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Review

Solvent Replacement Strategies for Processing Pharmaceuticals and Bio-Related Compounds—A Review

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Abstract: An overview of solvent replacement strategies shows that there is great progress in green chemistry for replacing hazardous di-polar aprotic solvents, such as N,N-dimethylformamide (DMF), 1-methyl-2-pyrrolidinone (NMP), and 1,4-dioxane (DI), used in processing active industrial ingredients (APIs). In synthetic chemistry, alcohols, carbonates, ethers, eucalyptol, glycols, furans, ketones, cycloalkanones, lactones, pyrrolidinone or solvent mixtures, 2-methyl tetrahydrofuran in methanol, HCl in cyclopentyl methyl ether, or trifluoroacetic acid in propylene carbonate or surfactant water (no organic solvents) are suggested replacement solvents. For the replacement of dichloromethane (DCM) used in chromatography, ethyl acetate ethanol or 2-propanol in heptanes, with or without acetic acid or ammonium hydroxide additives, are suggested, along with methanol acetic acid in ethyl acetate or methyl tert-butyl ether, ethyl acetate in ethanol in cyclohexane, CO_2-ethyl acetate, CO_2-methanol, CO_2-acetone, and CO_2-isopropanol. Supercritical CO_2 (scCO_2) can be used to replace many organic solvents used in processing materials from natural sources. Vegetable, drupe, legume, and seed oils used as co-extractants (mixed with substrate before extraction) can be used to replace the typical organic co-solvents (ethanol, acetone) used in scCO_2 extraction. Mixed solvents consisting of a hydrogen bond donor (HBD) solvent and a hydrogen bond acceptor (HBA) are not addressed in GSK or CHEM21 solvent replacement guides. Published data for 100 water-soluble and water-insoluble APIs in mono-solvents show polarity ranges appropriate for the processing of APIs with mixed solvents. When water is used, possible HBA candidate solvents are acetone, acetic acid, acetonitrile, ethanol, methanol, 2-methyl tetrahydrofuran, 2,2,5,5-tetramethyloxolane, dimethylisosorbide, Cyrene, Cygnet 0.0, or diformylxylose. When alcohol is used, possible HBA candidates are cyclopentanone, esters, lactone, eucalytol, MeSesamol, or diformylxylose. HBA—HBA mixed solvents, such as Cyrene—Cygnet 0.0, could provide interesting new combinations. Solubility parameters, Reichardt polarity, Kamlet—Taft parameters, and linear solvation energy relationships provide practical ways for identifying mixed solvents applicable to API systems.

Keywords: Reichardt polarity; Kamlet—Taft parameters; green chemistry; solvent substitution; pharmaceuticals

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1. Introduction

Solvents are commonly viewed as being polar or nonpolar, depending on whether their molecular structure contains highly electronegative (N, O, S, Cl, Br, I) elements or only (C, H) elements. However, for a molecule to be polar, it must contain a polar bond and have asymmetry in its structure that causes an imbalance in charge separation between two

(+ and −) poles referred to as dipoles. The presence of an asymmetrically arranged polar bond, such as C-Cl in chloromethane (CH_3C1), causes the molecule to be polar, whereas the presence of four symmetrically arranged C-Cl bonds in carbon tetrachloride (CCl_4) cause the molecule to be nonpolar. For two solvents to be miscible, similarity in molecular polarity is required, as given by the well-known adage, "like dissolves like", which in other words means that, for the solvation of polar molecules to occur, dipole—dipole interactions must exist, and conversely, for the solvation of nonpolar molecules to occur, dipole—dipole interactions must be absent. There are many exceptions to this adage, and certainly, system conditions (temperature, pressure) and van der Waals-London forces (dispersion) play important roles in solvation processes. Moreover, for solvent mixtures as discussed in this review, composition and interactions between hydrogen bond donor (HBD) and hydrogen bond acceptor (HBA) molecules are important.

Physical properties such as dipole moment (μ_D), dielectric constant (ε), octanol-water partition coefficient ($\log K_{ow}$ or logP), normal boiling point (T_b), melting temperature (T_m), entropy of fusion ($\Delta_{fus}S$), Hildebrand solubility parameter, and Hansen solubility parameter help to characterize the macroscopic polarity of a molecule. On the other hand, empirical polarity scales based on solvatochromic probes (dyes), such as Reichardt $E_T(30)$ [1] and normalized $E_T{}^N$ values [2], Kamlet—Taft (KT) acidity (α), basicity (β) and dipolar/polarizability (π*) values [3,4], and Catalán parameters [5], help to characterize the microscopic polarity of a solvent [6]. In solvent selection guides developed by the industry [7,8] and chemical societies [9–12], pure component solvent properties are analyzed in detail for developing solvent replacement strategies; however, as a focus of this review, considerable opportunities exist if mixtures of two kinds of polar solvents are used to create environments of microscopic polarity. For example, mixing an HBD solvent with an HBA solvent causes complex molecules (e.g., HBD—HBA pairs) to form, such that heterogeneity (local composition) is observed for simple alcohol—water mixtures [13,14] or ethylene glycol-water mixtures [15]. In this review, the emphasis is placed on taking advantage of the local composition and microscopic polarity of a solvent mixture as opposed to the bulk properties of a pure solvent, even though temperature and pressure can also be used to vary the properties of a pure solvent.

Solutes, in the context of this review, are active pharmaceutical ingredients (APIs) and bio-related molecules that can have multiple functional groups and can contain both polar (hydrophilic) and nonpolar (hydrophobic) regions in their structure. Functional groups in the solute can interact within the molecule (intramolecular) or between neighboring molecules (intermolecular) to form associated, cyclic, complex, network, or tertiary structures, and thus, the dissolution of an API into a solvent can be the result of many different molecular interactions. The composition of a solvent mixture can be used to fine-tune dipole—dipole interactions that sometimes lead to the solubility enhancement of the API in solution that is higher than that in either of the pure mono-solvents, which is known as synergistic behavior.

2. Substances of Very High Concern (SVHC)

In the synthesis and processing of APIs, polar protic (water, alcohols, carboxylic acids), dipolar aprotic (ketones, lactones, esters, ethers), or nonpolar aprotic (hydrocarbons) solvents are used. Notably, hazardous and unsafe dipolar aprotic chemicals (e.g., N,N-dimethylformamide (DMF), 1-methyl-2-pyrrolidinone (NMP), 1,4-dioxane (DI)) account for over 40% of total solvents used in synthetic, medicine-related, and process chemistry [16], and these solvents and more than 480 others are on the candidate list of substances of very high concern (SVHC), as designated under the European Chemicals Agency (ECHA), as the European Union Registration, Evaluation Authorization and Restriction of Chemicals (REACH) guidelines limit or prohibit the use of chemicals, especially those having reproductive toxicity, carcinogenicity, or explosive decomposition properties (Table 1). Thus, the key motivation of employing mixed solvents instead of mono-solvents, new solvents, or newly developed solvents is based on environmental health and safety (EHS) guidelines for compounds with known chemical properties and conformity with the "International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use" (ICH). Namely, EHS and ICH should be primary factors in solvent replacement, rather than apparent greenness or economic or sustainability factors, because few newly developed solvents or solvent systems have had sufficient time for scrutiny in all areas highlighted by governmental agencies and in the solvent guides discussed below. In this review, solvent replacement strategies are analyzed with the aim of highlighting a method for identifying safe solvent mixtures for the research development and chemical processing of organic compounds.

Table 1. Selected chemicals from candidate list of substances of very high concern (SVHC) for authorization by the European Chemicals Agency (ECHA) as of 2023. Chemicals shown in various categories are for educational purposes only. Specific hazards, detailed information, case decisions, or discussion should be accessed from ECHA website [17]. LD_{50} values from PubChem or online sources based on rat/mouse oral or dermal (*d*) studies.

Chemical (CAS No.)	**LD_{50} (mg/kg)**	**Chemical (CAS No.)**	**LD_{50} (mg/kg)**
Carcinogenic		Respiratory Sensitizing	
1,2,3-trichloropropane (96-18-4)	120	cis-cyclohexane-1,2-dicarboxylic anhydride (13149-00-3)	-
1,2-dichloroethane (107-06-2)	670	Cyclohexane-1,2-dicarboxylic anhydride (85-42-7)	958
1,4-dioxane (123-91-1) (DI)	1550	Glutaral (111-30-8)	134
2,4-dinitrotoluene (121-14-2)	268	Toxic to Reproduction	
4,4′-Diaminodiphenylmethane (101-77-9)	120	1-Methyl-2-pyrrolidone (NMP) (872-50-4)	3914
4-aminoazobenzene (60-09-3)	200	1-vinylimidazole (1072-63-5)	180
Acrylamide (79-06-1)	170	2-ethoxyethanol (110-80-5)	2125
Anthracene oil (90640-80-5)	2000 ^{d}	2-ethoxyethyl acetate (111-15-9)	2700
Biphenyl-4-ylamine (92-67-1)	205	2-methoxyethanol (109-86-4)	2370
Chrysene (218-01-9)	320	2-methoxyethyl acetate (110-49-6)	2900
Furan (110-00-9)	5.2	2-methylimidazole (693-98-1)	1400
Propylene oxide (75-56-9)	1245 ^{d}	4,4′-sulphonyldiphenol (80-09-1)	4556
N-(hydroxymethyl)acrylamide (924-42-5)	474	Dibutyl phthalate (84-74-2) (DBP)	7499
o-aminoazotoluene (97-56-3)	300 (dog)	Dicyclohexyl phthalate (84-61-7)	30
o-toluidine (95-53-4)	670	Dihexyl phthalate (84-75-3)	29,600
Phenolphthalein (77-09-8)	>1	Diisobutyl phthalate (84-69-5)	15
Potassium dichromate (7778-50-9)	25	Diisohexyl phthalate (71850-09-4)	-
Trichloroethylene (79-01-6)	1282	Diisopentyl phthalate (605-50-5)	2000
Endocrine disruptor		Dioctyltin dilaurate (3648-18-8)	6450
2-(isononylphenoxy)ethanol (85005-55-6)	-	Formamide (75-12-7)	5577
4-(1-ethyl-1-methylhexyl)phenol (52427-13-1)	-	Methoxyacetic acid (625-45-6)	1000
4,4′-(1-methylpropylidene)bisphenol (77-40-7)	500.1	N,N-dimethylformamide (68-12-2) (DMF)	2800
4-tert-butylphenol (98-54-4)	2951	Nitrobenzene (98-95-3)	349
Isobutyl 4-hydroxybenzoate (4247-02-3)	2600	N-methylacetamide (79-16-3)	5
Nonylphenol (25154-52-3)	1200	n-pentyl-isopentyl phthalate (776297-69-9)	-
Nonylphenol, ethoxylated (9016-45-9)	1300	Perfluoroheptanoic acid (375-85-9)	500
Human health effects		Phenol, 4-dodecyl, branched (210555-94-5)	2000
Melamine (108-78-1)	3161	Phenol, tetrapropylene- (57427-55-1)	2000
Persistent, Bioaccumulative and Toxic (PBT)		Very Persistent, Very Bioaccumulative (vPvB)	
Alkanes, C14-16, chloro (1372804-76-6)	23	Phenanthrene (85-01-8)	700
Anthracene (120-12-7)	>17	Terphenyl, hydrogenated (61788-32-7)	17,500
Dodecamethylcyclohexasiloxane (540-97-6)	>50		
Octamethylcyclotetrasiloxane (556-67-2)	1540		
Pyrene (129-00-0)	2700		

3. Solvent Guides

To address the issue of the overuse of hazardous dipolar aprotic chemicals in API synthesis and processing and to improve the awareness of chemical professionals who perform solvent selection on a day-to-day basis, pharmaceutical industries have developed solvent guides with ranking systems. Chemical agencies have developed lists for solvents evaluated as hazardous that require formal authorization for use in chemical processes.

The GlaxoSmithKline (GSK) solvent guide [7,18,19] contains detailed analyses of a total of 154 small molecules (e.g., alcohols, aromatics, carbonates, chlorinated, dipolar aprotics, esters, ethers, hydrocarbons, ketones, organic acids, water) commonly used in pharmaceutical industries. The GSK solvent guide has the following categories: (i) waste (incineration, recycling, biotreatment, VOC emissions), (ii) environment (aquatic impact, air impact), (iii) human health (health hazard, exposure potential), and (iv) safety (flammability and explosion, reactivity). The GSK solvent guide allows for the quick evaluation and qualitative comparison of replacement solvents based on four primary categories that include life-cycle assessment (LCA), and it ranks solvents in their categories on a scale from 1 (major issues) to 10 (few known issues).

The European consortium and Innovative Medicines Initiative (IMI) produced CHEM21 [8], which contains guidelines and metrics for solvent usage. Byrne et al. reported environmental, health, and safety (EHS) tools and guidelines for solvents and highlighted key points in available guidelines [11]. The CHEM21 solvent guide ranks solvents in EHS categories on a scale from 1 (recommended) to 10 (hazardous), which is contrary (and opposite in order) to the scale of the GSK solvent guide. Both solvent guides provide extremely useful evaluations of solvent risks and issues and provide solvent replacement recommendations.

The American Chemical Society (ACS) Green Chemistry Institute (CGI) and pharmaceutical roundtable produced a solvent selection website (Figure 1) [10,12] dedicated to solvent usage in pharmaceutical and chemical industries and a solvent guideline [9]. Figure 1 shows a sample screen of a solvent selection tool developed for the ACS GCI Pharmaceutical Roundtable (GCIPR) that uses principle component analysis (PCA) to identify potential solvent replacements. PCA combines many physical properties, characteristics (presence of functional groups), and environmental data to generate correlations and scores according to user constraints. The solvent selection tool (Figure 1) was described by Diorazio et al. [20] and was originally designed by AstraZeneca in Spotfire, and a version was donated to GCIPR. The GCIPR solvent selection tool is useful for identifying replacement solvents based on both quantitative and qualitative characteristics (Figure 1).

