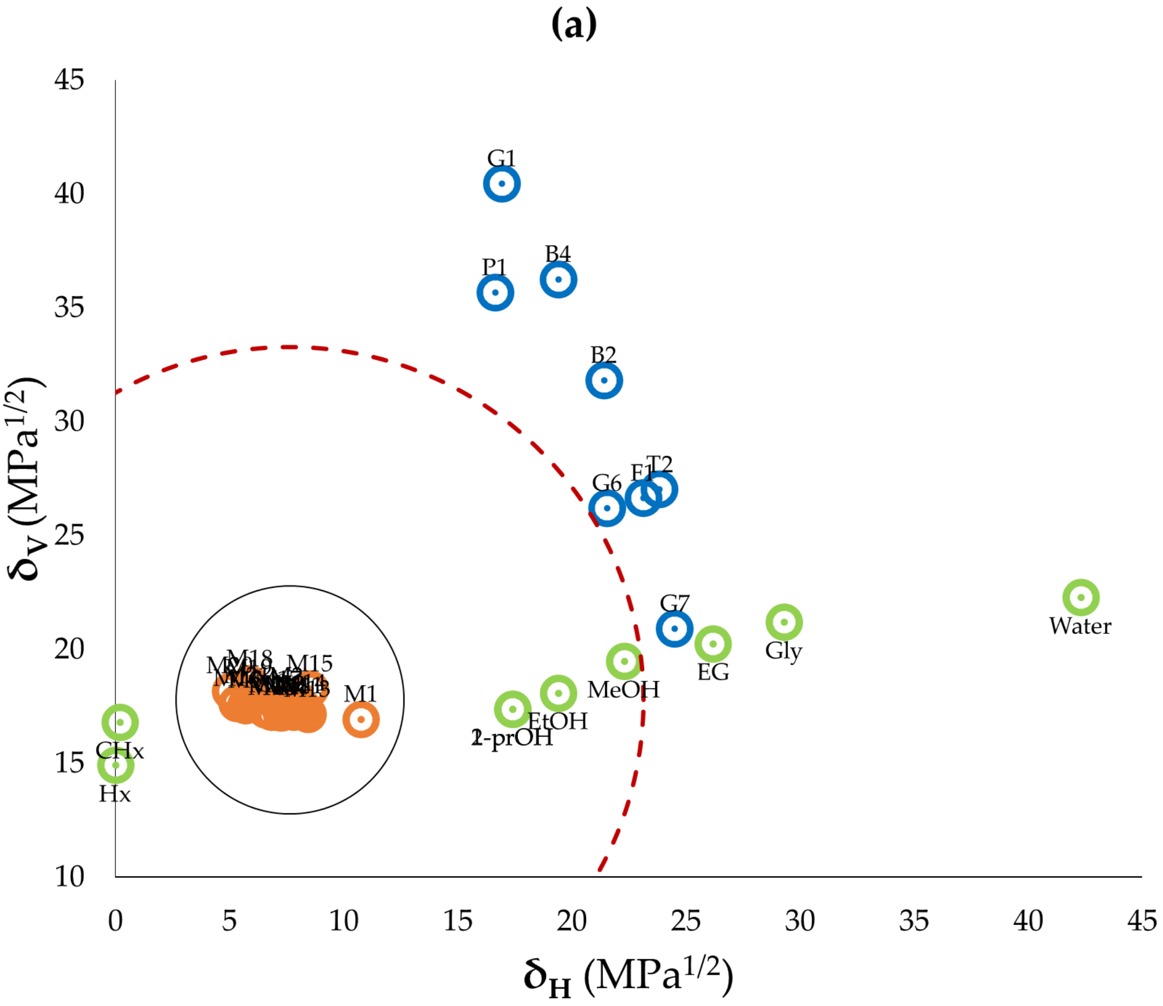


Figure A. 1: Bagley's 2D solubility charts (δ_V Vs δ_H) of organic solvents (green), hydrophilic (blue) and hydrophobic NADES (orange), predicted using the semi-empirical models (group I **(a)** and group II (b)) and the empirical model, StP (c), HK (d), HKF (e) and Ymt (f).

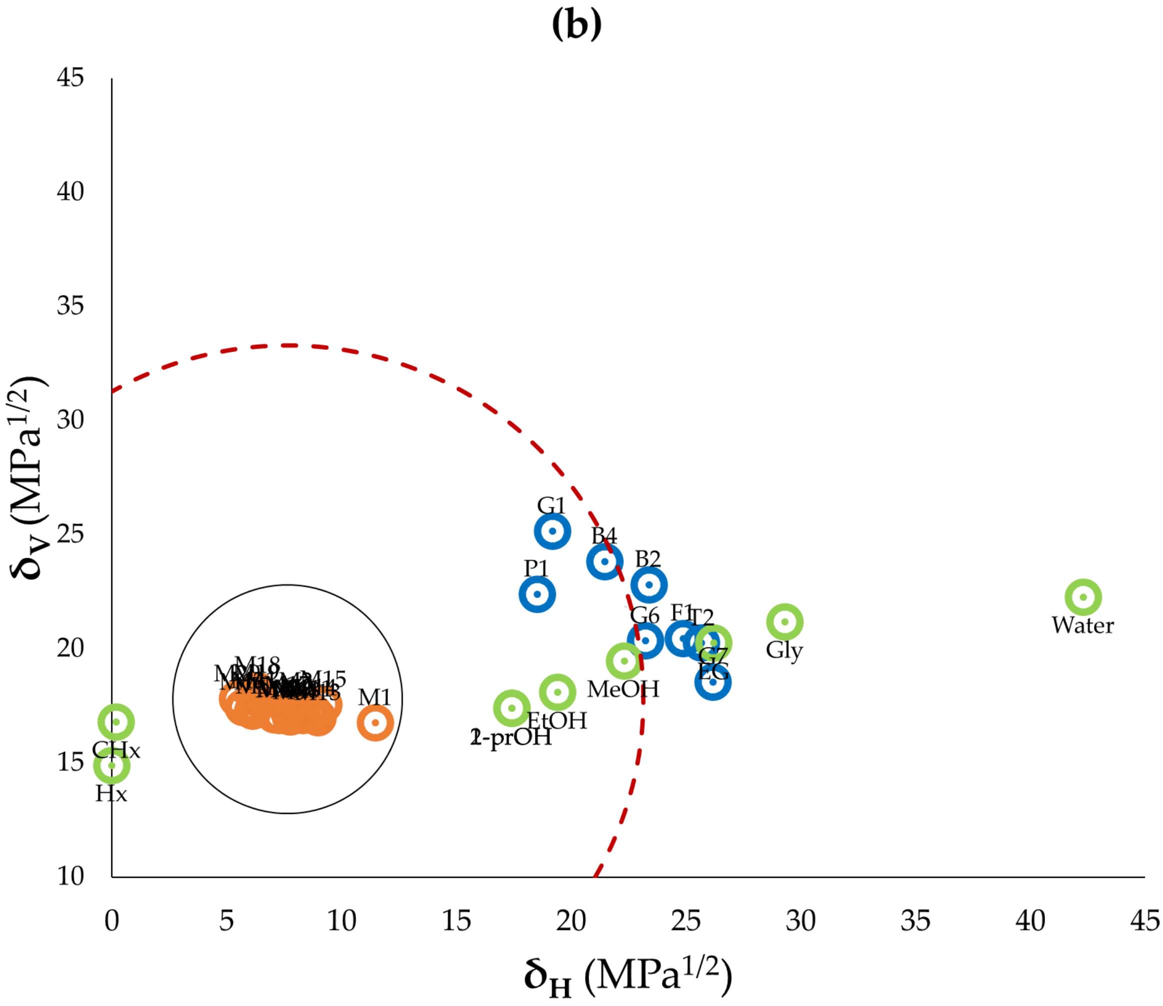


Figure A. 2: Bagley's 2D solubility charts (δ_V Vs δ_H) of organic solvents (green), hydrophilic (blue) and hydrophobic NADES (orange), predicted using the semi-empirical models (group I (a) and group II **(b)**) and the empirical model, StP (c), HK (d), HKF (e) and Ymt (f).

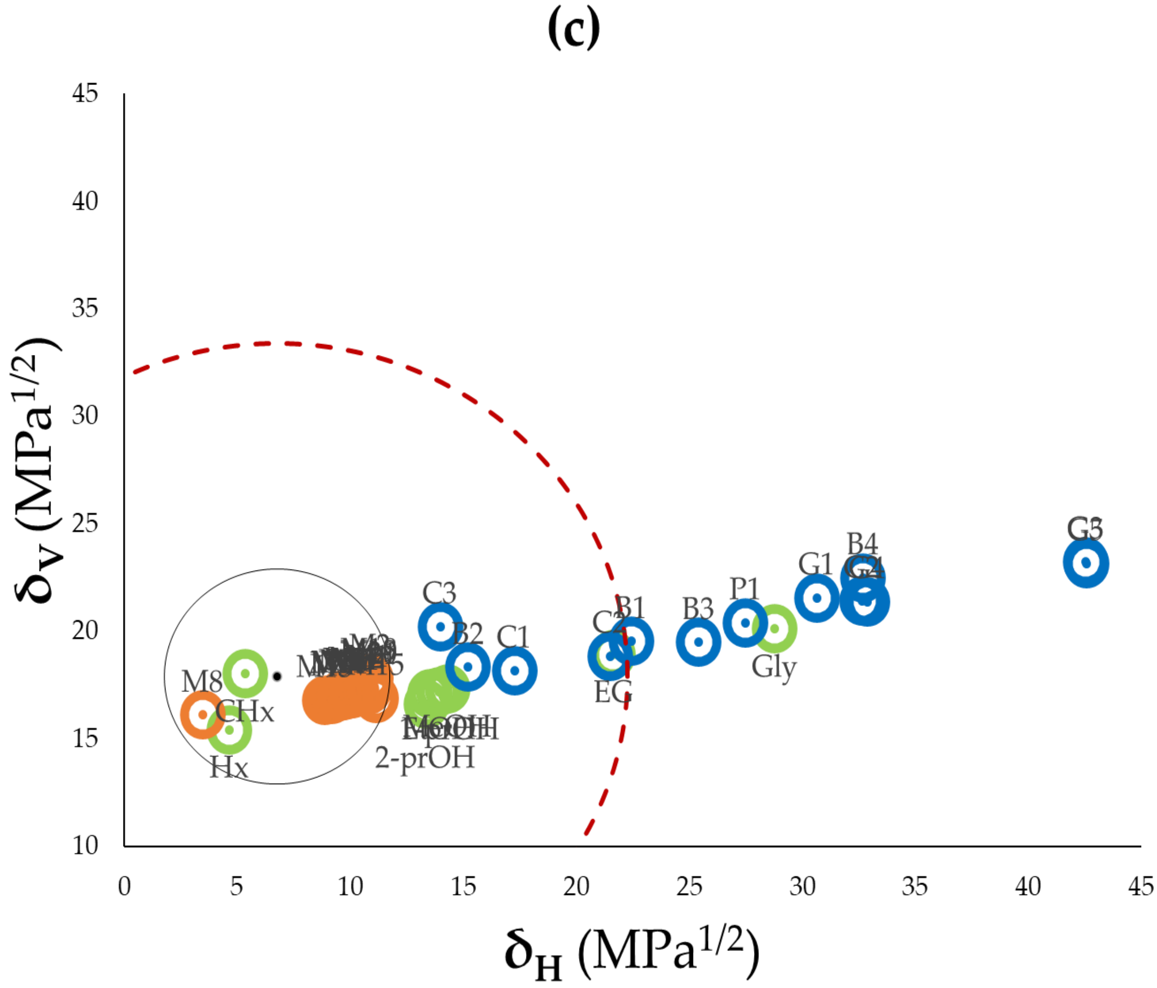


Figure A. 3: Bagley's 2D solubility charts (δv Vs δH) of organic solvents (green), hydrophilic (blue) and hydrophobic NADES (orange), predicted using the semi-empirical models (group I (a) and group II (b)) and the empirical model, StP **(c)**, HK (d), HKF (e) and Ymt (f).

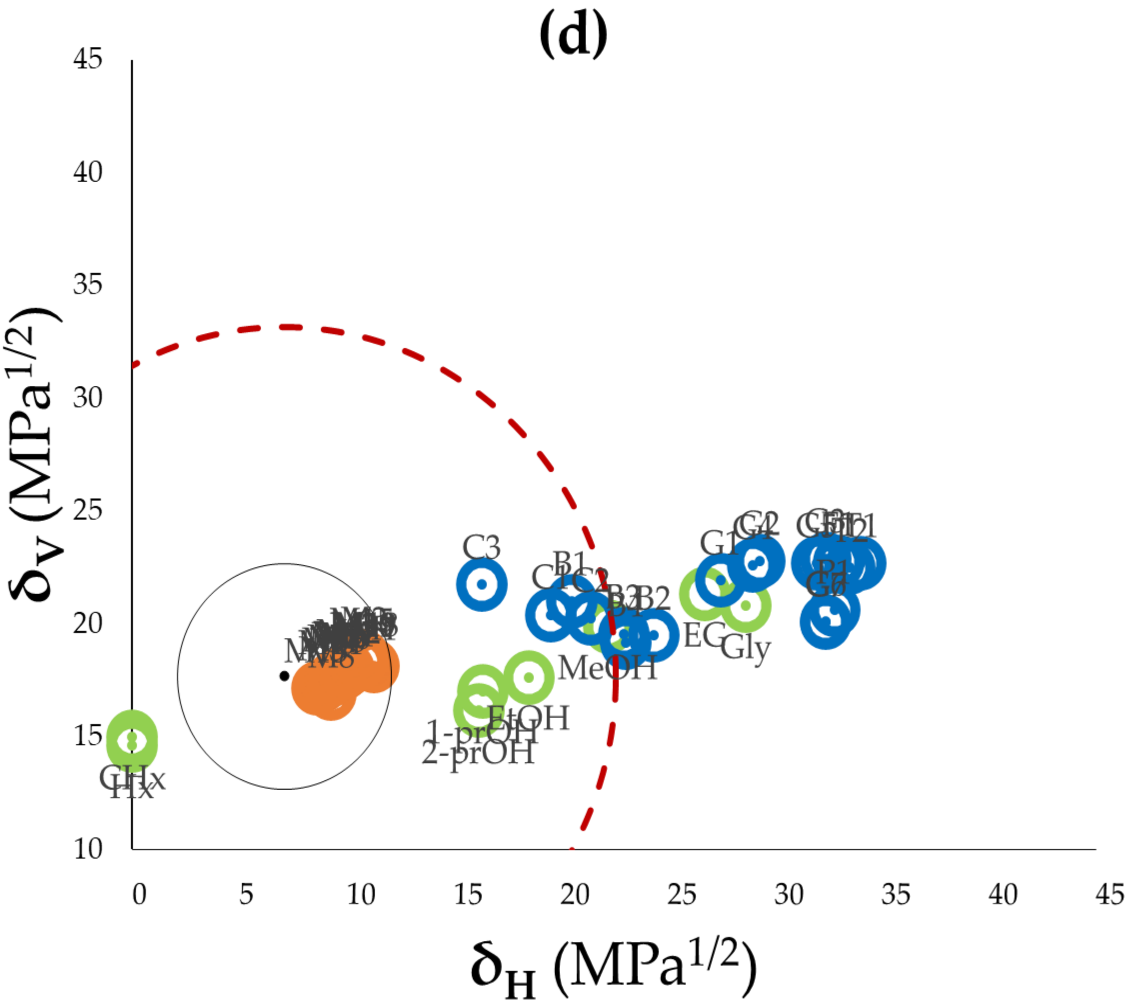


Figure A. 4: Bagley's 2D solubility charts (δ_V Vs δ_H) of organic solvents (green), hydrophilic (blue) and hydrophobic NADES (orange), predicted using the semi-empirical models (group I (a) and group II (b)) and the empirical model, StP (c), HK **(d)**, HKF (e) and Ymt (f).

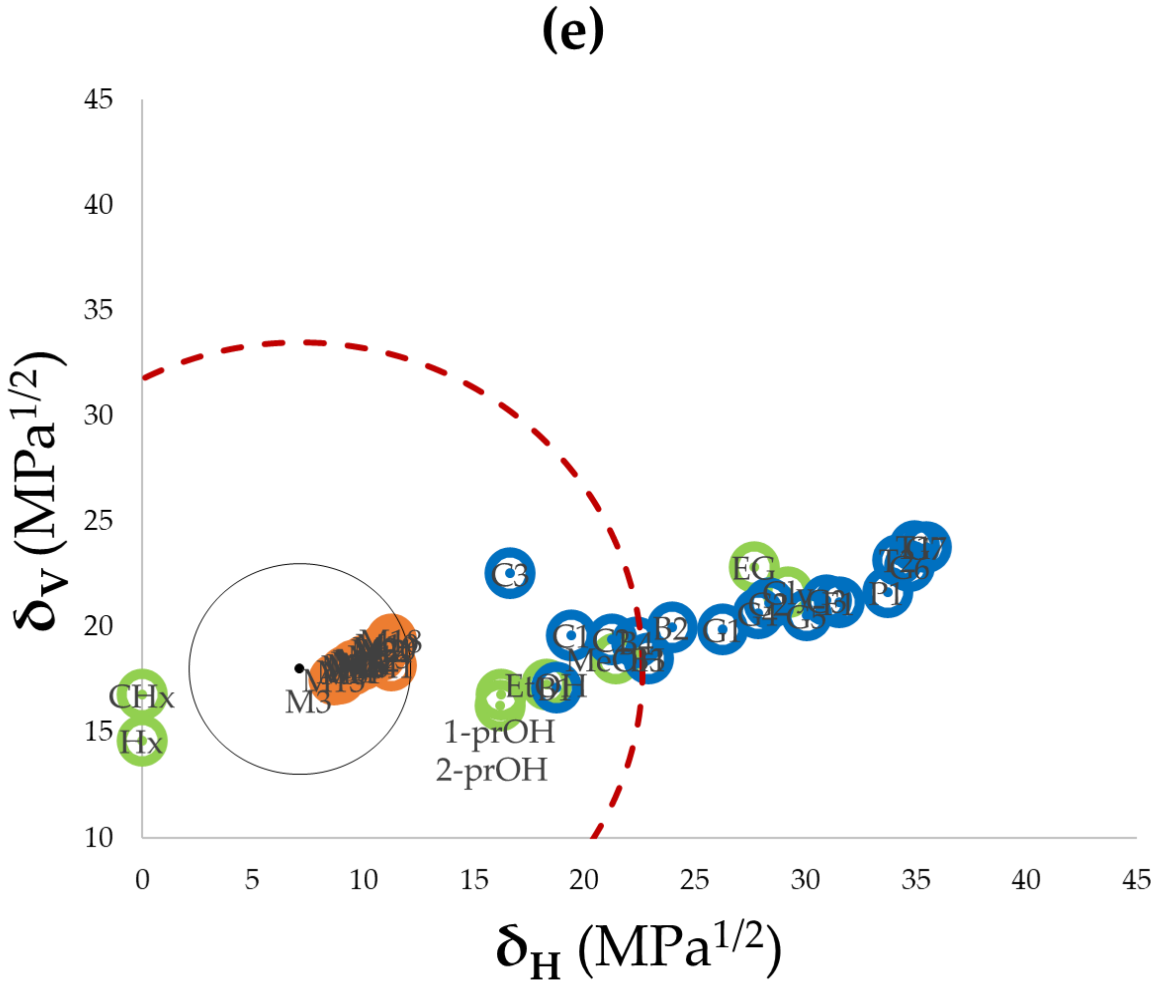


Figure A. 5: Bagley's 2D solubility charts (δV Vs δH) of organic solvents (green), hydrophilic (blue) and hydrophobic NADES (orange), predicted using the semi-empirical models (group I (a) and group II (b)) and the empirical model, StP (c), HK (d), HKF **(e)** and Ymt (f).