Figure 1. ACS Green Chemistry Institute and Pharmaceutical Roundtable (GCIPR) solvent selection tool https://www.acsgcipr.org/tools-for-innovation-in-chemistry/solvent-tool/ (accessed on 1 April 2024) described by Diorazio et al. [20]. Copyright ACS, 2023.

4. Replacement Solvents in Synthetic Chemistry

Syntheses of APIs are commonly performed in multistep batch processes that use hazardous or unsafe dipolar aprotic solvents in some of the key steps. Replacement strategies for non-green dipolar aprotic solvents used in reactions were suggested by Gao et al. [21].

Table 2 summarizes replacement solvents for 15 classes of synthetic reactions identified by Jordan et al. [16]. Possible replacement solvents for dipolar aprotics (Table 2) include novel water-surfactant (PS-750-M) systems that eliminate organic solvents [22], dipolar aprotic solvents with improved safety and sustainability, namely N-butyl-2-pyrrolidinone (NBP), propylene carbonate (PC), dimethylisosorbide (DMI) [23], dihydrolevoglucosenone (Cyrene) [24], eucalyptol [25], or dimethylcarbonate (DMC), or the use of mixed solvents, such as 2-methyltetrahydrofuran (2-MeTHF) with methanol (Table 2). Besides THF or DMF in Sonogashira cross-coupling reactions (Table 2), eucalyptol can possibly replace solvents such as anisole, bromobenzene, chlorobenzene, chloroform, diethyl ether (DE), N,N-dimethylacetamide (DMA), dimethyl ether (DME), DI, ethyl acetate, ethyl benzoate, and toluene [25].

Table 2. Possible replacement solvents for dipolar aprotic solvents used in synthetic chemistry transformations. Content was summarized and adapted from *Unified solvent selection guide for replacement of common dipolar aprotic solvents in synthetically useful transformations* contained in ref. [16]. Copyright ACS, 2022.

Reaction	Unsafe Dipolar Aprotics	Replacement Solvents
Amide formation	DCM; DMF	Cyrene; surfactant-water
Boc deprotection	DI	HCl in CPME; TFA in PC
Borylation chemistry	DI	2-MeTHF:MeOH (1:1); CPME; MTBE; CH
Buchwald—Hartwig amination	DI	2-MeTHF; tBuOH
Carbonylation	THF; DE	DMC
Carboxylation	THF; DE	2-MeTHF; DMI; DMC
C-H activation	THF; DMF; DI	2-MeTHF; CH
Mizoroki—Heck cross-coupling	DI; THF; DMF	NBP; DMI; PC
Nucleophilic aromatic substitution	THF; DMF; DI	2-MeTHF; PEG-400
Organometallic reaction	R-MgX; R-Li; hydrides	2-MeTHF; CPME
Solid-phase peptide synthesis	DMF; DMAc; NMP	NBP; GVL
Sonogashira cross-coupling	THF; DMF	Cyrene; NBP; DMI; Eucalyptol
Steglich Esterification	DMF	DMC
Suzuki-Miyaura cross-coupling	DI; THF; DMF	Cyrene; NBP; DMI; 2-MeTHF
Urea synthesis	DMF; THF	Cyrene

In the synthesis of APIs with solvents, the type of process employed is an important point that deserves attention. A less obvious way to lower risks associated with solvent usage in API synthesis is through continuous manufacturing (CM) [26], as opposed to batch processing. In a CM process, systems can be automated, quality can be improved, waste can be reduced, and, most importantly, solvent volumes can be greatly lowered over those quantities used in batch systems by lowering the total system volumes and by eliminating the storage of API reaction intermediates, such that overall safety of the synthesis can be improved. The number of papers published on the continuous manufacturing of APIs has roughly tripled in the past 5 years, making it a highly active research area. In CM processes, solvent selection and solvent additives play key roles in flow chemistry, product quality, system operability, economics, and sustainability. Furthermore, there are some recent new approaches for CM processes; amidation by reactive extrusion has been developed as a solventless synthesis method and has been used for the preparation of teriflunomide and moclobemide APIs [27].

5. Solubility Parameters

Solubility parameters (SP) are used to characterize substances in solvent replacement strategies. The Hildebrand SP (δ) has the basis of regular solution theory [28], and its development in solubility theory relates the cohesive energy density defined by Equation (1) to the activity coefficient [29].

$$\delta \equiv (\Delta \underline{U}^{\text{vap}} / \underline{V})^{1/2} \tag{1}$$

In Equation (1), $\underline{U}$ and $\underline{V}$ are the molar internal energy of vaporization and molar volume of the substance in its liquid state, respectively. The definition of the Hildebrand SP is typically simplified by replacing $\underline{U}$ with $(\underline{H} - P\underline{V})$ and assuming ideal gas behavior:

$$\delta = ((\Delta \underline{H}^{\text{vap}} - RT)/\underline{V})^{1/2} \tag{2}$$

Hansen [30] divided the total cohesive energy given in Equation (1) into three parts: (i) dispersion (van der Waals (London) forces) interactions (δ_{d}), hydrogen bonding interactions (δ_{h}), and polar (or dipole-dipole) interactions (δ_{p}). Hansen solubility parameters (HSPs) are used to determine a solubility parameter distance (Ra) between two substances "1" and "2" as follows:

$$(\text{Ra})^2 = 4 \cdot (\delta_{\text{d1}} - \delta_{\text{d2}})^2 + (\delta_{\text{h1}} - \delta_{\text{h2}})^2 + (\delta_{\text{p1}} - \delta_{\text{p2}})^2 \tag{3}$$

where the sphere provides a region of favorable solvation for a solute "1" and solvent "2", i.e., as values of Ra become closer to zero according to a chosen solvent with given HSP values, affinity becomes higher, and the solubility of the solute in the solvent should increase. The factor of four in Equation (3) is empirical and adds statistical weighting to dispersion interactions as being most important in solvation. By taking a substance such as a polymer or biomolecule and seeing whether it dissolves into solvents with known HSP values, the radius of interaction (Ro) can be determined for that compound. Then, a relative energy difference can be defined as follows:

$$\text{RED} = \text{Ra}/\text{Ro} \tag{4}$$

and solvents or solvent mixtures that have RED < 1 are candidates that dissolve the compound. It is possible, for example, for two solvents outside of the solvation sphere to be mixed, such that they form a good solvent as mixture for a polymer. HSP theory has been used to estimate the solubilities of anti-inflammatory drugs in pure and mixed solvents [31]. Fractional HSP values, which can be plotted on ternary diagrams to facilitate the assessment of interactions, have been used to identify green extraction solvents for alkaloids [32] and to screen solvent mixtures for pharmaceutical cocrystal formation [33]. HSP is a powerful tool used for solvent screening and is especially useful for large molecules, such as polymers or biomolecules, as highlighted by Abbott [34].

In comparing the Hildebrand solubility parameter theory with that of the Hansen solubility theory, the Hildebrand solubility parameter theory has some notable failures in predicting miscibility between materials [30]. However, in a critical comparison of solvent selection for 75 polymers, both theories gave similar results in predicting polymer—solvent miscibility [35]. Namely, Hildebrand SP had a prediction accuracy of 60% for solvents and 76% for non-solvents, whereas HSP had a prediction accuracy of 67% for solvents and 76% for non-solvents [35]. On the other hand, for polar polymers, the Hildebrand SP theory gave a prediction accuracy of only 57% [35]. Both Hildebrand solubility parameters and Hansen solubility parameters are useful screening tools for solvent replacement. Hildebrand SP theory is simple and provides qualitative estimation of solvent interactions for nonpolar molecules or slightly polar molecules; Hansen SP theory accounts for detailed molecular interactions and is applicable to both nonpolar and polar molecules. HSP can be applied to complex molecules, such as lignin [36] or phytochemicals [37]; however, HSP is qualitative when hydrogen bond donor (HBD) and hydrogen bond acceptor (HBA) molecular systems are considered [38].

6. Empirical Polarity Scales

Reichardt $E_T(30)$ parameters are based on the solvatochromic properties of Betaine 30 dye and provide the sensitive characterization of solvent polarity. Reichardt E_T^N values are normalized based on the $E_T(30)$ values of water and tetramethylsilane. Reichardt parameters are firmly established in the chemical literature and form the basis of a widely used polarity scale for organic chemicals [6].

Kamlet—Taft (KT) parameters are based on the solvatochromism of dyes specific to Lewis acidity (α), Lewis basicity (β), and dipolarity/polarizability (π^*) and have independent scales that depend on reference solvents [39]. The Kamlet—Taft polarity scales are meant to have values of α, β, and π^* that are between zero and one; however, when a solvent has a Lewis acidity, Lewis basicity, or dipolarity/polarizability that is outside of the range of reference compounds, ($\pi^* = 0$ (cyclohexane) and $\pi^* = 1$ (dimethylsulfoxide)) values of KT parameters can be greater than unity or less than zero.

Catalán parameters improved the KT parameter approach by using specific dyes for solvent polarizability (SP), solvent dipolarity (SdP), solvent acidity (SA), and solvent basicity (SB) parameters rather than by average values, as in the KT approach. Catalán parameters separate the polarizability (SP) and dipolarity (SdP) contributions of the KT parameter approach. All three scales have wide use in the chemical literature, although there are issues in data reduction methods and parameter values, as pointed out by Spange et al. [40], who reanalyzed polarity scales considering molar concentrations of the solvent (*N*), and Spange and Weiß [41], who proposed a method to unify the acid—based (pKa) and density effects of hydrogen bond donor solvents.

According to Reichardt and Welton [6], common molecular solvents (Figure 2) can be roughly divided into three groupings: (i) dipolar protic (HBD), $E_T^N > 0.5$; (ii) dipolar aprotic (HBA), $0.3 < E_T^N < 0.5$; and (iii) apolar (non-HBD or nonpolar), $E_T^N < 0.3$. Examination of the KT dipolarity/polarizability parameters (Figure 2) shows that longer chain hydrocarbons have π^* values less than zero, and water has a π^* greater than unity, which is due to the choice of reference solvents in the KT method. Most solvent replacement strategies consider Reichardt, Kamlet—Taft or Catalán parameters in their analysis. For example, dipolar aprotic solvents generally have high KT basicity and low KT acidity (Figure 3). Direct replacement solvents for dipolar aprotics could be N-butyl-2-pyrrolidinone (NBP), Cyrene^{TM} (Cyr), γ-valerolactone (GVL), γ-butyrolactone (GBL), eucalyptol (Eupt), tetramethyloxolane (TMO), dimethyl isosorbide (DMI), or cyclopentyl methyl ether (CPME). However, many solvents have E_T^N polarity values that are much lower than that of dipolar aprotics (Figure 2) and KT acidities that are either too high or KT basicities that are too low (Figure 3) to allow direct replacement of dipolar aprotics. Nevertheless, the range of Kamlet—Taft parameters of dipolar aprotics provide valuable information for considering mixed solvents and mixed solvent composition.

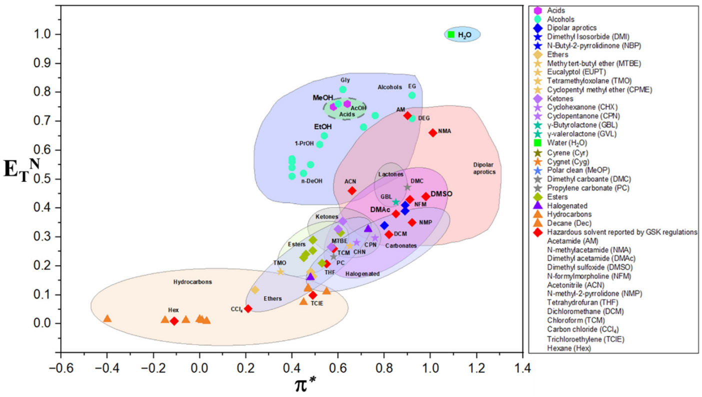

Figure 2. Reichardt E_T^N parameters plotted against Kamlet—Taft dipolarity/polarizability parameters for selected molecular solvents.

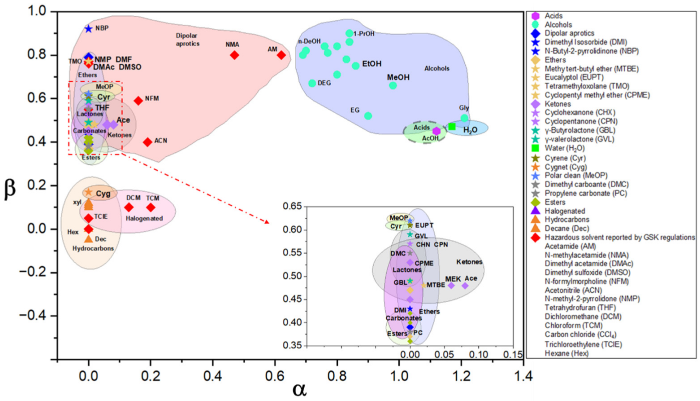

Figure 3. Kamlet—Taft basicity parameter plotted against acidity parameter for selected molecular solvents.

7. Opportunities with Mixed Solvents

Mixtures of solvents (mixed solvents) allow one to vary the chemical properties of the solution in a unique number of ways. For example, when an HBD solvent is mixed with an HBA solvent, KT parameters vary continuously with composition (Figure 4). KT parameters of mixed solvents can show synergistic behavior, which means that their β or π^* values can be higher than the KT parameters of the pure solvents (Figure 4), especially when water is the HBD solvent. Duereh et al. [42] showed that there is a clear relationship between microscopic (local) polarity, complex molecule (HBD—HBA solvent pairs) interactions, and synergistic behavior in thermodynamic properties (Figure 5).