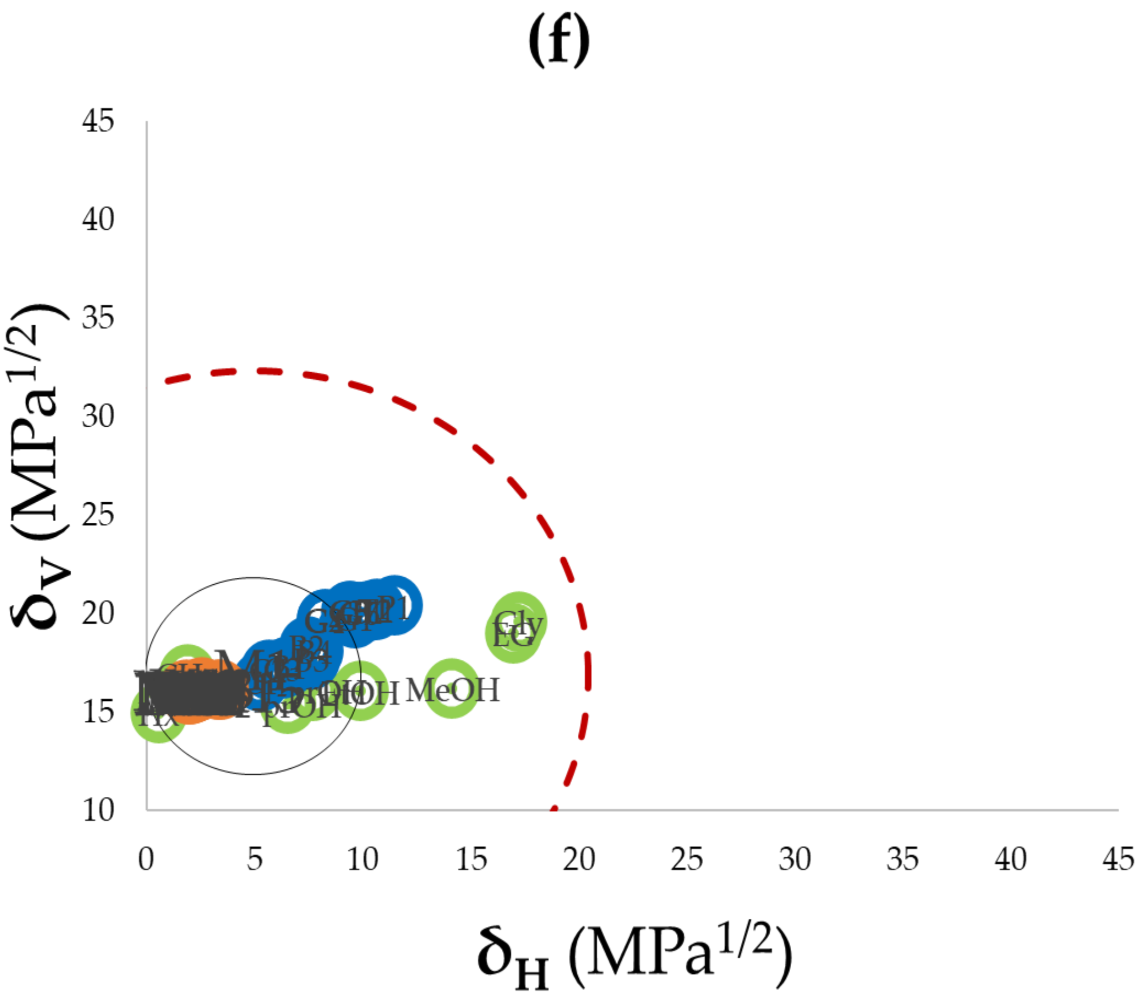


Figure A. 6: Bagley's 2D solubility charts (δ_V Vs δ_H) of organic solvents (green), hydrophilic (blue) and hydrophobic NADES (orange), predicted using the semi-empirical models (group I (a) and group II (b)) and the empirical model, StP (c), HK (d), HKF (e) and Ymt **(f)**.

A. 2 Empirical models (EM)

Table A. 11: Stefanis and Panayiotou group contributions for the partial HSPs [66].

Group	δ_d	δ_p	δ_{hb}	Group	δ_d	δ_p	δ_{hb}
$-CH_3$	-123.01	-1.6444	-0.7458	$CONH_2$	-1.22	5.9361	5.3646
$-CH_2$	1.82	-0.3141	-0.3877	$CON(CH_3)_2$	95.97	5.5309	3.2455
$-CH<$	82.94	0.6051	-0.2064	CH_2SH	214.84	-0.994	4.5321
$>C<$	182.13	2.0249	-0.0113	CH_3S	0	0.2451	-1.2669
$CH_2{=}CH-$	-126.15	-2.017	-1.1783	CH_2S	168.57	0.573	-0.0838
$-CH{=}CH-$	28.65	-0.5037	-0.1253	I	197.67	0.106	0.3321
$CH_2{=}C<$	-31.62	-0.9052	-0.7191	Br	109.79	0.5207	-0.9087
$-CH{=}C<$	62.48	-1.1018	-1.7171	CH_2Cl	47.17	0.5013	-0.4498
$>C{=}C<$	50.1	0.9957	-1.9773	CHCl	73.01	2.6796	-1.3563
$CH_2{=}C{=}CH-$	-161.71	0	-0.7545	CCl	385.39	1.8196	0.1473
$CH{\equiv}C-$	45.86	-1.5147	1.2582	$CHCl_2$	197.67	1.6255	-3.0669
$C{\equiv}C$	9.56	-0.9552	-1.0176	CCl_2	72.6	0.1035	-1.322
ACH	29.87	-0.5771	-0.3554	CCl_3	0	1.106	-2.5679
AC	98.84	0.7661	-0.1553	ACCl	141.54	-0.0941	-0.7512
$ACCH_3$	27.67	-0.6212	-1.1409	ACF	27.74	0.1293	-0.6613
$ACCH_2-$	89.07	0.8019	-0.2298	$Cl-(C{=}C)$	45.32	2.2673	-0.5258
CH_3CO	-29.41	2.1567	-1.1683	CF_3	-13.79	-2.1381	-1.2997
CH_2CO	114.74	3.6103	-0.3929	CH_2NO_2	0	6.6451	-1.0669
CHO (aldehyde)	-31.35	3.3159	0.2062	$CHNO_2$	0	7.7753	-2.1087
COOH	-38.16	0.7153	3.8422	$ACNO_2$	219.22	4.464	-0.7302
CH_3COO	-53.86	-0.6075	1.7051	CH_2CN	-29.09	6.3586	-0.7297
CH_2COO	89.11	3.4942	1.3893	CF_2	-103.83	0	0
HCOO	0	1.7056	2.3049	CF	20.32	0	0
COO	27.57	3.3401	1.1999	F (except as above)	-80.11	0	0
OH	-29.97	1.0587	7.3609	$CH_2{=}C{=}C<$	6.64	0	-1.7087
ACOH	58.52	1.052	6.9757	O (except as above)	18.09	3.5248	0.0883
CH_3O	-68.07	0.0089	0.2676	Cl (except as above)	76.35	1.7491	-0.2917
CH_2O	13.4	0.8132	-0.1196	$>C{=}N-$	-10.55	-0.1692	-5.382
CHO (ether)	111.46	1.6001	0.4873	$-CH{=}N-$	186.4	2.7015	0.5507
$C_2H_5O_2$	15.51	3.388	8.5893	NH (except as above)	0	-0.0746	2.0646
CH_2O (cyclic)	49.32	0.1227	0.1763	CN (except as above)	49.36	6.3705	-0.5239

Group	δ_d	δ_p	δ_{hb}	**Group**	δ_d	δ_p	δ_{hb}
CH_2NH_2	-49.96	-0.3449	2.728	**O=C=N–**	15.22	1.4695	4.1129
$CHNH_2$	18.53	-1.4337	0.5647	**SH (except as above)**	190.87	1.8229	4.9279
CH_3NH	0	0.506	5.7321	**S (except as above)**	201.91	8.5982	-0.4013
CH_2NH	96.18	0.2616	1.4053	**SO_2**	182.83	11.0254	-0.3602
CH_3N	170.59	1.0575	1.85	**>C=S**	-0.46	0.5216	3.0519
CH_2N	152.54	2.6766	1.5557	**>C=O (except as above)**	-127.16	0.7691	1.7033
$ACNH_2$	253.66	1.6493	4.4945	**N (except as above)**	267.06	2.2212	1.3655

Table A. 12: Hoftyzer-Van Krevelen [64] and Fedors [65] group contributions for the partial HSPs and volume molar ($\Delta\upsilon_i$), respectively.

Structural group	F_{di}	F_{pi}^2	E_{hi}	$\Delta\upsilon_i$
$-CH_3$	420	0	0	33.5
$-CH_2-$	270	0	0	16.1
>CH-	80	0	0	-1
>C<	-70	0	0	-19.2
$=CH_2$	400	0	0	28.5
=CH-	200	0	0	13.5
=C<	70	0	0	-5.5
R-cyclohexane	1620	0	0	16
Benzene	1430	12100	0	71.4
Benzene (bi-sub)	1270	12100	0	52.4
-F	220	0	0	18
-Cl	450	302500	400	24
-Br	550	0	0	30
-CN	430	1210000	2500	24
-OH (alcohol)	210	250000	20000	10
-O-	100	160000	3000	3.8
-COH	470	640000	4500	22.3
>C=O	290	592900	2000	10.8
-COOH	530	176400	10000	28.5
-COO-	390	240100	7000	18
-COOH	530	0	0	28.5
$-NH_2$	280	0	8400	19.2
>NH-	160	44100	3100	4.5
>N<	0	0	0	-30.8
-N<	20	640000	5000	-9
$-NO_2$	500	1144900	1500	24
-S-	440	0	0	12
$=PO_4-$	740	3572100	13000	28
ring (>=5 a)	190	0	0	16
ring (4/3 a)	190	0	0	18
1 plane o symmetry	0	x0.5	0	
2 planes of symmetry	0	x0.25	0	
>2 planes of symmetry	0	0	0	

Table A. 13: Yamamoto (Ymt) group contributions for the partial HSPs [48].

Label	dD	dDfg	dP	dH	CosVol	Mw
CH_3	12.9	7.5	0.7	0.1	28.85	15.034
CH_2	16.4	14.3	1.5	0.9	22.05	14.026
CH_2_R	17	13.7	1.7	1.9	21.65	14.026
CH_2=	11	0	3.2	4.2	26.5	14.026
CH	21.2	21.6	0.1	0	14.67	13.018
CH_R	19.1	18	0	0	14.57	13.018
CH=	19	16.8	0.1	0.1	18.26	13.018
CH=_R	17.3	14	2.3	5.3	17.95	13.018
CH=_reso	18.3	14.9	0.1	4.8	17.84	13.018
≡CH	14.2	9.2	3.6	4.1	24.5	13.018
C	33.3	37.2	0.1	5.3	5.48	12.01
C_R	31.7	32.5	0.1	0	6.58	12.01
C=	26	26.6	0	0	10.42	12.01
C=_R	25.4	25.3	0.1	4.7	10.64	12.01
C=_reso	24.5	24	1	0.1	10.12	12.01
C=_rrr	25.3	24.1	0.1	1.1	10.92	12.01
≡C	19.6	16.7	7.7	6.6	14.87	12.01
OH	18.4	11.3	16.6	36.6	18.05	17.008
2_OH	18.6	12.6	15	32.2	18.29	17.008
3_OH	19.8	15.7	12.4	25.3	18.58	17.008
OH@Ar	17.3	10.7	13.5	28.8	18.84	17.008
O	17.8	12.1	12.2	10.9	11.97	16
O_R	18	11.7	13.1	12.4	12.06	16
O@Ar	22	18	16.1	16.7	11.3	16
C=O	20.8	17.4	14	9.6	25.69	28.01
C=O_R	22.4	18.9	15.1	8.9	26.16	28.01
C=O@Ar	23.3	19.9	16.8	7.7	25.54	28.01
HCO	17.1	12.4	14.5	10.4	34.57	29.018
CHO@Ar	18.2	14	18.4	12.4	33.72	29.018
COOH	17.9	13.2	11.8	22.1	44.37	45.018
COOH@Ar	19.4	15.1	11.4	19.4	43.99	45.018
COO	19	15.2	8.1	10.8	37.02	44.01
COO_R	19.3	14.2	25.9	11.6	38.47	44.01
COO@Ar	17.6	14.3	13.6	6.3	37.69	44.01
NH_2	17.7	12.1	10.2	17.1	22.95	16.026
NH_2@Ar	20.6	16.2	13.7	24.2	22.3	16.026
NH	20.7	17.8	9.7	14.9	16.53	15.018
NH_R	19	15.5	14.1	18.3	16.41	15.018
NH@Ar	30.7	28.7	16.6	23.6	15.08	15.018

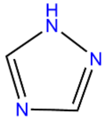
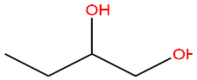
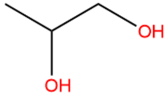
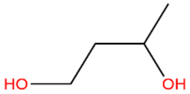
Label	dD	dDfg	dP	dH	CosVol	Mw
N	25.2	24.7	9.3	11.9	10.27	14.01
N_R	25	22.2	7.6	19.5	9.26	14.01
N@Ar	30.3	31.3	0	16.4	12.07	14.01
C≡N	17	12.5	21.8	9.6	34.12	26.02
C≡N@Ar	18.9	14.8	20.8	4.4	34	26.02
NO_2	17.9	12.4	20.6	6.9	40.26	46.01
NO_2@Ar	19.3	14	15.7	7.6	38.78	46.01
SH	19.1	15	9	9.7	36.4	33.078
SH@Ar	22.6	19	3.1	9.1	37.17	33.078
S	23.4	20.6	7	6.9	28.33	32.07
S_R	23.1	19.2	11.4	11.6	28.15	32.07
S@Ar	27.2	24.9	9.7	0	28.2	32.07
S=O	23.8	20.5	21	9.4	38.82	48.07
NHCO	21.3	17.2	23.1	17.5	42.13	43.028
NHCO_R	23.7	20.6	24	13.1	42.67	43.028
NCO	24.4	21.8	22.3	13.6	34.89	42.02
NCO_R	22.6	19.7	19.2	12.5	36.3	42.02
OCOO	17.6	13.5	10.9	9.6	47.85	60.01
OCOO_R	19.5	14.5	29	10.3	50.2	60.01
CF_3	10.7	0	1.8	0	52.73	69.01
CCl_3	17.9	13.2	0	0	94.36	118.36
CF_2	13.4	3.5	0	1.1	36.24	50.01
CCl_2	18.8	13.6	6.6	4.3	62.76	82.91
CF	15.9	7.8	0	0	21.27	31.01
CCl	20.6	18.2	6.7	3.9	36.98	47.46
F	0.1	0.1	0	4.6	14.84	19
Cl	16.4	8.7	0	0	27.46	35.45
Br	19.8	10.2	7.1	6.3	36.43	79.9
I	21	11.4	5.6	5.2	47.22	126.9
Si	10.7	11.3	0	0	29.98	28.09
P	17.7	13.7	6.5	0	30.3	30.97
Br	20.5	18.8	0.1	0	13.34	10.81

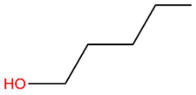
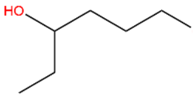
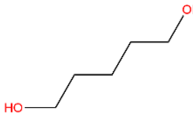
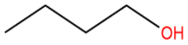
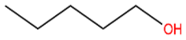
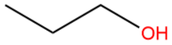
Table A. 14: Hoy group contributions for the partial HSPs [64], [68].

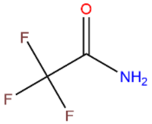
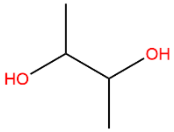
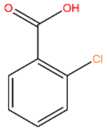
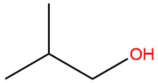
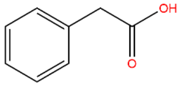
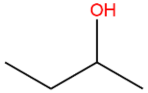
Groups	Ft,i	$F_{p,i}$	V_i	$\Delta_{T,i}^{*}$	$\Delta_{T,i}^{(P)}$
-CH_3	303.5	0	21.55	0.023	0.022
-CH_2-	269	0	15.55	0.02	0.02
>CH-	176	0	9.56	0.012	0.013
>C<	65.5	0	3.56	0	0.04
=CH_2	259	67	19.17	0.018	0.019
=CH-	249	59.5	13.18	0.018	0.0185
=C<	173	63	7.18	0	0.013
CH (ar)	241	62.5	13.42	0.011	0.018
>C< (ar)	201	65	7.42	0.011	0.015
-HC=O	600	532	23.3	0.048	0.045
>C=O	530	525	17.3	0.04	0.04
-COOH	565	415	26.1	0.039	0.039
-COO-	640	528	23.7	0.047	0.05
-CO-O-CO-	1160	1160	41	0.086	0.086
-CN	725	725	23.1	0.06	0.054
-N=C=O	736	8.5	25.9	0.054	0.054
HCON<	1020	725	35.8	0.062	0.055
-$CONH_2$	1200	900	34.3	0.071	0.084
-CONH-	1131	895	28.3	0.054	0.073
-OCONH	1265	890	34.8	0.078	0.094
-OH (H-bonded)	485	485	10.65	0.082	0.034
-OH (1º)	675	675	12.45	0.082	0.049
-OH (2º)	591	591	12.45	0.082	0.049
-OH (3º)	500	500	12.45	0.082	0.049
-OH (phenolic)	350	350	12.45	0.031	0.006
-O- (ether)	235	216	6.45	0.021	0.018
-O- (acetal)	236	102	6.45	0.018	0.018
-O- (epoxide)	361	156	6.45	0.027	0.027
-NH2	464	464	17	0.031	0.035
-NH-	368	368	11	0.031	0.027
>N-	125	125	12.6	0.014	0.009
-S-	428	428	18	0.015	0.032
-F	845	73.5	11.2	0.018	0.006
-Cl (1º)	419.5	307	19.5	0.017	0.031
-Cl (2º)	426	315	19.5	0.017	0.032
-Cl (ar)	330	81.5	19.5	0.017	0.025
<(Cl)2	705	572	39	0.034	0.052
-Br (aliph.)	528	123	25.3	0.01	0.039
-Br (ar)	422	100	25.3	0.01	0.031

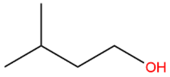
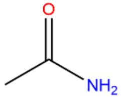
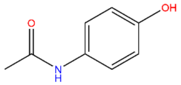
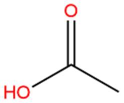
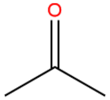
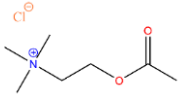
Groups	Ft,i	$F_{p,i}$	V_i	$\Delta_{T,i}{}^{*}$	$\Delta_{T,i}{}^{(P)}$
Base value (B)	277	0	0	0	0
ring non-aro (4member)	159	203	0	0	0.012
ring non-aro (5member)	43	85	0	0	0.003
ring non-aro (6member)	-48	61	0	0	-0.0035
ring non-aro (7member)	92	0	0	0	0.007
Conjugation isomerism	47.5	-19.8	0	0	0.0035
cis	-14.6	-14.6	0	0	-0.001
trans	-27.6	-27.6	0	0	-0.002
aromatic sub (ortho)	20.2	-13.3	0	0	0.0015
aromatic sub (meta)	13.5	-24.3	0	0	0.001
aromatic sub (para)	83	-34	0	0	0.006

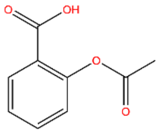
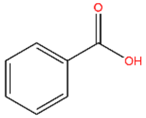
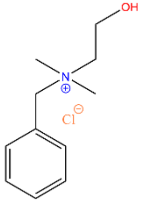
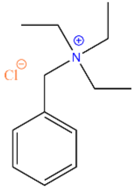
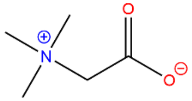
Table A. 15: Name, structure, molecular formula (MF), molecular weight (Mw, in g/mol), density (ρ, in g/cm³), molar volume (V_m, in cm³/mol) and HSPs estimated using the set of empirical models StP, HKF, Hoy and Ymt.