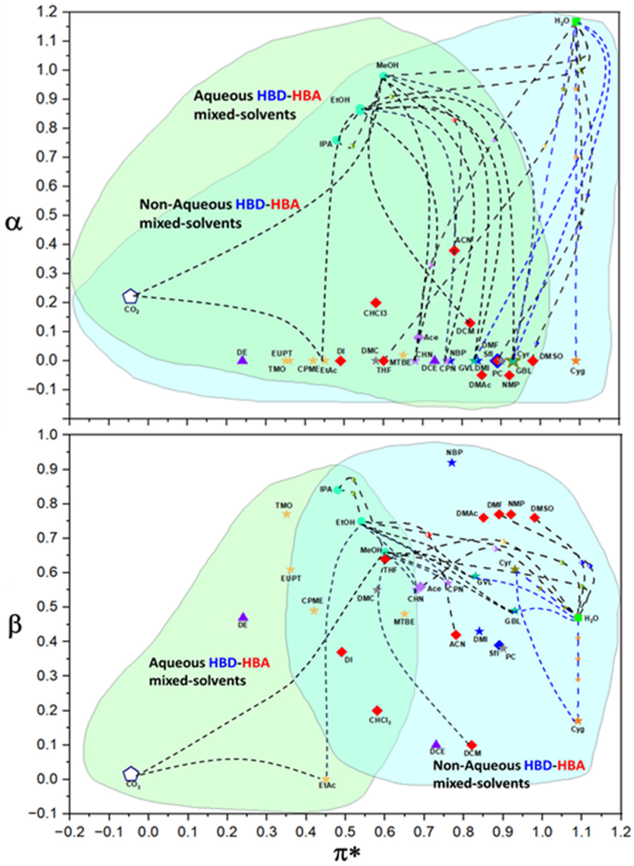

Figure 4. Kamlet—Taft acidity (α) and basicity (β) versus dipolar/polarizability (π^*) for aqueous and non-aqueous mixed solvents and pure solvents. Dashed lines show approximate behavior of mixed solvent KT parameters with composition.

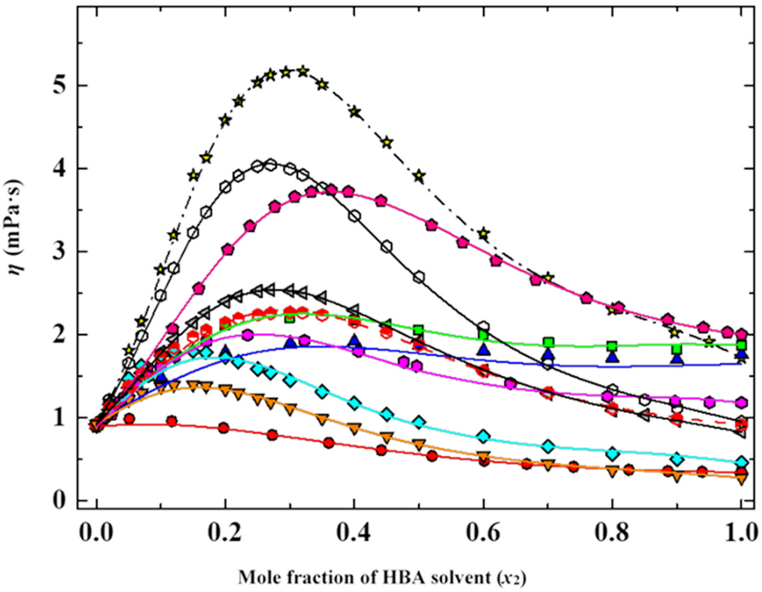

Figure 5. Dynamic viscosity (η) of water (HBD) –hydrogen bond acceptor (HBA) mixed solvent systems as a function of mole fraction of HBA solvent (x_2) at 25 °C. HBA solvents are ordered in terms of Hunter basicity (β_2^H) values (low to high): acetonitrile (● ACN), γ-valerolactone (🟩 GVL), γ-butyrolactone (▲ GBL), tetrahydrofuran (◇ THF), 1,4-dioxane (⬢ DI), acetone (▽ Ace), pyridine (⬣ PYR), *N*-methyl-2-pyrrolidone (★ NMP), *N*,*N*-dimethylformamide (◂ DMF), *N*,*N*-dimethylacetamide (⬡ DMA), and dimethyl sulfoxide (⬟ DMSO). Reprinted with permission from [42]. Copyright American Chemical Society, 2017.

Thus, solvent composition of mixed solvents allows one to vary microscopic polarity (local composition) and the concentration of HBD—HBA complex molecules that can be used advantageously in solvent replacement schemes.

In this section, strategies for using mixed solvents to replace hazardous chemicals are highlighted for chromatography solvents, CO_2 expanded liquids, supercritical fluids, low-transition temperature mixtures, switchable solvents, and HBD—HBA mixtures of molecular solvents.

7.1. Chromatography Solvents

In chromatographic methods, great progress has been made with the introduction of mixed solvents, such as ethyl acetate (EtAc)-ethanol (EtOH) in heptanes being demonstrated as a superior replacement for dichloromethane (DCM) [43]. Mixed solvent stock solutions are marketed by leading chemical suppliers for HPLC, TLC, and flash chromatography (FC) methods [44], confirming the success of the EtAc—ethanol mixtures.

The reason why EtAc—EtOH in a heptane mixed solvent system can replace DCM can be understood by examining the variation in KT parameters of the mixture compared with the KT parameters of the DCM—MeOH system. In this case, EtOH is the HBD solvent, EtAc is the HBA solvent, and the heptanes have low overall KT acidity for the mobile phase. Composition variation of EtAc–EtOH mixtures allows for the fine control of the basicity and dipolarity/polarizability that transverse methanol KT parameters (Figure 4).

To replace hexane, CO_2–EtAc has been suggested to be applicable to thin-layer chromatography (Table 3), and CO_2–MeOH has been demonstrated to be applicable to flash chromatography [45]. The entire corporate chemistry division of Syngenta (Table 3) reduced the overall volume of seven hazardous dipolar aprotic solvents (DCM, $CHCl_3$, DCE, DI, DME, DMF, DE) by 75% over a period of two years by using solvent replacement (e.g., EtAc–EtOH mixtures for DCM) and by emphasizing reverse phase chromatography for the separation of polar compounds [46] (Table 3); however, DMF usage increased during that period. Solvent pairs, such as cyclohexanone–MeOH, cyclohexanone–EtOH, cyclopentanone–MeOH, cyclopentanone–EtOH, GBL–MeOH, GBL–EtOH, GBL–water, GVL–MeOH, GVL–EtOH, and GVL–water, have been demonstrated as replacements for NMP or DMF in polyamide synthesis and, thus, have possibilities as solvent replacements in analytical method development [47].

Improvements in high-pressure liquid chromatography (HPLC) have been made with the introduction of ultra-high-pressure liquid chromatography (UHPLC), supercritical fluid chromatography (SFC), and ultra-high-pressure supercritical fluid chromatography (UHPSFC), which reduce the amount of solvents necessary in analyses while improving resolution [48]. When UHPSFC—tandem mass spectroscopy is employed, the determination of plant hormones (cytokinins) can be analyzed in 9 min at detection limits close to 0.03 fmol [49]. ACS has introduced the analytical method greenness score (AMGS) calculator developed by Hicks et al. [48] that ranks chromatography methods according to instrument energy, solvent energy, and solvent EHS scores [10].

Table 3. Replacement solvents for dichloromethane (DCM) in high-performance liquid (HPLC), thin-layer chromatography (TLC) and flash chromatography (FC) methods. Analytes consist of neutral, basic, acidic, and polar API.

Mixed Solvent [a]	**Analyte** [b]	**System**	**Ref.**
EtAc:EtOH (3:1) in heptanes	Neutral	LC	[43]
EtAc:EtOH in heptanes	Neutral	LC	[43]
iPrOH in heptanes	Neutral	LC	[43]
EtAc:EtOH (3:1) in MTBE	Neutral	LC	[43]
MeOH in MTBE	Neutral	LC	[43]
EtAc:EtOH (3:1) (2% NH_4OH) in heptanes	Basic	LC	[43]
MeOH: NH_4OH (10:1) in EtAc	Basic	LC	[43]
MeOH: NH_4OH (10:1) in MTBE	Basic	LC	[43]
EtAc:EtOH (3:1) (2% AcOH) in heptanes	Acidic	LC	[43]
MeOH:AcOH (10:1) in EtAc	Acidic	LC	[43]
MeOH:AcOH (10:1) in MTBE	Acidic	LC	[43]
EtAc:EtOH (3:1) in cyclohexane	n.s.	LC	[46]
acetonitrile:water	Polar	LC	[46]
tert-butyl acetate	All	LC	[50]
sec-butyl acetate	All	LC	[50]
ethyl isobutyrate	All	LC	[50]
methyl pivalate	All	LC	[50]
CO_2:EtAc	n.s.	TLC	[51]
EtAc in heptanes	n.s.	TLC	[51]
iPrOH in heptanes	n.s.	TLC	[51]
Ace in heptanes	n.s.	TLC	[51]
CO_2:MeOH	Neutral	FC	[45]
CO_2:EtAc	n.s.	FC	[51]
CO_2:Ace	n.s.	FC	[51]
CO_2:iPrOH	n.s.	FC	[51]

[a] AcOH: acetic acid; EtAc: ethyl acetate; MTBE: methyl tert-butyl ether; [b] n.s. not specified.

7.2. Expanded Liquids and Supercritical Fluids

Chemists and chemical engineers have introduced many new types of solvents through major research initiatives. CO_2-expanded bio-based liquids (CXL) have been demonstrated to be favorable for enantioselective biocatalysis [52], and supercritical fluids have been shown to be able to replace the hazardous solvents used in processing APIs [53]. Supercritical carbon dioxide ($scCO_2$) has been shown to have a wide application in processing bioactive lipids [54] and bioactive-related food ingredients [55]. A comprehensive review is available on the supercritical extraction of bioactive molecules from plant matrices [56]. A less-studied methodology in the supercritical extraction of bioactive molecules from natural sources is to eliminate organic co-solvents, such as ethanol or acetone, by replacing them with co-extractants that are typically oils from plant materials (Table 4).

Table 4. Co-extractant methodology for obtaining bio-products from supercritical CO_2 extraction of natural sources. Co-extractants: vegetable, drupe, legume, or seed oils or triacylglycerols (TAGs, triglycerides). Bio-product yields shown are maximum values normalized to 100%.

Natural Source	Co-Extractant	Bio-Product	T (°C)	P (MPa)	%Yield	Ref.
Algae	Soybean oil	astaxanthin	70	40	36	[57]
Brown seaweed	Sunflower oil	carotenoids	50	30	99	[58]
Carrots	Canola oil	carotenoids	70	55	92	[59]
Mangosteen	Virgin coconut oil	xanthonoids	70	43	31	[60]
Mangosteen	Virgin coconut oil	α-mangostin	60	35	76	[61]
Marigold	Medium-chain TAGs	lutein esters	65	43	98	[62]
Marigold	Soybean oil	lutein esters	53	30	93	[63]
Propolis	Virgin coconut oil	flavonoids	50	15	25	[64]
Pumpkin	Olive oil	carotenoid	50	25	41	[65]
Red sage	Peanut oil	diterpenoids	50	38	90	[66]
Tomato	Canola oil	lycopene	40	40	86	[67]
Tomato	Hazelnut oil	lycopene	66	45	40	[68]
Tomato skin	Olive oil	lycopene	75	35	58	[69]

In co-extractant methodology (Table 4), natural source substrates (petals, pericarp, etc.) are mixed with a natural oil (co-extractant) from a vegetable, drupe, legume, or seed (or fruit) before extraction with pure $scCO_2$. The co-extractant serves to increase the mass transfer of active components from the natural source to the supercritical phase by solubilization and polarity matching, and the co-extractant properties are enhanced due to $scCO_2$ dissolution into the co-extractant phase that causes the reduction of both surface tension and viscosity while enhancing heat transfer and related properties. Thus, with co-extractant methodology (Table 4), organic co-solvents are completely eliminated in $scCO_2$ extraction such that the contamination of extracts with organic compounds is not an issue. Furthermore, with co-extractant methodology, a final product is realized directly, the cultural processing of many types of food is possible, and food safety is strictly enhanced [70].

Related to developments in supercritical fluid theory, entropy based solubility parameters have been proposed that allow the extension of traditional solubility parameter theory to chemical systems containing supercritical fluids and ethanol [71] or systems at high temperatures or high pressures [72]. Experimental systems for measuring the KT parameters of methanol, ethanol, 2-propanol, and 1,1,1,2-tetrafluoroethane (HFC134a) co-solvents in CO_2 have been developed for assessing the HBD alcohol interactions with the HBA Lewis acidity of CO_2 in the supercritical state for quantifying polarity enhancements [73].

7.3. Low Transition Temperature Mixtures

Low transition temperature mixtures (LTTMs) are special combinations of mixed solvents made up of a hydrogen bond donor (HBD) molecule and a hydrogen bond acceptor (HBA) molecule for the purpose of liquefying the mixture [74]. Ionic liquids (ILs) are combinations of discrete organic moiety containing cations and anions that are in the liquid state at room temperature. Deep eutectic solvents (DESs) are mixtures of Lewis or Brønsted acids and bases that are in the liquid state at room temperature.

The possibility of using either ILs or DESs as solvent replacements or for processing APIs allows them to have many potential innovative applications due to their solvation and tailorable properties [75]. Issues with ILs are their cost, recyclability, and relatively higher viscosity compared to molecular solvents. While DESs are inexpensive, they share some of the same issues as ILs, and in addition, their separation from chemical products may be problematic due to the formation of strong HBD—HBA complexes with the API. One innovative approach that addresses some of these issues is to incorporate the IL chemical structure into the API to improve the bioavailability in drug delivery systems [76,77]. Reviews in the area of combining HBD- or HBA-containing APIs into the structure of ILs for drug delivery systems and other purposes show that there is much activity in this research area [78,79].