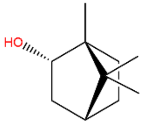
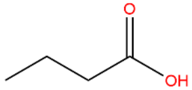
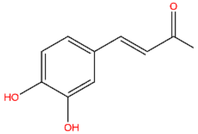
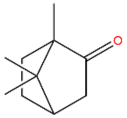
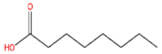
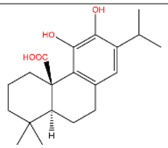
						HSPs ($MPa^{0.5}$)															
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V_m**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
1,2,4-triazole		$C_2H_3N_3$	69.07	1.349	51.20	N/A	N/A	N/A	N/A	19.5	12.9	10.9	**25.8**	10.4	19.7	15.1	**26.9**	25.9	3.4	12.3	**28.9**	**18.2**
1,2-butanediol		$C_4H_{10}O_2$	90.12	1.006	89.58	N/A	N/A	N/A	N/A	16.3	8.1	20.7	**27.5**	17.2	8.3	21.7	**29.0**	16.5	5.3	10.4	**20.2**	**27.3**
1,2-propanediol		$C_3H_8O_2$	76.09	1.036	73.45	N/A	N/A	N/A	N/A	16.3	8.4	21.1	**27.9**	17.3	10.3	24.1	**31.5**	16.5	6.2	12.5	**21.6**	**29.3**
1,3-butanediol		$C_4H_{10}O_2$	90.12	1.005	89.67	16.6	10.0	21.5	28.9	16.3	8.1	20.7	**27.5**	17.2	8.3	21.7	**29.0**	16.5	5.3	10.4	**20.2**	**27.3**

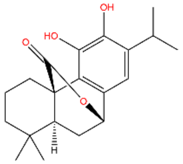
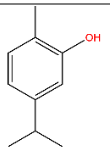
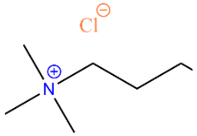
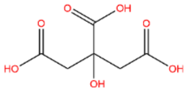
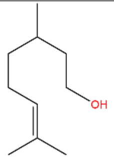
Name	Structure	MF	Mw^a	ρ^a	V_m	HSPs (MPa$^{0.5}$)																
						Hansen [38]				StP*				HKF*				Ymt*				Hoy*
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
1,4-butanediol		$C_4H_{10}O_2$	90.12	1.017	88.61	16.6	15.3	21.7	**31.3**	16.6	8.5	20.9	**28.0**	17.8	8.4	21.8	**29.3**	16.9	5.9	11.3	**21.1**	**29.0**
1,4-hexanediol		$C_6H_{14}O_2$	118.17	1.000	118.17	N/A	N/A	N/A	N/A	16.3	7.4	19.9	**26.8**	17.1	6.0	18.5	**25.9**	16.5	4.3	7.9	**18.8**	**24.9**
1,5-pentanediol		$C_5H_{12}O_2$	104.15	0.994	104.78	N/A	N/A	N/A	N/A	16.6	8.2	20.5	**27.6**	17.6	7.0	20.0	**27.5**	16.8	5.2	9.7	**20.1**	**27.3**
1-butanol		$C_4H_{10}O$	74.12	0.810	91.51	16.0	5.7	15.8	**23.2**	15.9	6.1	13.2	**21.5**	15.7	5.4	14.8	**22.2**	15.7	3.7	6.4	**17.3**	**23.0**
1-pentanol		$C_5H_{12}O$	88.15	0.811	108.69	15.9	4.5	13.9	**21.6**	15.9	5.8	12.8	**21.2**	15.8	4.6	13.6	**21.4**	15.8	3.3	5.5	**17.1**	**22.2**
1-propanol		C_3H_8O	60.10	0.804	74.75	16.0	6.8	17.4	**24.6**	15.8	6.4	13.5	**21.8**	15.5	6.6	16.3	**23.4**	15.5	4.2	7.7	**17.8**	**24.2**

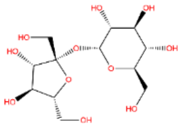
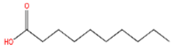
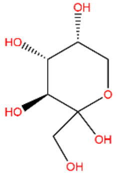
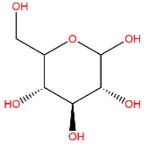
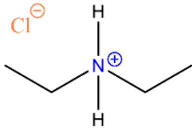
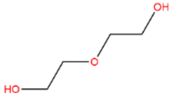
Name	**Structure**	**MF**	**Mw**^{a}	**ρ**^{a}	**V**$_m$	**HSPs (MPa**$^{0.5}$**)**																
						Hansen [38]				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_T**
2,2,2-trifluoracetamide		$C_2H_2F_3NO$	113.04	1.400	80.74	15.6	9.9	11.6	**21.8**	16.9	11.4	11.8	**23.5**	16.9	9.1	11.1	**22.2**	14.3	6.8	6.3	**17.0**	**54.3**
2,3-butanediol		$C_4H_{10}O_2$	90.12	1.002	89.94	N/A	N/A	N/A	N/A	15.9	7.7	20.5	**27.1**	16.7	8.3	21.7	**28.6**	16.1	4.8	9.6	**19.3**	**25.6**
2-chloro benzoic acid		$C_7H_5ClO_2$	156.57	1.544	101.40	N/A	N/A	N/A	N/A	19.1	6.7	9.2	**22.3**	21.4	6.7	10.0	**24.6**	18.1	4.2	8.9	**20.6**	**22.9**
2-Methyl-1-propanol		$C_4H_{10}O$	74.12	0.803	92.31	15.1	5.7	15.9	**22.7**	15.5	5.7	13.0	**21.0**	15.2	5.4	14.7	**21.9**	15.1	3.3	6.1	**16.6**	**22.3**
2-Phenylacetic acid		$C_8H_8O_2$	136.15	1.081	125.95	N/A	N/A	N/A	N/A	18.4	6.2	9.5	**21.6**	19.2	3.7	9.3	**21.7**	17.9	4.6	9.1	**20.6**	**20.1**
2-propanol		C_3H_8O	60.09	0.785	76.55	15.8	6.1	16.4	**23.6**	15.5	6.0	13.4	**21.3**	14.9	6.6	16.2	**23.0**	15.0	3.5	6.6	**16.7**	**22.0**

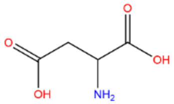
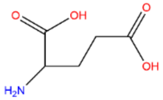
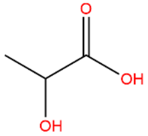
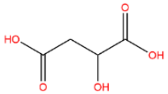
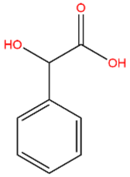
Name	Structure	MF	Mw[a]	ρ[a]	V_m	HSPs ($MPa^{0.5}$) Hansen [38]				StP*				HKF*				Ymt*				Hoy*
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
3-Methyl-1-butanol		$C_5H_{12}O$	88.15	0.809	108.96	15.8	5.2	13.3	**21.3**	15.5	5.4	12.6	**20.7**	15.4	4.6	13.6	**21.1**	15.3	3.0	5.2	**16.5**	**21.6**
Acetamide		C_2H_5NO	59.07	1.159	50.96	17.3	18.7	22.4	**33.9**	16.0	11.9	12.3	**23.5**	19.8	12.1	12.8	**26.5**	16.5	7.9	8.3	**20.1**	**28.0**
Acetaminophen		$C_8H_9NO_2$	151.16	1.293	116.90	17.8	10.5	13.9	**24.9**	17.2	6.2	16.1	**24.4**	21.1	8.5	15.0	**27.3**	18.4	7.9	9.0	**22.0**	**30.9**
Acetic acid		CH_3COOH	60.05	1.049	57.25	14.5	8.0	13.5	**21.4**	15.8	6.7	10.8	**20.2**	15.3	6.8	12.7	**21.0**	15.9	7.4	13.4	**22.1**	**18.9**
Acetone		C_3H_6O	58.08	0.791	73.42	15.5	10.4	7.0	**19.9**	15.8	8.1	5.8	**18.7**	14.5	9.9	5.1	**18.3**	15.0	4.8	3.0	**16.0**	**19.6**
Acetyl choline chloride		$C_7H_{16}ClNO_2$	181.66	1.124	161.69	N/A	N/A	N/A	N/A	18.4	9.2	10.2	**22.9**	15.5	5.5	7.9	**18.2**	14.7	2.3	2.4	**15.1**	**17.7**

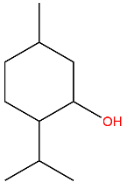
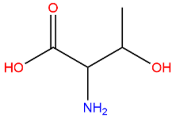
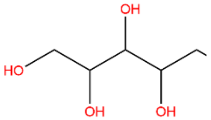
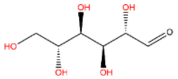
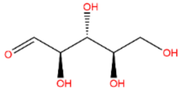
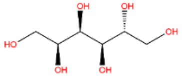
						HSPs ($MPa^{0.5}$)																
Name	**Structure**	**MF**	**Mw**^{a}	**ρ**^{a}	**V**$_m$	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
Aspirin		$C_9H_8O_4$	180.16	1.350	133.45	N/A	N/A	N/A	N/A	18.9	7.6	9.8	**22.6**	19.7	4.9	11.3	**23.3**	17.9	4.3	8.6	**20.3**	**22.3**
Benzoic acid		$C_7H_6O_2$	122.12	1.080	113.08	18.2	6.9	9.8	**21.8**	18.4	6.2	9.6	**21.7**	19.6	4.3	10.0	**22.4**	18.1	5.1	10.4	**21.5**	**20.4**
Benzyldimethyl(2-Hydroxyethyl) ammonium chloride		$C_{13}H_{22}ClNO$	215.72	1.000	215.72	N/A	N/A	N/A	N/A	18.2	9.2	13.3	**24.3**	17.8	5.2	11.0	**21.5**	16.1	2.7	4.9	**17.0**	**21.0**
Benzyltriethylammonium chloride		$C_{13}H_{22}ClN$	227.77	0.900	253.08	N/A	N/A	N/A	N/A	18.6	3.3	3.1	**19.1**	16.9	3.9	4.6	**17.9**	15.6	1.6	2.4	**15.9**	**18.4**
Betaine		$C_5H_{10}NO_2$	117.15	1.000	117.15	N/A	N/A	N/A	N/A	15.7	6.8	8.1	**18.9**	13.8	6.7	9.3	**17.9**	15.3	3.1	3.5	**16.0**	**18.5**

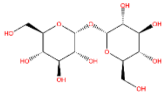
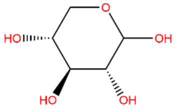
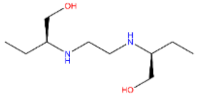
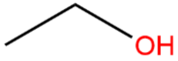
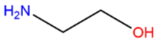
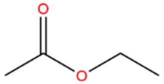
						HSPs (MPa$^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V$_m$**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ$_D$	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_T$**
Borneol		$C_{10}H_{18}O$	154.25	1.010	152.72	N/A	N/A	N/A	N/A	18.0	8.1	11.2	**22.7**	19.2	3.3	11.4	**22.6**	16.1	2.1	3.6	**16.6**	**19.6**
Butyric acid		$C_4H_8O_2$	88.11	0.964	91.40	14.9	4.1	10.6	**18.7**	15.8	6.1	10.0	**19.7**	15.8	4.5	10.3	**19.4**	16.1	5.2	8.7	**19.0**	**18.6**
Caffeic acid		$C_9H_8O_4$	180.16	1.293	139.30	N/A	N/A	N/A	N/A	19.0	9.0	24.1	**32.0**	17.7	6.2	19.4	**27.0**	18.3	7.1	15.3	**24.9**	**29.8**
Camphor		$C_{10}H_{16}O$	152.23	0.990	153.77	N/A	N/A	N/A	N/A	18.4	10.3	4.1	**21.4**	19.5	5.0	3.6	**20.4**	16.5	2.8	1.9	**16.9**	**18.2**
Caprylic acid		$C_8H_{16}O_2$	144.21	0.900	160.23	N/A	N/A	N/A	N/A	15.8	4.8	8.5	**18.6**	16.2	2.6	7.9	**18.2**	16.2	3.6	5.4	**17.5**	**18.3**
Carnosic acid		$C_{20}H_{28}O_4$	332.43	1.184	280.77	N/A	N/A	N/A	N/A	19.9	10.8	21.3	**31.1**	19.5	3.1	13.8	**24.1**	16.9	3.2	6.3	**18.3**	**18.0**