7.4. Switchable Solvents

Switchable polarity solvents (SPS) [80], switchable hydrophilicity solvents (SHS) [81], switchable water (SW) [82], solvent-assisted switchable water (SASW) [83], and high-pressure switchable water (HPSW) [84] are new types of mixed solvents that can change their polarity, hydrophilicity, or characteristics through the introduction or removal of CO_2. Switchable solvent systems would seem to have many applications in processing API, and furthermore, it could be highly advantageous if APIs with an existing or added amidine group could have modified hydrophilicity with CO_2 [85] for the purposes of separation, purification, or analysis.

7.5. HBD—HBA Mixtures of Molecular Solvents

The attractiveness of using molecular solvents to form HBD—HBA mixtures is that their EHS data are available, making it possible to assess their safety. With the EHS safety of the solvents assessed, it becomes possible to focus on the technical issue of solubilizing the API in the mixed solvent for processing operations.

Duereh et al. [86] developed a methodology for replacing dipolar aprotic solvents with safe HBD—HBA solvent pairs based on solubility and Kamlet—Taft windows (Figure 6). In the methodology [86], solvent pairs are evaluated from a database with user-defined solubility parameter and KT parameter windows of an API to determine working compositions and a prioritized list of mixed solvents according to a composite GSK score. The open-access software given in ref. [86] can be extended with activity coefficient models or quantum chemistry methods to broaden the scope of the methodology.

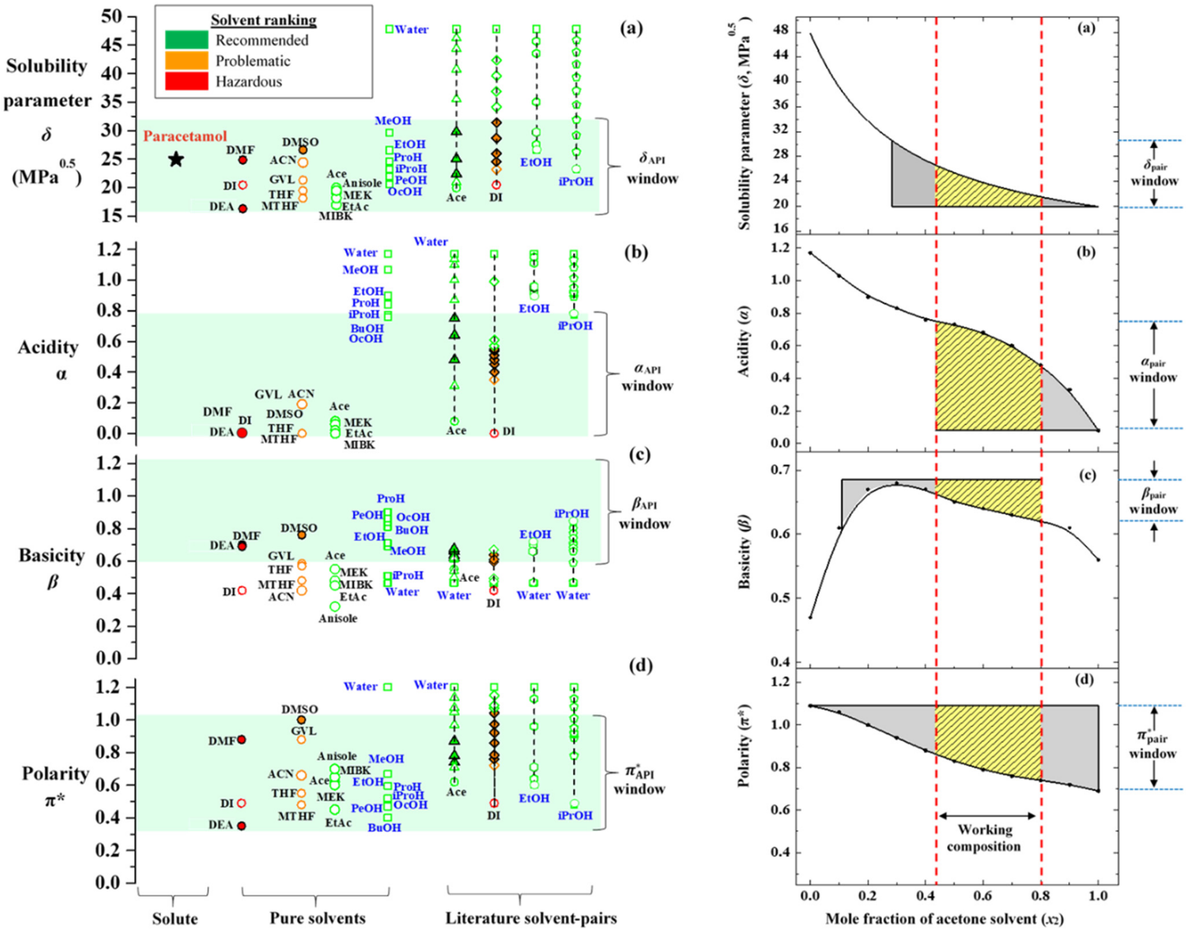

Figure 6. Concept of solubility parameter and Kamlet—Taft windows for identifying replacement solvents of an API (paracetamol): (**a**) window for solubility parameter, (**b**) window for API acidity,

(**c**) window for API basicity, (**d**) window for API dipolarity/polarizability. (**left**): Range of solubility and Kamlet—Taft parameters for dissolution of API in known solvents, including hazardous ones. (**right**): Range of solubility and Kamlet—Taft parameters superimposed onto theoretical calculations and available literature data to determine working composition ranges for a given mixed solvent pair (acetone—water). Reprinted with permission from ref. [86]. Copyright American Chemical Society, 2016.

In developing solvent replacement methodologies, physical properties can be important attributes for solvent selection. Jouyban and Acree [87] developed a single functional form for the correlation of viscosity, density, dielectric constant, surface tension, speed of sound, Reichardt E_T^N, molar volume, and isentropic compressibility of binary mixed solvents. Nazemieh et al. [88] reported data for a new set of mixed solvents, namely p-cymene with α-pinene, limonene, and citral correlated with the Jouyban—Acree model for physico-chemical properties (PCPs). Lee et al. [89] developed a local composition regular solution theory model for the correlation and prediction of API solubility in mixed solvents that had a single functional form for all compounds studied. The advantage of similar functional forms in correlative and predictive schemes for PCPs and activity coefficients is that machine learning techniques can be applied as the size of the database increases.

8. Kamlet—Taft Parameter Windows for APIs

APIs are commonly designated as being water soluble or non-water soluble. When the Reichardt E_T^N and KT parameters are plotted for mono-solvents that solvate 45 water-soluble APIs (Figure 7) and 47 water-insoluble APIs (Figure 8), the range of E_T^N and KT parameter values becomes visible, which characterizes the apparent polarity of the API. Although many water-soluble APIs are solvated by dipolar protic solvents ($E_T^N > 0.5$) and dipolar aprotic solvents ($0.3 < E_T^N < 0.5$) over a wide range of KT acidities (α), there are minimum values of π* and β required for solvation (Figure 7). On the other hand, water-insoluble APIs are solvated by a relatively narrow range of solvent polarities ($0.2 < E_T^N < 0.75$) and KT acidities (α), in which there are maximum values of π* and minimum values of β required for solvation (Figure 8).

When an API is dipolar protic, it interacts with basic dipolar aprotic solvents by forming hydrogen bonds with the solvent that must be stronger than those in the solid phase for solvation to occur. If the dipolar aprotic solvent is not basic or if it has insufficient basicity, then the dipolar protic API will have low solubility in the solvent, because dipole-dipole interactions generally do not have sufficient strength to break hydrogen bonds in the solid phase. On the other hand, when an API is dipolar aprotic, it interacts with dipolar aprotic solvents through dipole—dipole interactions that must be stronger than those in the solid phase for solvation to occur.

Conversely, if a solvent is dipolar protic, then the API must have sufficient basicity to accept hydrogen bonds that must be stronger than those in the solvent phase. Thus, scales for molecular basicity are extremely important in identifying potential new solvents and solvent systems. However, note that all KT α, β, and π* parameters influence API solubility in a mixed solvent and that they depend on the mixed solvent local composition, frequently in a non-linear or synergistic way [90,91].

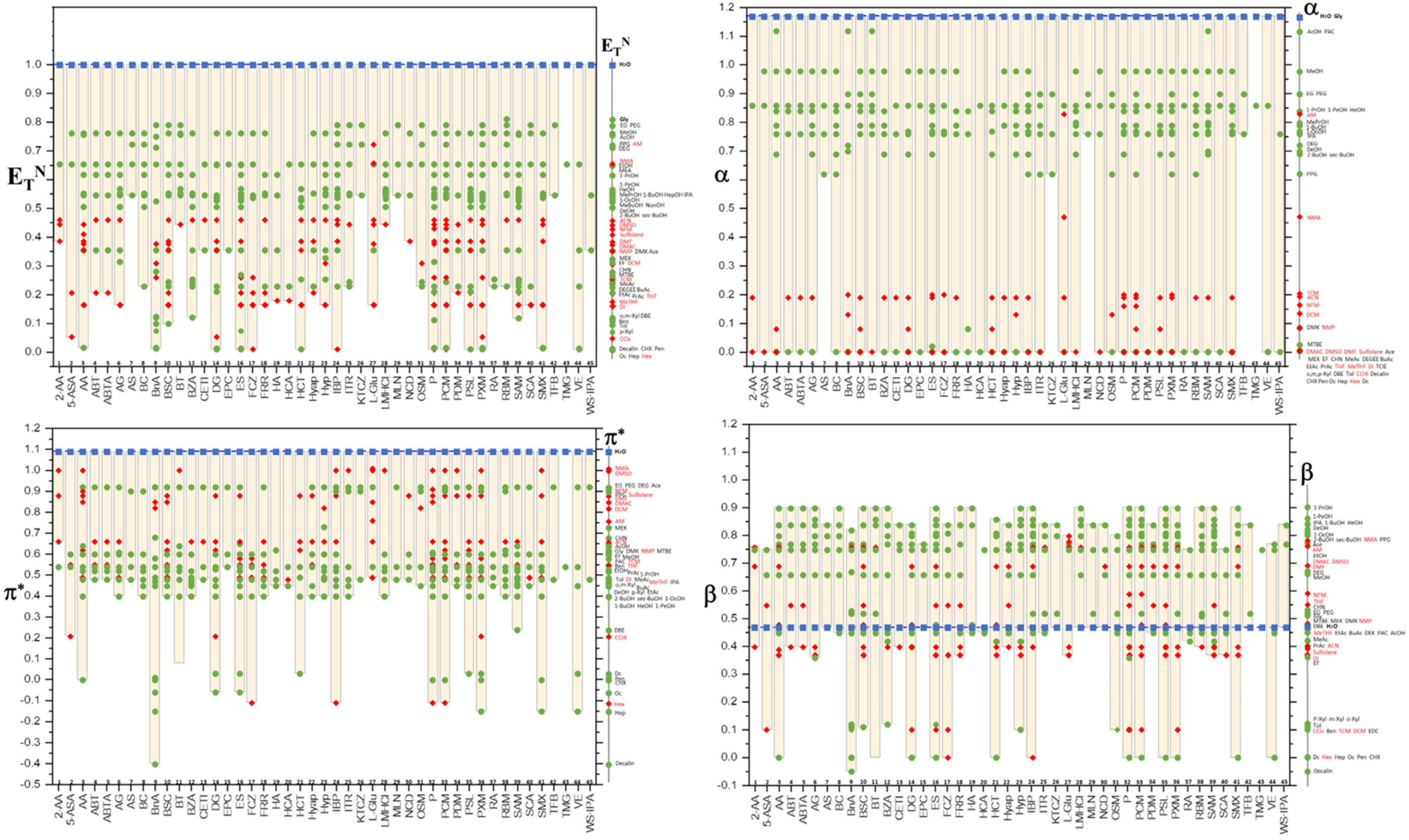

Figure 7. Reichardt E_T^N and Kamlet—Taft parameters of mono-solvents that solvate water-soluble APIs at ca. 25 °C. Data from refs. [1,92–302]. Water (Blue). Less-hazardous solvents (Green). Hazardous solvents (Red). Detailed information in Supplementary Materials.