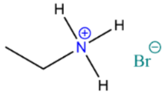
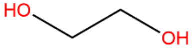
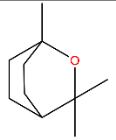
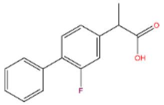
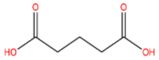
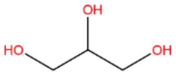
						HSPs ($MPa^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V_m**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
Carnosol		$C_{20}H_{26}O_4$	330.42	1.260	262.24	N/A	N/A	N/A	N/A	20.8	12.8	16.9	**29.7**	19.9	3.6	14.0	**24.6**	17.2	4.4	5.1	**18.5**	**18.6**
Carvacrol		$C_{10}H_{14}O$	150.22	0.977	153.75	N/A	N/A	N/A	N/A	16.3	3.7	8.4	**18.8**	17.9	3.3	11.3	**21.4**	16.4	1.7	4.0	**17.0**	**19.2**
Choline Chloride		$C_5H_{14}ClNO$	139.62	1.024	136.38	N/A	N/A	N/A	N/A	15.7	7.9	13.7	**22.3**	15.7	6.9	12.7	**21.4**	14.5	2.8	4.5	**15.4**	**19.8**
Citric acid		$C_6H_8O_7$	192.12	1.660	115.74	N/A	N/A	N/A	N/A	17.3	12.2	25.8	**33.4**	20.9	8.1	21.5	**31.1**	18.0	9.3	17.3	**26.6**	**23.4**
Citronellol		$C_{10}H_{20}O$	156.27	0.855	182.77	N/A	N/A	N/A	N/A	15.0	2.0	9.3	**17.8**	22.5	2.8	10.5	**25.0**	15.7	2.1	3.2	**16.2**	**20.0**

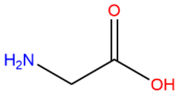
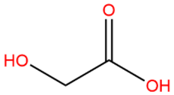
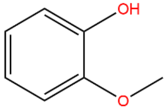
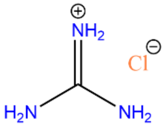
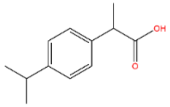
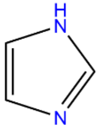
						HSPs (MPa$^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V$_m$**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ$_D$	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_T$**
D (+)-Sucrose		$C_{12}H_{22}O_{11}$	342.30	1.581	216.57	23.4	18.4	20.8	**36.3**	21.3	25.0	65.8	**73.6**	23.4	9.9	32.6	**41.3**	17.9	7.6	14.6	**24.3**	**33.9**
Decanoic acid		$C_{10}H_{20}O_2$	172.26	0.893	192.91	N/A	N/A	N/A	N/A	15.9	4.2	7.7	**18.1**	16.3	2.2	7.2	**18.0**	16.3	3.2	4.6	**17.2**	**18.3**
D-Fructose		$C_6H_{12}O_6$	180.16	1.690	106.60	N/A	N/A	N/A	N/A	19.2	16.2	43.3	**50.1**	18.4	7.8	26.0	**32.8**	18.3	8.1	16.0	**25.6**	**35.3**
D-Glucose		$C_6H_{12}O_6$	180.16	1.560	115.48	N/A	N/A	N/A	N/A	19.1	15.7	43.3	**49.8**	17.1	6.9	24.4	**30.6**	18.2	8.1	17.1	**26.3**	**35.1**
Diethylamine hydrochloride		$C_4H_{12}ClN$	109.60	1.000	109.60	N/A	N/A	N/A	N/A	15.3	5.4	8.3	**18.2**	14.8	3.9	7.9	**17.2**	14.4	2.2	2.9	**14.9**	**19.1**
Diethylene glycol		$C_4H_{10}O_3$	106.12	1.100	96.47	16.6	12.0	20.7	**29.1**	17.4	10.1	21.4	**29.3**	18.1	9.2	22.1	**30.0**	16.9	6.4	11.2	**21.3**	**29.6**

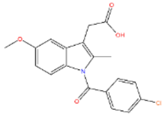
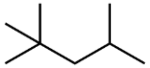
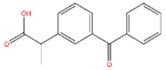
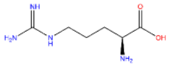
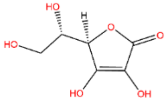
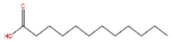
						HSPs ($MPa^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V_m**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_T**
DL-Aspartic acid		$C_4H_7NO_4$	133.10	1.700	78.30	N/A	N/A	N/A	N/A	16.6	7.3	15.6	**23.9**	18.5	6.5	17.6	**26.4**	17.8	8.9	16.0	**25.5**	**22.5**
DL-Glutamic acid		$C_5H_9NO_4$	147.13	1.400	105.09	N/A	N/A	N/A	N/A	16.6	7.0	15.2	**23.5**	18.2	5.5	16.3	**25.1**	17.6	7.9	14.0	**23.9**	**21.8**
DL-Lactic acid		$C_3H_6O_3$	90.08	1.206	74.69	17.0	8.3	28.4	**34.1**	16.2	8.3	18.0	**25.6**	17.5	9.2	20.6	**28.5**	16.9	7.7	14.8	**23.7**	**24.5**
DL-Malic acid		$C_4H_6O_5$	134.09	1.610	83.28	N/A	N/A	N/A	N/A	16.8	10.4	22.2	**29.7**	19.7	9.5	22.1	**31.1**	15.9	9.5	18.0	**25.8**	**24.0**
DL-Mandelic acid		$C_8H_8O_3$	152.15	1.300	117.04	N/A	N/A	N/A	N/A	20.4	3.1	4.0	**21.0**	20.7	6.1	16.6	**27.2**	15.8	3.6	7.6	**17.9**	**21.9**

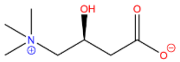
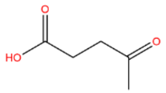
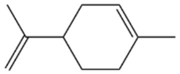
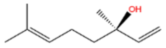
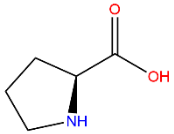
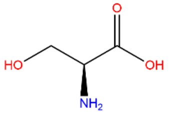
						HSPs ($MPa^{0.5}$)																
Name	**Structure**	**MF**	**Mw**^{a}	**ρ**^{a}	**V**$_m$	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
DL-Menthol		$C_{10}H_{20}O$	156.27	0.890	175.58	16.6	4.7	10.6	**20.2**	16.5	5.2	10.8	**20.4**	18.6	2.9	10.8	**21.7**	15.7	2.0	3.2	**16.1**	**19.4**
DL-Threonine		$C_4H_9NO_3$	119.12	1.313	90.75	N/A	N/A	N/A	N/A	16.9	7.5	18.3	**26.1**	17.9	7.3	20.7	**28.4**	17.2	7.3	13.7	**23.1**	**24.6**
DL-Xylitol		$C_{12}H_{16}O_6$	152.15	1.515	100.43	N/A	N/A	N/A	N/A	17.7	14.1	43.1	**48.7**	23.1	14.1	35.5	**44.7**	18.3	8.3	17.5	**26.6**	**35.8**
D-Mannose		$C_6H_{12}O_6$	180.16	1.539	117.06	N/A	N/A	N/A	N/A	18.1	18.3	43.5	**50.5**	25.0	16.3	35.2	**46.1**	18.4	9.4	16.4	**26.4**	**34.5**
D-Ribose		$C_5H_{10}O_5$	150.13	1.190	126.19	N/A	N/A	N/A	N/A	17.7	16.7	36.3	**43.7**	24.1	17.0	33.5	**44.6**	18.3	9.6	16.2	**26.2**	**34.2**
D-Sorbitol		$C_6H_{14}O_6$	182.17	1.489	122.35	N/A	N/A	N/A	N/A	18.1	15.8	50.3	**55.7**	20.0	11.5	33.6	**40.8**	18.4	8.3	17.5	**26.7**	**35.9**

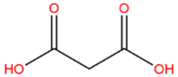
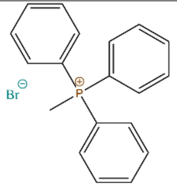
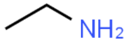
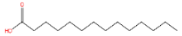
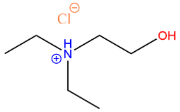
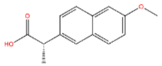
						HSPs (MPa$^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V$_m$**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_T**
D-Threhalose		$C_{12}H_{22}O_{11}$	342.30	1.580	216.64	N/A	N/A	N/A	N/A	21.2	24.5	65.8	**73.4**	28.1	12.0	35.8	**47.1**	17.9	7.5	14.3	**24.1**	**33.5**
D-Xylose		$C_5H_{10}O_5$	150.13	1.520	98.77	N/A	N/A	N/A	N/A	18.8	14.1	36.1	**43.1**	27.4	19.3	38.5	**51.0**	18.1	7.9	15.7	**25.3**	**34.7**
Ethambutol		$C_{10}H_{24}N_2O_2$	204.31	1.100	185.74	N/A	N/A	N/A	N/A	17.4	6.3	21.0	**28.0**	17.6	3.7	15.6	**23.8**	16.6	4.0	6.7	**18.3**	**24.0**
Ethanol		C_2H_5OH	46.07	0.789	58.39	15.8	8.8	19.4	**26.5**	15.8	6.7	13.9	**22.1**	15.1	8.4	18.3	**25.2**	15.2	5.1	9.9	**18.9**	**26.2**
Ethanolamine		C_2H_7NO	61.08	1.012	60.36	17.0	15.5	21.2	**31.3**	16.4	8.0	17.4	**25.2**	16.8	8.1	21.5	**28.5**	16.9	7.0	12.8	**22.4**	**29.0**
Ethyl acetate		$C_4H_8O_2$	88.11	0.902	97.68	15.8	5.3	7.2	**18.2**	15.6	5.0	8.3	**18.4**	14.8	4.8	8.3	**17.7**	15.4	3.2	3.6	**16.1**	**19.2**