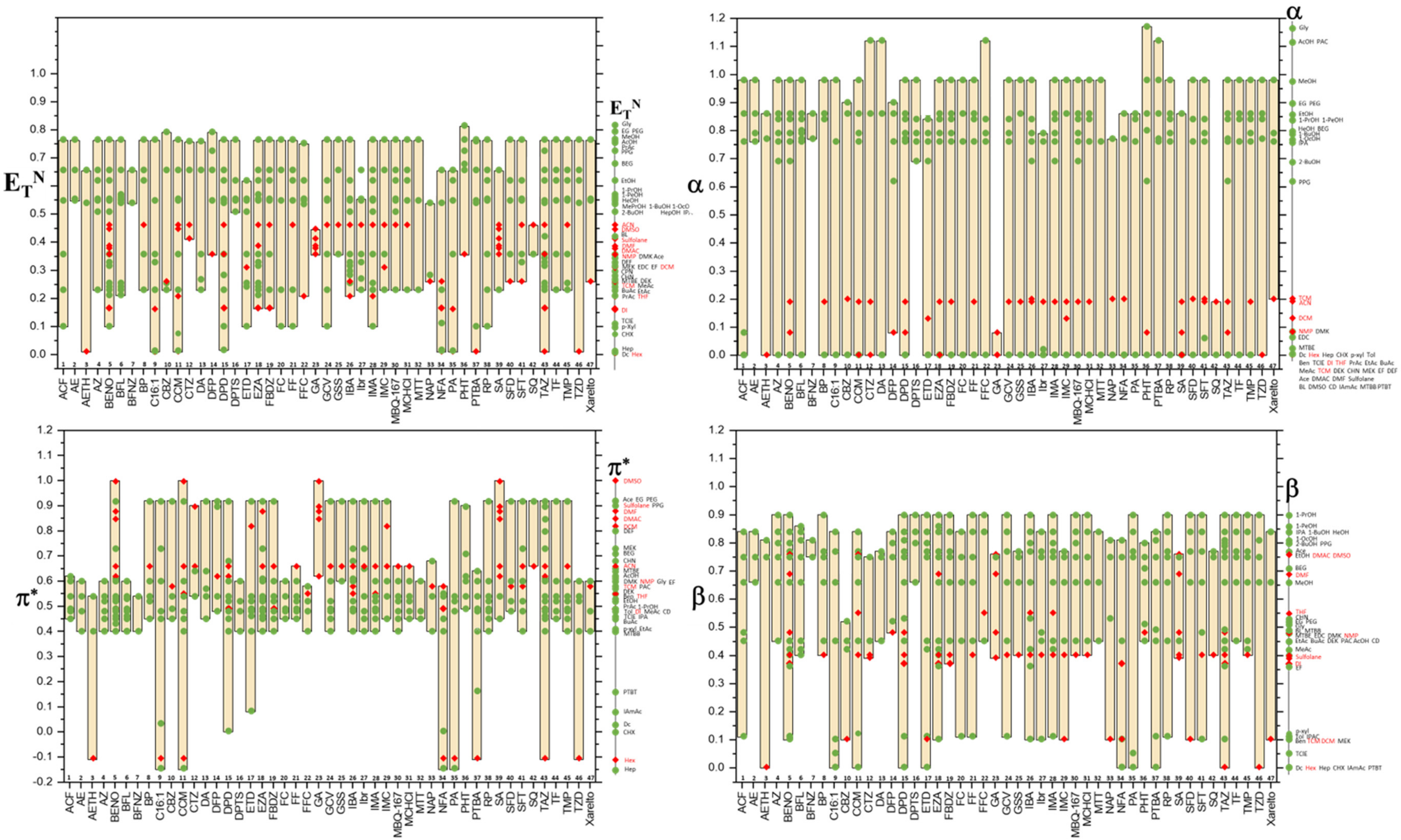

Figure 8. Reichardt E_T^N and Kamlet—Taft parameters of mono-solvents that solvate water-insoluble APIs at ca. 25 °C. Data from refs. [1,92–302]. Less-hazardous solvents (Green). Hazardous solvents (Red). Detailed information in Supplementary Materials.

Consider the HBD—HBA mixed-solvent systems shown in Figure 9. When water is used as the HBD solvent (Figure 9a–c), the HBA solvent addition (increasing x_2) lowers the KT α and generally lowers π^* values depending on the HBA polarity and causes KT β values to initially sharply increase, during which the microscopic polarity changes greatly due to the formation of complex molecules [91]. For example, water—lactone mixed solvents have been shown to exhibit synergy in KT basicity [91]. For an alcohol as the HBD solvent, the addition of an HBA solvent lowers the KT α, and it causes the KT π^* and KT β values to linearly increase or decrease with bulk composition depending on whether the pure alcohol KT π^* or KT β values are less than, equal to, or greater than those of the HBA solvent alcohol KT π^* or KT β values (Figure 9d–i). Duereh et al. showed examples of the case of ethanol (HBD) –cyclopentanone (HBA), in which mixed solvent composition can be used to favorably solvate an API (paracetamol), and they also showed a case of methanol (HBD) –cyclopentanone (HBA), in which mixed solvent composition failed to provide any solvation benefit, along with examples of 12 APIs [90].

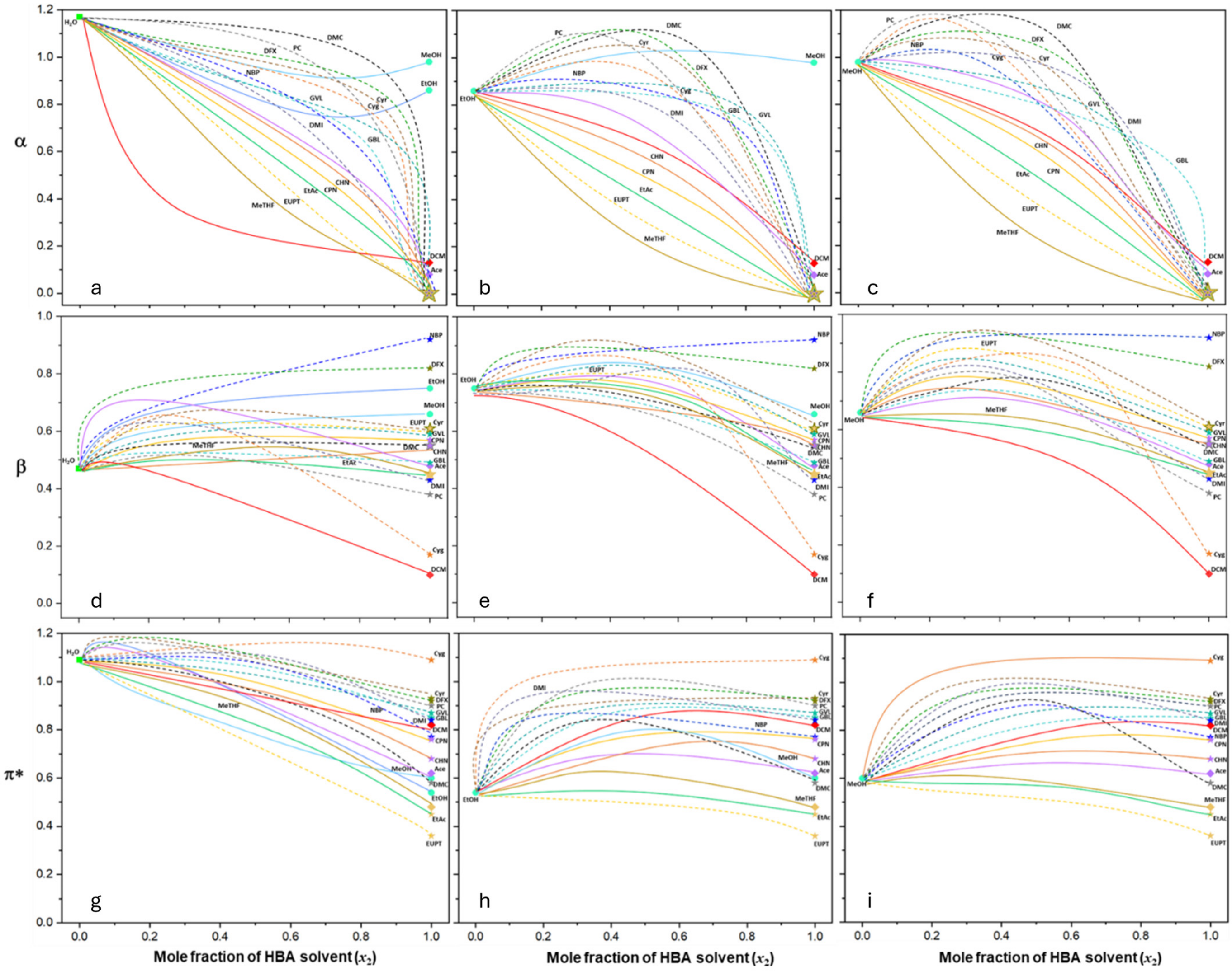

Figure 9. Kamlet—Taft acidity, basicity, and polarity for selected mixed solvents versus HBA solvent mole fraction: (**a**,**d**,**g**) water—HBA; (**b**,**e**,**h**) methanol—HBA; (**c**,**f**,**i**) ethanol—HBA. Trends shown are based on estimations (dashed lines) and actual data (solid lines) [51,86,90,91].

There are a number of HBD—HBA solvent combinations that could be replacements for hazardous solvents (Figure 9). For possible HBD solvents, water, methanol, and ethanol are good candidates. When water is the HBD solvent, possible candidate HBA solvents are acetone, acetic acid, acetonitrile, EtOH, MeOH, 2-MeTHF, water-2,2,5,5-tetramethyloxolane (TMO), DMI, Cyrene, Cygnet 0.0, or possibly diformylxylose. Safety and conditions must be considered carefully. For example, 2-MeTHF forms peroxides more rapidly than IPE, THF, or CPME when inhibitors are not present; ethereal solvents form peroxides [7]. Cygnet 0.0 is solid at room temperature [303], and 2-MeTHF in water has inverse temperature behavior up until temperatures of 340 K [304], meaning that its solubility in water decreases with increasing temperature.

When alcohols are used as the HBD solvent, cyclohexanone (CHN), cyclopentanone (CPN), many kinds of esters, GBL, GVL, eucalytol (water insoluble), or possibly MeSesamol (water insoluble) [305] or diformylxylose [306] are candidates. Furthermore, interesting HBA—HBA combinations, such as Cyrene—Cygnet 0.0, are being suggested for polymer syntheses [303] to replace hazardous dipolar aprotic solvents, and these types of HBA—HBA mixed solvents could have advantages in processing APIs.

9. Linear Solvation Energy Relationships (LSER)

Polarity parameters originally reported by Kamlet, Abboud, Abraham, and Taft were intended for use in linear solvation energy relationships (LSER) [307], expressed as follows:

$$XYZ = XYZ_0 + s(\pi^* + \mathrm{d}\delta) + a\alpha + b\beta + h\delta_\mathrm{H} + e\xi \tag{5}$$

where XYZ is a chemical phenomenon, XYZ_0 is a reference phenomenon, and s, a, b, h, and e are descriptors that are used to correlate polarity parameters to XYZ. Many adaptations have been made of Equation (5), and a well-known one is due to Abraham [308], which expressed water—octanol partition coefficients (*log* P) and gas—solvent partition coefficient (*log* K) as follows [309]:

$$\mathit{log}\ (P) = \mathrm{c} + \mathrm{e}\mathbf{E} + \mathrm{s}\mathbf{S} + \mathrm{a}\mathbf{A} + \mathrm{b}\mathbf{B} + \mathrm{v}\mathbf{V} \tag{6}$$

$$\mathit{log}\ (K) = \mathrm{c} + \mathrm{e}\mathbf{E} + \mathrm{s}\mathbf{S} + \mathrm{a}\mathbf{A} + \mathrm{b}\mathbf{B} + \mathrm{v}\mathbf{L} \tag{7}$$

Where the bold symbols are properties of the solute related to excess molar refraction (**E**), dipolarity/polarizability (**S**), hydrogen bond acidity (**A**), Lewis basicity (**B**), McGowan's molecular volume (**V**), and gas-to-hexadecane partition coefficient (**L**). LSER models are directly applicable to predict the solubility of APIs in solvents [309]. LSER models are widely used in the field of chromatography for characterizing columns and estimating retention times [310,311] or in the analysis of petroleum distillate conditions with group contribution activity coefficient models such as UNIFAC [312], but they do not appear to have been used more broadly (in reverse) in mixed solvent replacement schemes, although environmentally related partition coefficients are incorporated into life-cycle assessment tools, such as EPA's CompTox chemical dashboard system [313] or machine learning studies for solvent characterization factors [314].

10. Conclusions

In this work, several strategies were highlighted for the replacement of hazardous dipolar aprotic solvents related to pharmaceutical and bio-related compounds. Solvent guides form the basis of solvent replacement and consider categories of safety, human health, environment, waste, and sustainability. Linking online solvent selection sites with GSK, CHEM21, ECHA, and other guidelines would allow for the efficient dissemination of solvent replacements.

An example of drop-in replacement solvents and several mixed solvent combinations for synthesizing APIs is one strategy that shows it is possible for academia and the industry to replace hazardous dipolar aprotic solvents by adopting new chemical systems that are both efficient and safe. The universal guide for the replacement of hazardous dipolar aprotic solvents in synthetic chemistry is one of the key strategies.

Mixed solvents can be used in many ways to replace hazardous solvents, often with a performance benefit. Dichloromethane can be replaced by ethanol (HBD) and ethyl acetate (HBA) mixed solvents, as is evident from marketed stock solutions by chemical companies. The use of CO_2 with esters or alcohols instead of hexane or chlorinated hydrocarbons is seen to be effective for thin-layer, flash, and supercritical chromatography, and with the introduction of marketed industrial analytical equipment, it is clear that the new technology will become established.

Expanded liquids, supercritical fluids, low-transition temperature (HBD—HBA) mixtures, and switchable solvents all offer safer chemical systems that have low energy, performance, and sustainability benefits. Chemical systems based on HBD—HBA mixtures of molecular solvents for processing APIs offer a simple way to replace hazardous solvents by considering the range of solubility parameters, Reichardt polarity, and Kamlet—Taft parameters of the pure components. Reichardt polarity and Kamlet—Taft parameters of pure components are necessary physical properties for the development of solvent replacement strategies. By using the available solubility data of APIs in mono-solvents, new mixed solvent combinations can be seen.

11. Future Outlook

Presently, there are many measurements of Reichardt polarity and Kamlet—Taft parameters of pure compounds, but far fewer measurements have been made for mixed solvent systems that can potentially replace hazardous dipolar aprotic solvents. Many new measurements are needed of Reichardt polarity and Kamlet—Taft parameters of HBD—HBA and HBA—HBA mixed solvents, especially those systems such as ethanol—ethyl acetate, to understand fundamental interactions of complex molecules with APIs.

Theoretical methods applied to HBD—HBA systems could greatly accelerate the identification of new chemical systems for processing APIs. COSMO-RS is able to quantitatively predict Kamlet—Taft parameters for both molecular solvents and deep eutectic solvents [315]. COSMO-RS gives qualitative predictions of Hansen solubility parameters [316], which is encouraging because the values of APIs could lead to a great reduction in experimental effort.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/liquids4020018/s1, Table S1. Water-soluble APIs solvated by monosolvents and their solvent polarity ($E_T{}^N$), Kamlet-Taft acidity (α), basicity (β) window, dipolarity/polarizability (π*) and corresponding literature. Solvents listed as hazardous in GSK solvent guide are highlighted in red. Table S2. Water-insoluble APIs solvated by monosolvents and their solvent polarity ($E_T{}^N$), Kamlet-Taft acidity (α), basicity (β) window, dipolarity/polarizability (π*) and corresponding literature. Solvents listed as hazardous in GSK solvent guide are highlighted in red.

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References

1. Reichardt, C. Empirical Parameters of Solvent Polarity as Linear Free-Energy Relationships. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 98–110. [CrossRef]
2. Krygowski, T.M.; Wrona, P.K.; Zielkowska, U.; Reichardt, C. Empirical parameters of lewis acidity and basicity for aqueous binary solvent mixtures. *Tetrahedron* **1985**, *41*, 4519–4527. [CrossRef]
3. Reichardt, C. Solvation Effects in Organic Chemistry: A Short Historical Overview. *J. Org. Chem.* **2022**, *87*, 1616–1629. [CrossRef] [PubMed]
4. Kamlet, M.J.; Taft, R.W. The Solvatochromic Comparison Method. I. The β-Scale Of Solvent Hydrogen-Bond Acceptor (HBA) Basicities. *J. Am. Chem. Soc.* **1976**, *98*, 377–383. [CrossRef]
5. Catalán, J. On the empirical scales of organic solvents established using probe/homomorph pairs. *J. Phys. Org. Chem.* **2021**, *34*, e4206. [CrossRef]
6. Reichardt, C.; Welton, T. *Solvents and Solvent Effects in Organic Chemistry*; Wiley-VCH Verlag GmbH & Co.: Weinheim, Germany, 2011. [CrossRef]
7. Alder, C.M.; Hayler, J.D.; Henderson, R.K.; Redman, A.M.; Shukla, L.; Shuster, L.E.; Sneddon, H.F. Updating and further expanding GSK's solvent sustainability guide. *Green Chem.* **2016**, *18*, 3879–3890. [CrossRef]
8. Prat, D.; Wells, A.; Hayler, J.; Sneddon, H.; McElroy, C.R.; Abou-Shehada, S.; Dunn, P.J. CHEM21 selection guide of classical- and less classical-solvents. *Green Chem.* **2016**, *18*, 288–296. [CrossRef]
9. ACS. ACS GCI Pharmaceutical Roundtable. Collaboration to Deliver a Solvent Selection Guide for the Pharmaceutical Industry. 2018. Available online: https://www.acs.org/content/dam/acsorg/greenchemistry/industriainnovation/roundtable/solvent-selection-guide.pdf (accessed on 16 December 2023).
10. ACS. Tools for Innovation in Chemistry. 2023. Available online: https://www.acsgcipr.org/tools-for-innovation-in-chemistry/ (accessed on 16 December 2023).
11. Byrne, F.P.; Jin, S.; Paggiola, G.; Petchey, T.H.M.; Clark, J.H.; Farmer, T.J.; Hunt, A.J.; Robert McElroy, C.; Sherwood, J. Tools and techniques for solvent selection: Green solvent selection guides. *Sustain. Chem. Process.* **2016**, *4*, 7. [CrossRef]
12. Diorazio, L.J.; Richardson, P.; Sneddon, H.F.; Moores, A.; Briddell, C.; Martinez, I. Making Sustainability Assessment Accessible: Tools Developed by the ACS Green Chemistry Institute Pharmaceutical Roundtable. *ACS Sustain. Chem. Eng.* **2021**, *9*, 16862–16864. [CrossRef]
13. Dixit, S.; Crain, J.; Poon, W.C.K.; Finney, J.L.; Soper, A.K. Molecular segregation observed in a concentrated alcohol–water solution. *Nature* **2002**, *416*, 829–832. [CrossRef]
14. Ono, T.; Horikawa, K.; Ota, M.; Sato, Y.; Inomata, H. Insight into the local composition of the Wilson equation at high temperatures and pressures through molecular simulations of methanol-water mixtures. *J. Chem. Eng. Data* **2014**, *59*, 1024–1030. [CrossRef]
15. Ono, T.; Ito, Y.; Ota, M.; Takebayashi, Y.; Furuya, T.; Inomata, H. Difference in aqueous solution structure at 293.2 and 473.2 K between ethanol and ethylene glycol via molecular dynamics. *J. Mol. Liq.* **2022**, *368*, 120764. [CrossRef]
16. Jordan, A.; Hall, C.G.J.; Thorp, L.R.; Sneddon, H.F. Replacement of Less-Preferred Dipolar Aprotic and Ethereal Solvents in Synthetic Organic Chemistry with More Sustainable Alternatives. *Chem. Rev.* **2022**, *122*, 6749–6794. [CrossRef] [PubMed]
17. ECHA. Candidate List of Substances of Very High Concern for Authorisation. 2023. Available online: https://echa.europa.eu/candidate-list-table (accessed on 24 December 2023).
18. Henderson, R.K.; Jiménez-González, C.; Constable, D.J.C.; Alston, S.R.; Inglis, G.G.A.; Fisher, G.; Sherwood, J.; Binks, S.P.; Curzons, A.D. Expanding GSK's solvent selection guide—Embedding sustainability into solvent selection starting at medicinal chemistry. *Green Chem.* **2011**, *13*, 854–862. [CrossRef]
19. Jiménez-González, C.; Curzons, A.D.; Constable, D.J.C.; Cunningham, V.L. Expanding GSK's Solvent Selection Guide—Application of life cycle assessment to enhance solvent selections. *Clean Technol. Environ. Policy* **2004**, *7*, 42–50. [CrossRef]
20. Diorazio, L.J.; Hose, D.R.J.; Adlington, N.K. Toward a More Holistic Framework for Solvent Selection. *Org. Process Res. Dev.* **2016**, *20*, 760–773. [CrossRef]
21. Gao, F.; Bai, R.; Ferlin, F.; Vaccaro, L.; Li, M.; Gu, Y. Replacement strategies for non-green dipolar aprotic solvents. *Green Chem.* **2020**, *22*, 6240–6257. [CrossRef]
22. Gabriel, C.M.; Keener, M.; Gallou, F.; Lipshutz, B.H. Amide and Peptide Bond Formation in Water at Room Temperature. *Org. Lett.* **2015**, *17*, 3968–3971. [CrossRef]
23. Dalla Torre, D.; Annatelli, M.; Aricò, F. Acid catalyzed synthesis of dimethyl isosorbide via dimethyl carbonate chemistry. *Catal. Today* **2023**, *423*, 113892. [CrossRef]
24. Sherwood, J.; Constantinou, A.; Moity, L.; McElroy, C.R.; Farmer, T.J.; Duncan, T.; Raverty, W.; Hunt, A.J.; Clark, J.H. Dihydrolevoglucosenone (Cyrene) as a bio-based alternative for dipolar aprotic solvents. *Chem. Commun.* **2014**, *50*, 9650–9652. [CrossRef]
25. Campos, J.F.; Scherrmann, M.-C.; Berteina-Raboin, S. Eucalyptol: A new solvent for the synthesis of heterocycles containing oxygen, sulfur and nitrogen. *Green Chem.* **2019**, *21*, 1531–1539. [CrossRef]
26. Domokos, A.; Nagy, B.; Szilágyi, B.; Marosi, G.; Nagy, Z.K. Integrated Continuous Pharmaceutical Technologies—A Review. *Org. Process Res. Dev.* **2021**, *25*, 721–739. [CrossRef]
27. Lavayssiere, M.; Lamaty, F. Amidation by reactive extrusion for the synthesis of active pharmaceutical ingredients teriflunomide and moclobemide. *Chem. Commun.* **2023**, *59*, 3439–3442. [CrossRef] [PubMed]

28. Hildebrand, J.H. solubility. xii. Regular solutions1. *J. Am. Chem. Soc.* **1929**, *51*, 66–80. [CrossRef]
29. Prausnitz, J.M.; Lichtenthaler, R.N.; Azevedo, E.G.D. *Molecular Thermodynamics of Fluid-Phase Equilibria*, 3rd ed.; Prentice Hall PTR: London, UK, 1999.
30. Hansen, C.M. Hansen Solubility Parameters. In *A User's Handbook*, 2nd ed.; CRC Press: Boca Raton, FL, USA, 2007. [CrossRef]
31. Takebayashi, Y.; Sue, K.; Furuya, T.; Yoda, S. Solubilities of Organic Semiconductors and Nonsteroidal Anti-inflammatory Drugs in Pure and Mixed Organic Solvents: Measurement and Modeling with Hansen Solubility Parameter. *J. Chem. Eng. Data* **2018**, *63*, 3889–3901. [CrossRef]
32. Wu, Y.; Li, W.; Vovers, J.; Thuan Lu, H.; Stevens, G.W.; Mumford, K.A. Investigation of green solvents for the extraction of phenol and natural alkaloids: Solvent and extractant selection. *Chem. Eng. J.* **2022**, *442*, 136054. [CrossRef]
33. Kumar, A.; Nanda, A. In-silico methods of cocrystal screening: A review on tools for rational design of pharmaceutical cocrystals. *J. Drug Deliv. Sci. Technol.* **2021**, *63*, 102527. [CrossRef]
34. Abbott, S. Solubility, similarity, and compatibility: A general-purpose theory for the formulator. *Curr. Opin. Colloid Interface Sci.* **2020**, *48*, 65–76. [CrossRef]
35. Venkatram, S.; Kim, C.; Chandrasekaran, A.; Ramprasad, R. Critical Assessment of the Hildebrand and Hansen Solubility Parameters for Polymers. *J. Chem. Inf. Model.* **2019**, *59*, 4188–4194. [CrossRef]
36. Ma, Q.; Yu, C.; Zhou, Y.; Hu, D.; Chen, J.; Zhang, X. A review on the calculation and application of lignin Hansen solubility parameters. *Int. J. Biol. Macromol.* **2024**, *256*, 128506. [CrossRef]
37. Novaes, F.J.M.; de Faria, D.C.; Ferraz, F.Z.; de Aquino Neto, F.R. Hansen Solubility Parameters Applied to the Extraction of Phytochemicals. *Plants* **2023**, *12*, 3008. [CrossRef] [PubMed]
38. Otárola-Sepúlveda, J.; Cea-Klapp, E.; Aravena, P.; Ormazábal-Latorre, S.; Canales, R.I.; Garrido, J.M.; Valerio, O. Assessment of Hansen solubility parameters in deep eutectic solvents for solubility predictions. *J. Mol. Liq.* **2023**, *388*, 122669. [CrossRef]
39. Kamlet, M.J.; Abboud, J.L.; Taft, R.W. The solvatochromic comparison method. 6. The .pi.* scale of solvent polarities. *J. Am. Chem. Soc.* **1977**, *99*, 6027–6038. [CrossRef]
40. Spange, S.; Weiß, N.; Schmidt, C.H.; Schreiter, K. Reappraisal of Empirical Solvent Polarity Scales for Organic Solvents. *Chem. Methods* **2021**, *1*, 42–60. [CrossRef]
41. Spange, S.; Weiß, N. Empirical Hydrogen Bonding Donor (HBD) Parameters of Organic Solvents Using Solvatochromic Probes—A Critical Evaluation. *ChemPhysChem* **2023**, *24*, e202200780. [CrossRef] [PubMed]
42. Duereh, A.; Sato, Y.; Smith, R.L.; Inomata, H.; Pichierri, F. Does Synergism in Microscopic Polarity Correlate with Extrema in Macroscopic Properties for Aqueous Mixtures of Dipolar Aprotic Solvents? *J. Phys. Chem. B* **2017**, *121*, 6033–6041. [CrossRef]
43. Taygerly, J.P.; Miller, L.M.; Yee, A.; Peterson, E.A. A convenient guide to help select replacement solvents for dichloromethane in chromatography. *Green Chem.* **2012**, *14*, 3020–3025. [CrossRef]
44. Sigma-Aldrich. Greener Chromatography Solvents. 2015. Available online: https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Sigma-Aldrich/General_Information/1/greener-chromatography-solvents-82207.pdf (accessed on 27 December 2023).
45. McClain, R.; Rada, V.; Nomland, A.; Przybyciel, M.; Kohler, D.; Schlake, R.; Nantermet, P.; Welch, C.J. Greening Flash Chromatography. *ACS Sustain. Chem. Eng.* **2016**, *4*, 4905–4912. [CrossRef]
46. Dutta, P.; McGranaghan, A.; Keller, I.; Patil, Y.; Mulholland, N.; Murudi, V.; Prescher, H.; Smith, A.; Carson, N.; Martin, C.; et al. A case study in green chemistry: The reduction of hazardous solvents in an industrial R&D environment. *Green Chem.* **2022**, *24*, 3943–3956. [CrossRef]
47. Duereh, A.; Sato, Y.; Smith, R.L.; Inomata, H. Replacement of Hazardous Chemicals Used in Engineering Plastics with Safe and Renewable Hydrogen-Bond Donor and Acceptor Solvent-Pair Mixtures. *ACS Sustain. Chem. Eng.* **2015**, *3*, 1881–1889. [CrossRef]
48. Hicks, M.B.; Farrell, W.; Aurigemma, C.; Lehmann, L.; Weisel, L.; Nadeau, K.; Lee, H.; Moraff, C.; Wong, M.; Huang, Y.; et al. Making the move towards modernized greener separations: Introduction of the analytical method greenness score (AMGS) calculator. *Green Chem.* **2019**, *21*, 1816–1826. [CrossRef]
49. Petřík, I.; Pěnčík, A.; Stýskala, J.; Tranová, L.; Amakorová, P.; Strnad, M.; Novák, O. Rapid profiling of cytokinins using supercritical fluid chromatography coupled with tandem mass spectrometry. *Anal. Chim. Acta* **2024**, *1285*, 342010. [CrossRef]
50. Lynch, J.; Sherwood, J.; McElroy, C.R.; Murray, J.; Shimizu, S. Dichloromethane replacement: Towards greener chromatography via Kirkwood–Buff integrals. *Anal. Methods* **2023**, *15*, 596–605. [CrossRef] [PubMed]
51. Duereh, A.; Smith, R.L. Strategies for using hydrogen-bond donor/acceptor solvent pairs in developing green chemical processes with supercritical fluids. *J. Supercrit. Fluids* **2018**, *141*, 182–197. [CrossRef]
52. Hoang, H.N.; Nagashima, Y.; Mori, S.; Kagechika, H.; Matsuda, T. CO_2-expanded bio-based liquids as novel solvents for enantioselective biocatalysis. *Tetrahedron* **2017**, *73*, 2984–2989. [CrossRef]
53. Kankala, R.K.; Zhang, Y.S.; Wang, S.-B.; Lee, C.-H.; Chen, A.-Z. Supercritical Fluid Technology: An Emphasis on Drug Delivery and Related Biomedical Applications. *Adv. Healthc. Mater.* **2017**, *6*, 1700433. [CrossRef] [PubMed]
54. Temelli, F. Perspectives on supercritical fluid processing of fats and oils. *J. Supercrit. Fluids* **2009**, *47*, 583–590. [CrossRef]
55. Temelli, F. Perspectives on the use of supercritical particle formation technologies for food ingredients. *J. Supercrit. Fluids* **2018**, *134*, 244–251. [CrossRef]
56. De Melo, M.M.R.; Silvestre, A.J.D.; Silva, C.M. Supercritical fluid extraction of vegetable matrices: Applications, trends and future perspectives of a convincing green technology. *J. Supercrit. Fluids* **2014**, *92*, 115–176. [CrossRef]