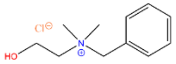
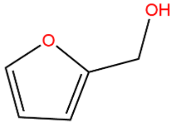
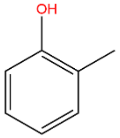
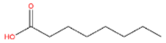
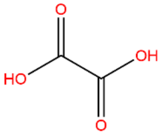
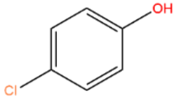
Name	Structure	MF	Mw^a	ρ^a	V_m	HSPs ($MPa^{0.5}$)																
						Hansen [38]				StP*				HKF*				Ymt*				Hoy*
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
Ethylammonium bromide		C_2H_8BrN	126.00	1.521	82.85	N/A	N/A	N/A	N/A	18.7	8.4	7.0	**21.7**	18.0	15.0	9.1	**25.1**	17.7	2.0	1.9	**17.9**	**16.8**
Ethylene glycol		$C_2H_6O_2$	62.07	1.110	55.92	17.0	11.0	26.0	**33.0**	16.6	9.1	21.6	**28.7**	18.4	13.5	27.7	**35.9**	17.1	8.3	17.0	**25.5**	**35.1**
Eucalyptol		$C_{10}H_{18}O$	154.25	0.922	167.30	16.7	4.6	3.4	**17.7**	17.9	6.2	3.9	**19.4**	27.2	3.1	4.8	**27.8**	15.9	1.7	1.3	**16.0**	**17.5**
Flurbiprofen		$C_{15}H_{13}FO_2$	244.26	1.180	207.09	N/A	N/A	N/A	N/A	20.7	5.9	6.5	**22.4**	20.0	2.5	7.6	**21.5**	18.1	2.1	5.7	**19.1**	**20.7**
Glutaric acid		$C_5H_8O_4$	132.11	1.300	101.63	N/A	N/A	N/A	N/A	16.5	8.1	14.2	**23.2**	17.8	5.6	13.8	**23.2**	17.3	7.4	13.0	**22.9**	**20.4**
Glycerol		$C_3H_8O_3$	92.09	1.260	73.09	17.4	12.1	29.3	**36.2**	17.0	10.8	28.8	**35.1**	17.8	12.3	29.2	**36.4**	17.7	8.3	17.2	**26.1**	**35.5**

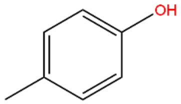
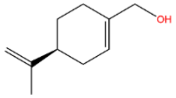
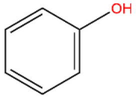
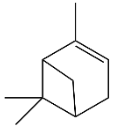
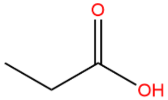
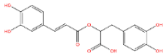
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V_m**	**HSPs ($MPa^{0.5}$)**																
						Hansen [38]				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_T**
Glycine		$C_2H_5NO_2$	75.07	1.595	47.06	N/A	N/A	N/A	N/A	16.3	8.0	14.3	**23.1**	16.9	6.6	17.0	**24.9**	17.4	8.8	15.6	**25.0**	**23.0**
Glycolic acid		$C_2H_4O_3$	76.05	1.250	60.84	N/A	N/A	N/A	N/A	16.5	9.1	18.5	**26.4**	18.5	12.0	23.4	**32.2**	17.5	10.1	19.7	**28.2**	**29.0**
Guaiacol		$C_7H_8O_2$	124.14	1.129	109.95	N/A	N/A	N/A	N/A	15.7	8.1	21.6	**27.9**	20.1	6.5	15.2	**26.0**	17.5	4.0	7.9	**19.6**	**23.1**
Guanidinium hydrochloride		$CH_5N_3 \cdot HCl$	95.53	1.180	80.96	N/A	N/A	N/A	N/A	17.5	9.2	2.0	**19.8**	33.6	7.4	18.3	**39.0**	17.0	6.6	11.0	**21.3**	**26.6**
Ibuprofen		$C_{13}H_{18}O_2$	206.28	1.036	199.04	N/A	N/A	N/A	N/A	17.5	3.5	6.8	**19.1**	17.9	2.2	7.2	**19.4**	16.7	2.4	4.9	**17.5**	**18.1**
Imidazole		$C_3H_4N_2$	68.08	1.030	66.09	N/A	N/A	N/A	N/A	18.5	9.7	10.2	**23.2**	15.6	16.0	12.7	**25.7**	23.0	3.2	10.0	**25.3**	**20.3**

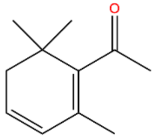
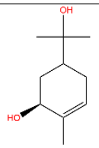
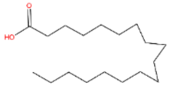
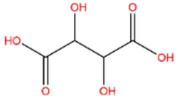
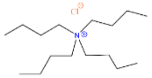
Name	Structure	MF	Mw^a	ρ^a	V$_m$	HSPs (MPa$^{0.5}$)																
						Hansen [38]				StP*				HKF*				Ymt*				Hoy*
						δ$_D$	δ$_P$	δ$_H$	δ$_T$	δ$_D$	δ$_P$	δ$_H$	δ$_T$	δ$_D$	δ$_P$	δ$_H$	δ$_T$	δ$_D$	δ$_P$	δ$_H$	δ$_T$	δ$_T$
Indomethacin		$C_{19}H_{16}ClNO_4$	357.79	1.214	294.84	N/A	N/A	N/A	N/A	19.8	10.0	4.7	**22.7**	22.2	6.0	9.4	**24.8**	18.7	3.7	5.7	**19.9**	**22.2**
Isooctane		C_8H_{18}	114.23	0.692	165.07	14.1	0.0	0.0	**14.1**	14.1	1.7	3.4	**14.6**	14.6	0.0	0.0	**14.6**	13.8	0.7	0.3	**13.8**	**15.6**
Ketoprofen		$C_{16}H_{14}O_3$	254.28	1.157	219.87	N/A	N/A	N/A	N/A	19.4	5.2	8.6	**21.8**	20.6	4.6	7.8	**22.5**	18.0	4.2	7.3	**19.9**	**21.1**
L-Arginine		$C_6H_{14}N_4O_2$	174.20	0.640	272.19	N/A	N/A	N/A	N/A	18.2	6.3	8.4	**21.0**	20.1	3.6	16.7	**26.4**	18.3	6.6	10.8	**22.2**	**24.2**
L-Ascorbic acid		$C_6H_8O_6$	176.12	1.650	106.74	18.0	12.6	27.6	**35.3**	18.2	18.1	33.6	**42.3**	21.0	15.4	31.5	**40.9**	19.1	9.0	15.4	**26.2**	**35.0**
Lauric acid		$C_{12}H_{24}O_2$	200.32	0.880	227.63	N/A	N/A	N/A	N/A	15.9	3.5	6.9	**17.7**	16.4	1.9	6.7	**17.8**	16.3	3.0	4.0	**17.0**	**18.2**

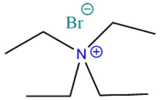
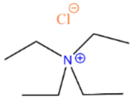
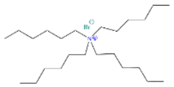
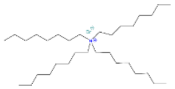
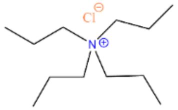
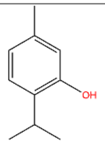
						HSPs (MPa$^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V$_m$**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_D**	**δ_P**	**δ_H**	**δ_T**	**δ_T**
L-Carnitine		$C_7H_{15}NO_3$	161.20	1.063	151.67	N/A	N/A	N/A	N/A	16.0	10.0	15.0	**24.1**	16.6	7.1	14.6	**23.2**	16.0	3.8	5.5	**17.3**	**20.2**
Levulinic acid		$C_5H_8O_3$	116.12	1.134	102.39	N/A	N/A	N/A	N/A	14.7	6.8	11.7	**20.0**	17.0	8.4	10.7	**21.7**	15.9	6.0	10.1	**19.8**	**18.6**
Limonene		$C_{10}H_{16}$	136.23	0.841	161.99	N/A	N/A	N/A	N/A	16.0	2.0	2.4	**16.3**	20.6	0.5	0.0	**20.6**	14.7	1.4	1.6	**14.9**	**17.4**
L-Linalool		$C_{10}H_{18}O$	154.25	0.858	179.78	N/A	N/A	N/A	N/A	14.8	1.7	8.8	**17.3**	24.1	3.2	11.1	**26.7**	12.5	2.4	3.6	**13.2**	**17.9**
L-Proline		$C_5H_9NO_2$	115.13	1.350	85.28	N/A	N/A	N/A	N/A	18.0	8.3	11.6	**23.0**	19.7	5.2	12.8	**24.0**	17.7	6.2	10.0	**21.3**	**21.4**
L-Serine		$C_3H_7NO_3$	105.09	1.600	65.68	N/A	N/A	N/A	N/A	16.6	7.6	19.1	**26.4**	18.8	9.0	23.0	**31.0**	17.7	8.9	16.8	**26.0**	**27.7**

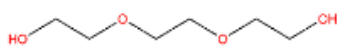
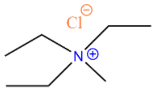
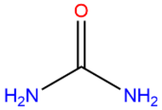
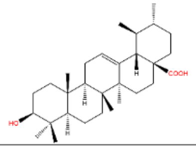
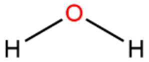
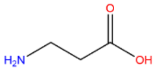
						HSPs ($\mathrm{MPa}^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V_m**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
Malonic acid		$C_3H_4O_4$	104.06	1.620	64.24	N/A	N/A	N/A	N/A	16.4	8.7	15.0	**23.9**	18.2	8.1	16.5	**25.9**	15.2	9.8	18.0	**25.5**	**20.2**
Methyl triphenylphosphonium bromide		$C_{19}H_{18}BrP$	357.22	1.300	274.79	N/A	N/A	N/A	N/A	21.5	0.1	0.2	**21.5**	19.0	2.1	1.2	**19.2**	17.4	2.3	4.2	**18.0**	**19.9**
Monoethanolamine		C_2H_7NO	61.08	1.012	60.36	N/A	N/A	N/A	N/A	16.9	6.9	15.2	**23.8**	16.8	8.1	21.5	**28.5**	16.9	7.0	12.8	**22.4**	**28.8**
Myristic acid		$C_{14}H_{28}O_2$	228.37	0.862	264.93	N/A	N/A	N/A	N/A	15.9	2.9	6.1	**17.3**	16.4	1.6	6.3	**17.6**	16.3	2.8	3.6	**16.9**	**18.2**
N, N diethylethanol ammonium chloride		$C_6H_{13}NO.HCl$	153.64	-	-	N/A	N/A	N/A	N/A	18.2	9.0	15.3	**25.4**	16.6	7.0	12.7	**22.1**	15.2	3.0	4.8	**16.2**	**22.1**
Naproxen		$C_{14}H_{14}O_3$	230.26	1.350	170.56	N/A	N/A	N/A	N/A	19.8	6.9	8.1	**22.5**	19.1	3.3	8.5	**21.2**	17.6	3.5	6.8	**19.2**	**21.7**

Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V$_m$**	**HSPs (MPa$^{0.5}$)**																
						Hansen [38]				**StP***				**HKF***				**Ymt***				**Hoy***
						δ$_D$	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_D$**	**δ$_P$**	**δ$_H$**	**δ$_T$**	**δ$_T$**
N-benzyl-2-hydroxy-N.N-dimethyl ethanaminium chloride		$C_{11}H_{18}NO$	215.72	1.500	143.81	N/A	N/A	N/A	N/A	18.3	7.4	12.4	**23.4**	17.8	5.2	11.0	**21.5**	16.1	2.7	4.9	**17.0**	**20.1**
Nfurfuryl alcohol		$C_5H_6O_2$	98.10	1.135	86.43	N/A	N/A	N/A	N/A	17.8	15.4	20.4	**31.1**	17.8	7.9	16.9	**25.8**	18.1	5.3	10.0	**21.3**	**29.0**
***O*-Cresol**		C_7H_8O	108.14	1.048	103.18	N/A	N/A	N/A	N/A	18.4	5.7	12.1	**22.8**	19.8	5.3	14.4	**25.1**	17.3	3.1	7.3	**19.1**	**20.3**
Octanoic acid		$C_8H_{16}O_2$	144.21	0.910	158.47	15.1	3.3	8.2	**17.5**	15.8	4.8	8.5	**18.6**	16.2	2.6	7.9	**18.2**	16.2	3.6	5.4	**17.5**	**18.3**
Oxalic acid		$C_2H_2O_4$	90.03	1.900	47.39	17.0	14.3	22.0	**31.3**	16.4	9.0	15.4	**24.3**	18.6	10.4	18.7	**28.4**	17.9	11.8	22.1	**30.8**	**22.5**
***p*-Chlorophenol**		C_6H_5ClO	128.56	1.306	98.44	N/A	N/A	N/A	N/A	19.1	6.3	12.5	**23.7**	22.3	8.7	15.4	**28.5**	18.1	3.0	7.3	**19.7**	**27.4**

Name	Structure	MF	Mw^a	ρ^a	V_m	HSPs ($MPa^{0.5}$)															
						Hansen [38]				StP*				HKF*				Ymt*				Hoy*
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
***p*-Cresol**		C_7H_8O	108.14	1.034	104.58	N/A	N/A	N/A	N/A	18.4	5.7	12.1	**22.8**	19.8	5.3	14.4	**25.1**	17.3	3.1	7.3	**19.1**	**22.2**
Perillyl alcohol		$C_{10}H_{16}O$	152.23	0.960	158.58	N/A	N/A	N/A	N/A	16.8	4.4	10.1	**20.1**	28.1	3.9	12.4	**31.0**	15.5	2.7	4.9	**16.5**	**21.5**
Phenol		C_6H_6O	94.11	1.070	87.95	18.0	5.9	14.9	**24.1**	18.4	5.8	12.9	**23.2**	20.1	6.3	15.7	**26.3**	18.4	2.3	8.2	**20.3**	**20.9**
Pinene		$C_{10}H_{16}$	136.23	0.860	158.41	16.9	1.8	3.1	**17.3**	17.3	4.2	2.5	**18.0**	27.5	0.0	0.0	**27.5**	15.8	0.9	0.9	**15.9**	**17.3**
Propionic acid		$C_3H_6O_2$	74.08	0.993	74.60	14.7	5.3	12.4	**19.9**	15.8	6.4	10.4	**19.9**	15.6	5.4	11.3	**20.0**	16.0	6.1	10.5	**20.1**	**18.7**
Rosmarinic acid		$C_{18}H_{16}O_8$	360.31	1.330	270.91	N/A	N/A	N/A	N/A	21.4	14.0	37.9	**45.7**	18.5	4.9	20.0	**27.7**	18.7	4.9	10.3	**21.9**	**23.5**

						HSPs ($MPa^{0.5}$)																
Name	Structure	MF	Mw^a	ρ^a	V_m	Hansen [38]				StP*				HKF*				Ymt*				Hoy*
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
Safranal		$C_{10}H_{14}O$	150.22	0.973	154.39	N/A	N/A	N/A	N/A	15.9	8.2	3.2	**18.2**	26.2	5.9	5.8	**27.4**	15.5	3.2	2.8	**16.1**	**19.7**
Sobrerol		$C_{10}H_{18}O_2$	170.25	0.958	177.69	N/A	N/A	N/A	N/A	16.9	6.3	17.3	**25.0**	20.2	4.1	15.2	**25.6**	16.2	3.1	6.1	**17.6**	**21.9**
Stearic acid		$C_{18}H_{36}O_2$	284.48	0.941	302.31	16.3	3.3	5.5	**17.5**	16.0	1.7	4.6	**16.7**	16.5	1.3	5.6	**17.5**	16.3	2.5	3.1	**16.8**	**18.2**
Tartaric acid		$C_4H_6O_6$	150.09	1.790	83.85	N/A	N/A	N/A	N/A	17.2	12.4	29.7	**36.5**	21.9	12.3	28.3	**37.8**	18.4	10.3	20.3	**29.3**	**28.8**
Tetrabutylammonium bromide		$C_{16}H_{36}BrN$	322.37	1.039	310.27	N/A	N/A	N/A	N/A	15.4	0.8	1.1	**15.4**	15.8	2.3	3.8	**16.4**	15.4	1.4	0.9	**15.5**	**17.0**
Tetrabutylammonium chloride		$C_{16}H_{36}ClN$	277.92	0.980	283.59	N/A	N/A	N/A	N/A	14.8	14.8	14.8	**25.7**	15.8	2.8	4.0	**16.5**	15.1	15.1	15.1	**26.2**	**17.0**

						HSPs (MPa$^{0.5}$)																
Name	**Structure**	**MF**	**Mw^a**	**ρ^a**	**V$_m$**	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_D	δ_P	δ_H	δ_T	δ_T
Tetraethylammonium bromide		$C_8H_{20}NBr$	210.16	1.397	150.43	N/A	N/A	N/A	N/A	15.2	3.3	4.2	**16.1**	15.2	3.6	4.8	**16.3**	14.7	1.4	0.9	**14.8**	**16.3**
Tetraethylammonium chloride		$C_8H_{20}ClN$	165.70	1.080	153.43	N/A	N/A	N/A	N/A	14.9	4.5	4.8	**16.3**	15.1	4.5	5.0	**16.6**	14.3	1.3	0.9	**14.4**	**16.3**
Tetrahexylammonium bromide		$C_{24}H_{52}BrN$	434.58	1.063	408.90	N/A	N/A	N/A	N/A	15.5	-1.7	-2.0	**15.7**	16.0	1.7	3.2	**16.4**	15.7	1.4	0.9	**15.7**	**17.3**
Tetraoctylammonium bromide		$C_{32}H_{68}BrN$	546.79	1.526	358.32	N/A	N/A	N/A	N/A	15.6	-4.2	-5.1	**16.9**	16.2	1.3	2.9	**16.5**	15.8	1.5	0.9	**15.9**	**17.5**
Tetrapropylammonium chloride		$C_{12}H_{28}ClN$	221.81	0.946	234.45	N/A	N/A	N/A	N/A	15.0	3.3	3.3	**15.7**	15.5	3.5	4.4	**16.5**	14.8	1.3	0.9	**14.9**	**16.8**
Thymol		$C_{10}H_{14}O$	150.22	0.960	156.48	19.0	4.5	10.8	**22.3**	17.4	4.1	10.9	**20.9**	19.7	3.6	11.8	**23.3**	16.4	1.7	4.0	**17.0**	**19.2**

						HSPs ($MPa^{0.5}$)																
Name	**Structure**	**MF**	**Mw**^{a}	**ρ**^{a}	**V**$_m$	**Hansen [38]**				**StP***				**HKF***				**Ymt***				**Hoy***
						δ$_D$	**δ**$_P$	**δ**$_H$	**δ**$_T$	**δ**$_D$	**δ**$_P$	**δ**$_H$	**δ**$_T$	**δ**$_D$	**δ**$_P$	**δ**$_H$	**δ**$_T$	**δ**$_D$	**δ**$_P$	**δ**$_H$	**δ**$_T$	**δ**$_T$
Triethylene glycol		$C_6H_{14}O_4$	150.17	1.124	133.61	16.0	12.5	18.6	**27.5**	16.8	11.4	22.2	**30.0**	18.0	7.3	19.2	**27.4**	16.8	5.7	8.8	**19.8**	**27.3**
Triethylmethylammonium chloride		$C_7H_{18}ClN$	151.68	0.800	189.60	N/A	N/A	N/A	N/A	16.1	4.5	5.9	**17.7**	15.0	4.9	5.2	**16.6**	14.1	1.3	0.9	**14.2**	**16.2**
Urea		CH_4N_2O	60.06	1.320	45.50	20.9	18.7	26.4	**38.5**	18.8	15.8	14.4	**28.5**	23.2	21.0	22.6	**38.6**	18.2	11.6	14.4	**25.9**	**33.7**
Ursolic acid		$C_{30}H_{48}O_3$	456.70	1.026	445.08	N/A	N/A	N/A	N/A	20.5	7.7	7.2	**23.1**	18.2	1.6	8.5	**20.1**	16.6	2.2	3.5	**17.1**	**18.6**
Water		H_2O	18.01	0.997	18.06	15.5	16.0	42.3	**47.8**	15.5	16.0	42.3	**47.8**	15.5	16.0	42.3	**47.8**	15.5	16.0	42.3	**47.8**	**47.8**
β-Alanine		$C_3H_7NO_2$	89.09	1.440	61.87	N/A	N/A	N/A	N/A	16.4	7.4	13.5	**22.4**	16.9	5.3	15.2	**23.3**	17.2	7.4	12.7	**22.6**	**22.0**

^{a} Data acquired from the *Chemical book* website (reference [91]).

* **StP**- Stefanis-Panayiotou [66], [67]; **HKF** - Hoftyzer-Van Krevelen-Fedors [64], [65]; **Hoy** [68]; **Ymt** - Yamamoto [48], [69]. Instead of HKF which uses the molar volume estimated by the Fedors method, for HK the experimental value of density is used to calculate the molar volume.

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