57. Krichnavaruk, S.; Shotipruk, A.; Goto, M.; Pavasant, P. Supercritical carbon dioxide extraction of astaxanthin from Haematococcus pluvialis with vegetable oils as co-solvent. *Bioresour. Technol.* **2008**, *99*, 5556–5560. [CrossRef]
58. Saravana, P.S.; Getachew, A.T.; Cho, Y.-J.; Choi, J.H.; Park, Y.B.; Woo, H.C.; Chun, B.S. Influence of co-solvents on fucoxanthin and phlorotannin recovery from brown seaweed using supercritical CO_2. *J. Supercrit. Fluids* **2017**, *120*, 295–303. [CrossRef]
59. Sun, M.; Temelli, F. Supercritical carbon dioxide extraction of carotenoids from carrot using canola oil as a continuous co-solvent. *J. Supercrit. Fluids* **2006**, *37*, 397–408. [CrossRef]
60. Kok, S.L.; Lee, W.J.; Smith, R.L.; Suleiman, N.; Jom, K.N.; Vangnai, K.; Bin Sharaai, A.H.; Chong, G.H. Role of virgin coconut oil (VCO) as co-extractant for obtaining xanthones from mangosteen (*Garcinia mangostana*) pericarp with supercritical carbon dioxide extraction. *J. Supercrit. Fluids* **2021**, *176*, 105305. [CrossRef]
61. Lee, W.J.; Ng, C.C.; Ng, J.S.; Smith, R.L.; Kok, S.L.; Hee, Y.Y.; Lee, S.Y.; Tan, W.K.; Zainal Abidin, N.H.; Halim Lim, S.A.; et al. Supercritical carbon dioxide extraction of α-mangostin from mangosteen pericarp with virgin coconut oil as co-extractant and in-vitro bio-accessibility measurement. *Process Biochem.* **2019**, *87*, 213–220. [CrossRef]
62. Gao, Y.; Liu, X.; Xu, H.; Zhao, J.; Wang, Q.; Liu, G.; Hao, Q. Optimization of supercritical carbon dioxide extraction of lutein esters from marigold (*Tagetes erecta* L.) with vegetable oils as continuous co-solvents. *Sep. Purif. Technol.* **2010**, *71*, 214–219. [CrossRef]
63. Ma, Q.; Xu, X.; Gao, Y.; Wang, Q.; Zhao, J. Optimisation of supercritical carbon dioxide extraction of lutein esters from marigold (*Tagetes erect* L.) with soybean oil as a co-solvent. *Int. J. Food Sci. Technol.* **2008**, *43*, 1763–1769. [CrossRef]
64. Pattiram, P.D.; Abas, F.; Suleiman, N.; Mohamad Azman, E.; Chong, G.H. Edible oils as a co-extractant for the supercritical carbon dioxide extraction of flavonoids from propolis. *PLoS ONE* **2022**, *17*, e0266673. [CrossRef]
65. Shi, X.; Wu, H.; Shi, J.; Xue, S.J.; Wang, D.; Wang, W.; Cheng, A.; Gong, Z.; Chen, X.; Wang, C. Effect of modifier on the composition and antioxidant activity of carotenoid extracts from pumpkin (Cucurbita maxima) by supercritical CO_2. *LWT-Food Sci. Technol.* **2013**, *51*, 433–440. [CrossRef]
66. Fikri, I.; Yulianah, Y.; Lin, T.-C.; Lin, R.-W.; Chen, U.-C.; Lay, H.-L. Optimization of supercritical fluid extraction of dihydrotanshinone, cryptotanshinone, tanshinone I, and tanshinone IIA from Salvia miltiorrhiza with a peanut oil modifier. *Chem. Eng. Res. Des.* **2022**, *180*, 220–231. [CrossRef]
67. Saldaña, M.D.A.; Temelli, F.; Guigard, S.E.; Tomberli, B.; Gray, C.G. Apparent solubility of lycopene and β-carotene in supercritical CO_2, CO_2+ethanol and CO_2+canola oil using dynamic extraction of tomatoes. *J. Food Eng.* **2010**, *99*, 1–8. [CrossRef]
68. Vasapollo, G.; Longo, L.; Rescio, L.; Ciurlia, L. Innovative supercritical CO_2 extraction of lycopene from tomato in the presence of vegetable oil as co-solvent. *J. Supercrit. Fluids* **2004**, *29*, 87–96. [CrossRef]
69. Shi, J.; Yi, C.; Xue, S.J.; Jiang, Y.; Ma, Y.; Li, D. Effects of modifiers on the profile of lycopene extracted from tomato skins by supercritical CO_2. *J. Food Eng.* **2009**, *93*, 431–436. [CrossRef]
70. Yara-Varón, E.; Li, Y.; Balcells, M.; Canela-Garayoa, R.; Fabiano-Tixier, A.S.; Chemat, F. Vegetable oils as alternative solvents for green oleo-extraction, purification and formulation of food and natural products. *Molecules* **2017**, *22*, 1474. [CrossRef] [PubMed]
71. Ota, M.; Hashimoto, Y.; Sato, M.; Sato, Y.; Smith, R.L.; Inomata, H. Solubility of flavone, 6-methoxyflavone and anthracene in supercritical CO_2 with/without a co-solvent of ethanol correlated by using a newly proposed entropy-based solubility parameter. *Fluid Phase Equilibria* **2016**, *425*, 65–71. [CrossRef]
72. Ota, M.; Sugahara, S.; Sato, Y.; Smith, R.L.; Inomata, H. Vapor-liquid distribution coefficients of hops extract in high pressure CO_2 and ethanol mixtures and data correlation with entropy-based solubility parameters. *Fluid Phase Equilibria* **2017**, *434*, 44–48. [CrossRef]
73. Duereh, A.; Sugimoto, Y.; Ota, M.; Sato, Y.; Inomata, H. Kamlet-Taft Dipolarity/Polarizability of Binary Mixtures of Supercritical Carbon Dioxide with Cosolvents: Measurement, Prediction, and Applications in Separation Processes. *Ind. Eng. Chem. Res.* **2020**, *59*, 12319–12330. [CrossRef]
74. Francisco, M.; van den Bruinhorst, A.; Kroon, M.C. Low-Transition-Temperature Mixtures (LTTMs): A New Generation of Designer Solvents. *Angew. Chem. Int. Ed.* **2013**, *52*, 3074–3085. [CrossRef] [PubMed]
75. Smith, E.L.; Abbott, A.P.; Ryder, K.S. Deep Eutectic Solvents (DESs) and Their Applications. *Chem. Rev.* **2014**, *114*, 11060–11082. [CrossRef]
76. Moshikur, R.M.; Goto, M. Ionic Liquids as Active Pharmaceutical Ingredients (APIs). In *Application of Ionic Liquids in Drug Delivery*; Goto, M., Moniruzzaman, M., Eds.; Springer Singapore: Singapore, 2021; pp. 13–33. [CrossRef]
77. Md Moshikur, R.; Goto, M. Pharmaceutical Applications of Ionic Liquids: A Personal Account. *Chem. Rec.* **2023**, *23*, e202300026. [CrossRef]
78. Wu, X.; Zhu, Q.; Chen, Z.; Wu, W.; Lu, Y.; Qi, J. Ionic liquids as a useful tool for tailoring active pharmaceutical ingredients. *J. Control. Release* **2021**, *338*, 268–283. [CrossRef]
79. Moshikur, R.M.; Carrier, R.L.; Moniruzzaman, M.; Goto, M. Recent Advances in Biocompatible Ionic Liquids in Drug Formulation and Delivery. *Pharmaceutics* **2023**, *15*, 1179. [CrossRef] [PubMed]
80. Jessop, P.G.; Mercer, S.M.; Heldebrant, D.J. CO_2-triggered switchable solvents, surfactants, and other materials. *Energy Environ. Sci.* **2012**, *5*, 7240–7253. [CrossRef]
81. Cunha, I.T.; McKeeman, M.; Ramezani, M.; Hayashi-Mehedy, K.; Lloyd-Smith, A.; Bravi, M.; Jessop, P.G. Amine-free CO_2-switchable hydrophilicity solvents and their application in extractions and polymer recycling. *Green Chem.* **2022**, *24*, 3704–3716. [CrossRef]

82. Mercer, S.M.; Jessop, P.G. "Switchable water": Aqueous solutions of switchable ionic strength. *ChemSusChem* **2010**, *3*, 467–470. [CrossRef] [PubMed]
83. Liberato, V.S.; Ferreira, T.F.; MacDonald, A.R.; Dias Ribeiro, B.; Zarur Coelho, M.A.; Jessop, P.G. A CO_2-responsive method for separating hydrophilic organic molecules from aqueous solutions: Solvent-assisted switchable water. *Green Chem.* **2023**, *25*, 4705–4712. [CrossRef]
84. Cunha, I.T.; Yang, H.; Jessop, P.G. High pressure switchable water: An alternative method for separating organic products from water. *Green Chem.* **2021**, *23*, 3996–4007. [CrossRef]
85. Phan, L.; Jessop, P.G. Switching the hydrophilicity of a solute. *Green Chem.* **2009**, *11*, 307–330. [CrossRef]
86. Duereh, A.; Sato, Y.; Smith, R.L.; Inomata, H. Methodology for replacing dipolar aprotic solvents used in API processing with safe hydrogen-bond donor and acceptor solvent-pair mixtures. *Org. Process Res. Dev.* **2017**, *21*, 114–124. [CrossRef]
87. Jouyban, A.; Acree, W.E. A single model to represent physico-chemical properties of liquid mixtures at various temperatures. *J. Mol. Liq.* **2021**, *323*, 115054. [CrossRef]
88. Nazemieh, A.; Acree, W.E.; Jouyban, A. Further computations on physico-chemical properties of binary mixtures of p-cymene with α-pinene, limonene and citral. *J. Mol. Liq.* **2022**, *350*, 118211. [CrossRef]
89. Lee, J.L.; Chong, G.H.; Kanno, A.; Ota, M.; Guo, H.; Smith, R.L. Local composition-regular solution theory for analysis of pharmaceutical solubility in mixed-solvents. *J. Mol. Liq.* **2024**, *397*, 124012. [CrossRef]
90. Duereh, A.; Guo, H.; Honma, T.; Hiraga, Y.; Sato, Y.; Lee Smith, R.; Inomata, H. Solvent Polarity of Cyclic Ketone (Cyclopentanone, Cyclohexanone): Alcohol (Methanol, Ethanol) Renewable Mixed-Solvent Systems for Applications in Pharmaceutical and Chemical Processing. *Ind. Eng. Chem. Res.* **2018**, *57*, 7331–7344. [CrossRef]
91. Duereh, A.; Sato, Y.; Smith, R.L.; Inomata, H. Analysis of the Cybotactic Region of Two Renewable Lactone-Water Mixed-Solvent Systems that Exhibit Synergistic Kamlet-Taft Basicity. *J. Phys. Chem. B* **2016**, *120*, 4467–4481. [CrossRef] [PubMed]
92. Abbasi, M.; Vaez-Gharamaleki, J.; Fazeli-Bakhtiyari, R.; Martinez, F.; Jouyban, A. Prediction of deferiprone solubility in some non-aqueous binary solvent mixtures at various temperatures. *J. Mol. Liq.* **2015**, *203*, 16–19. [CrossRef]
93. Acree, W.E. IUPAC-NIST Solubility Data Series. 102. Solubility of Nonsteroidal Anti-inflammatory Drugs (NSAIDs) in Neat Organic Solvents and Organic Solvent Mixtures. *J. Phys. Chem. Ref. Data* **2014**, *43*, 023102. [CrossRef]
94. Akay, S.; Kayan, B.; Martínez, F. Solubility of fluconazole in (ethanol + water) mixtures: Determination, correlation, dissolution thermodynamics and preferential solvation. *J. Mol. Liq.* **2021**, *333*, 115987. [CrossRef]
95. Akay, S.; Kayan, B.; Peña, M.Á.; Jouyban, A.; Martínez, F. Solubility of Salicylic Acid in Some (Ethanol + Water) Mixtures at Different Temperatures: Determination, Correlation, Thermodynamics and Preferential Solvation. *Int. J. Thermophys.* **2023**, *44*, 121. [CrossRef]
96. Ali, H.S.M.; York, P.; Blagden, N.; Soltanpour, S.; Acree, W.E.; Jouyban, A. Solubility of Budesonide, Hydrocortisone, and Prednisolone in Ethanol + Water Mixtures at 298.2 K. *J. Chem. Eng. Data* **2009**, *55*, 578–582. [CrossRef]
97. Almandoz, M.C.; Sancho, M.I.; Blanco, S.E. Spectroscopic and DFT study of solvent effects on the electronic absorption spectra of sulfamethoxazole in neat and binary solvent mixtures. *Spectrochim. Acta Part A Mol. Biomol. Spectrosc.* **2014**, *118*, 112–119. [CrossRef]
98. Alsubaie, M.; Aljohani, M.; Erxleben, A.; McArdle, P. Cocrystal Forms of the BCS Class IV Drug Sulfamethoxazole. *Cryst. Growth Des.* **2018**, *18*, 3902–3912. [CrossRef]
99. Alvani-Alamdari, S.; Rezaei, H.; Rahimpour, E.; Hemmati, S.; Martinez, F.; Barzegar-Jalali, M.; Jouyban, A. Mesalazine solubility in the binary mixtures of ethanol and water at various temperatures. *Phys. Chem. Liq.* **2019**, *59*, 12–25. [CrossRef]
100. Aniya, V.; De, D.; Mohammed, A.M.; Thella, P.K.; Satyavathi, B. Measurement and modeling of solubility of para-tert-butylbenzoic acid in pure and mixed organic solvents at different temperatures. *J. Chem. Eng. Data* **2017**, *62*, 1411–1421. [CrossRef]
101. Anwer, M.K.; Mohammad, M.; Fatima, F.; Alshahrani, S.M.; Aldawsari, M.F.; Alalaiwe, A.; Al-Shdefat, R.; Shakeel, F. Solubility, solution thermodynamics and molecular interactions of osimertinib in some pharmaceutically useful solvents. *J. Mol. Liq.* **2019**, *284*, 53–58. [CrossRef]
102. Assis, G.P.; Garcia, R.H.L.; Derenzo, S.; Bernardo, A. Solid-liquid equilibrium of paracetamol in water-ethanol and water-propylene glycol mixtures. *J. Mol. Liq.* **2021**, *323*, 114617. [CrossRef]
103. Aydi, A.; Claumann, C.A.; Wüst Zibetti, A.; Abderrabba, M. Differential Scanning Calorimetry Data and Solubility of Rosmarinic Acid in Different Pure Solvents and in Binary Mixtures (Methyl Acetate + Water) and (Ethyl Acetate + Water) from 293.2 to 313.2 K. *J. Chem. Eng. Data* **2016**, *61*, 3718–3723. [CrossRef]
104. Banerjee, D.; Laha, A.K.; Bagchi, S. Preferential solvation in mixed binary solvent. *J. Chem. Soc. Faraday Trans.* **1995**, *91*, 631. [CrossRef]
105. Barzegar-Jalali, M.; Mirheydari, S.N.; Rahimpour, E.; Shekaari, H.; Martinez, F.; Jouyban, A. Experimental determination and correlation of bosentan solubility in (PEG 200+ water) mixtures at T = (293.15–313.15) K. *Phys. Chem. Liq.* **2018**, *57*, 504–515. [CrossRef]
106. Bernal-García, J.M.; Guzmán-López, A.; Cabrales-Torres, A.; Estrada-Baltazar, A.; Iglesias-Silva, G.A. Densities and viscosities of (*N*,*N*-dimethylformamide+ water) at atmospheric pressure from (283.15 to 353.15) K. *J. Chem. Eng. Data* **2008**, *53*, 1024–1027. [CrossRef]
107. Bhesaniya, K.; Nandha, K.; Baluja, S. Thermodynamics of Fluconazole Solubility in Various Solvents at Different Temperatures. *J. Chem. Eng. Data* **2014**, *59*, 649–652. [CrossRef]

108. Blanco-Márquez, J.H.; Ortiz, C.P.; Cerquera, N.E.; Martínez, F.; Jouyban, A.; Delgado, D.R. Thermodynamic analysis of the solubility and preferential solvation of sulfamerazine in (acetonitrile + water) cosolvent mixtures at different temperatures. *J. Mol. Liq.* **2019**, *293*, 111507. [CrossRef]
109. Blokhina, S.V.; Sharapova, A.V.; Ol'khovich, M.V.; Levshin, I.B.; Perlovich, G.L. Solid–liquid phase equilibrium and thermodynamic analysis of novel thiazolidine-2,4-dione derivative in different solvents. *J. Mol. Liq.* **2021**, *326*, 115273. [CrossRef]
110. Bosch, E.; Rived, F.; Rosés, M. Solute–solvent and solvent–solvent interactions in binary solvent mixtures. Part 4. Preferential solvation of solvatochromic indicators in mixtures of 2-methylpropan-2-ol with hexane, benzene, propan-2-ol, ethanol and methanol. *J. Chem. Soc. Perkin Trans.* **1996**, *2*, 2177–2184. [CrossRef]
111. Bosch, E.; Rosés, M.; Herodes, K.; Koppel, I.; Leito, I.; Koppel, I.; Taal, V. Solute-solvent and solvent-solvent interactions in binary solvent mixtures. 2. Effect of temperature on the ET(30) polarity parameter of dipolar hydrogen bond acceptor-hydrogen bond donor mixtures. *J. Phys. Org. Chem.* **1996**, *9*, 403–410. [CrossRef]
112. Calvo, B.; Cepeda, E.A. Solubilities of Stearic Acid in Organic Solvents and in Azeotropic Solvent Mixtures. *J. Chem. Eng. Data* **2008**, *53*, 628–633. [CrossRef]
113. Calvo, B.; Collado, I.; Cepeda, E.A. Solubilities of Palmitic Acid in Pure Solvents and Its Mixtures. *J. Chem. Eng. Data* **2008**, *54*, 64–68. [CrossRef]
114. Cañadas, R.; González-Miquel, M.; González, E.J.; Díaz, I.; Rodríguez, M. Evaluation of bio-based solvents for phenolic acids extraction from aqueous matrices. *J. Mol. Liq.* **2021**, *338*, 116930. [CrossRef]
115. Carmen Grande, M.d.; Juliá, J.A.; García, M.; Marschoff, C.M. On the density and viscosity of (water+dimethylsulphoxide) binary mixtures. *J. Chem. Thermodyn.* **2007**, *39*, 1049–1056. [CrossRef]
116. Castro, G.T.; Filippa, M.A.; Peralta, C.M.; Davin, M.V.; Almandoz, M.C.; Gasull, E.I. Solubility and Preferential Solvation of Piroxicam in Neat Solvents and Binary Systems. *Z. Für Phys. Chem.* **2017**, *232*, 257–280. [CrossRef]
117. Chen, F.; Zhao, M.; Feng, L.; Ren, B. Measurement and Correlation for Solubility of Diosgenin in Some Mixed Solvents. *Chin. J. Chem. Eng.* **2014**, *22*, 170–176. [CrossRef]
118. Chen, F.-X.; Zhao, M.-R.; Ren, B.-Z.; Zhou, C.-R.; Peng, F.-F. Solubility of diosgenin in different solvents. *J. Chem. Thermodyn.* **2012**, *47*, 341–346. [CrossRef]
119. Chen, S.; Liu, Q.; Dou, H.; Zhang, L.; Pei, L.; Huang, R.; Shu, G.; Yuan, Z.; Lin, J.; Zhang, W.; et al. Solubility and dissolution thermodynamic properties of Mequindox in binary solvent mixtures. *J. Mol. Liq.* **2020**, *303*, 112619. [CrossRef]
120. Chen, Y.; Xu, X.; Xie, L. Thermodynamic parameters on corresponding solid-liquid equilibrium of hydroxyapatite in pure and mixture organic solvents. *J. Mol. Liq.* **2017**, *229*, 189–197. [CrossRef]
121. Chen, Z.; Zhai, J.; Liu, X.; Mao, S.; Zhang, L.; Rohani, S.; Lu, J. Solubility measurement and correlation of the form A of ibrutinib in organic solvents from 278.15 to 323.15 K. *J. Chem. Thermodyn.* **2016**, *103*, 342–348. [CrossRef]
122. Cui, Z.; Yao, L.; Ye, J.; Wang, Z.; Hu, Y. Solubility measurement and thermodynamic modelling of curcumin in twelve pure solvents and three binary solvents at different temperature (T = 278.15–323.15 K). *J. Mol. Liq.* **2021**, *338*, 116795. [CrossRef]
123. Cysewski, P.; Jeliński, T.; Przybyłek, M.; Nowak, W.; Olczak, M. Solubility Characteristics of Acetaminophen and Phenacetin in Binary Mixtures of Aqueous Organic Solvents: Experimental and Deep Machine Learning Screening of Green Dissolution Media. *Pharmaceutics* **2022**, *14*, 2828. [CrossRef] [PubMed]
124. De la Rosa, M.V.G.; Santiago, R.; Romero, J.M.; Duconge, J.; Monbaliu, J.-C.; López-Mejías, V.; Stelzer, T. Solubility Determination and Correlation of Warfarin Sodium 2-Propanol Solvate in Pure, Binary, and Ternary Solvent Mixtures. *J. Chem. Eng. Data* **2019**, *64*, 1399–1413. [CrossRef] [PubMed]
125. del Mar Muñoz, M.; Delgado, D.R.; Peña, M.Á.; Jouyban, A.; Martínez, F. Solubility and preferential solvation of sulfadiazine, sulfamerazine and sulfamethazine in propylene glycol + water mixtures at 298.15K. *J. Mol. Liq.* **2015**, *204*, 132–136. [CrossRef]
126. Delgado, D.R.; Martínez, F. Solubility and solution thermodynamics of sulfamerazine and sulfamethazine in some ethanol+water mixtures. *Fluid Phase Equilibria* **2013**, *360*, 88–96. [CrossRef]
127. Delgado, D.R.; Martínez, F. Preferential solvation of sulfadiazine, sulfamerazine and sulfamethazine in ethanol+water solvent mixtures according to the IKBI method. *J. Mol. Liq.* **2014**, *193*, 152–159. [CrossRef]
128. Dizechi, M.; Marschall, E. Viscosity of some binary and ternary liquid mixtures. *J. Chem. Eng. Data* **1982**, *27*, 358–363. [CrossRef]
129. Domańska, U.; Pobudkowska, A.; Pelczarska, A.; Winiarska-Tusznio, M.; Gierycz, P. Solubility and pKa of select pharmaceuticals in water, ethanol, and 1-octanol. *J. Chem. Thermodyn.* **2010**, *42*, 1465–1472. [CrossRef]
130. Dong, Q.; Yu, S.; Wang, X.; Ding, S.; Li, E.; Cai, Y.; Xue, F. Solubility Measurement and Correlation of Itraconazole Hydroxy Isobutyltriazolone in Four Kinds of Binary Solvent Mixtures with Temperature from 283.15 to 323.15 K. *ACS Omega* **2023**, *8*, 39390–39400. [CrossRef] [PubMed]
131. Elizalde-Solis, O.; Arenas-Quevedo, M.G.; Verónico-Sánchez, F.J.; García-Morales, R.; Zúñiga-Moreno, A. Solubilities of Binary Systems α-Tocopherol + Capsaicin and α-Tocopherol + Palmitic Acid in Supercritical Carbon Dioxide. *J. Chem. Eng. Data* **2019**, *64*, 1948–1955. [CrossRef]
132. Fakhree, M.A.A.; Ahmadian, S.; Panahi-Azar, V.; Acree, W.E.; Jouyban, A. Solubility of 2-Hydroxybenzoic Acid in Water, 1-Propanol, 2-Propanol, and 2-Propanone at (298.2 to 338.2) K and Their Aqueous Binary Mixtures at 298.2 K. *J. Chem. Eng. Data* **2012**, *57*, 3303–3307. [CrossRef]
133. Filippa, M.A.; Gasull, E.I. Ibuprofen solubility in pure organic solvents and aqueous mixtures of cosolvents: Interactions and thermodynamic parameters relating to the solvation process. *Fluid Phase Equilibria* **2013**, *354*, 185–190. [CrossRef]

134. Gheitasi, N.; Nazari, A.H.; Haghtalab, A. Thermodynamic Modeling and Solubility Measurement of Cetirizine Hydrochloride and Deferiprone in Pure Solvents of Acetonitrile, Ethanol, Acetic Acid, Sulfolane, and Ethyl Acetate and Their Mixtures. *J. Chem. Eng. Data* **2019**, *64*, 5486–5496. [CrossRef]
135. Gonçalves Bonassoli, A.B.; Oliveira, G.; Bordón Sosa, F.H.; Rolemberg, M.P.; Mota, M.A.; Basso, R.C.; Igarashi-Mafra, L.; Mafra, M.R. Solubility measurement of lauric, palmitic, and stearic acids in ethanol, n-propanol, and 2-propanol using differential scanning calorimetry. *J. Chem. Eng. Data* **2019**, *64*, 2084–2092. [CrossRef]
136. Guo, S.; Yang, W.; Hu, Y.; Wang, K.; Luan, Y. Measurement and Correlation of the Solubility of N-Acetylglycine in Different Solvents at Temperatures from 278.15 to 319.15 K. *J. Solut. Chem.* **2013**, *42*, 1879–1887. [CrossRef]
137. Guo, Y.; He, H.; Huang, H.; Qiu, J.; Han, J.; Hu, S.; Liu, H.; Zhao, Y.; Wang, P. Solubility determination and thermodynamic modeling of *n*-acetylglycine in different solvent systems. *J. Chem. Eng. Data* **2021**, *66*, 1344–1355. [CrossRef]
138. Gusain, K.; Garg, S.; Kumar, R. Solubility Prediction of Pharmaceutical Compounds in Pure Solvent by Different Correlations and Thermodynamic Models. *SSRN Electron. J.* **2020**. [CrossRef]
139. Ha, E.-S.; Lee, S.-K.; Jeong, J.-S.; Sim, W.-Y.; Yang, J.-I.; Kim, J.-S.; Kim, M.-S. Solvent effect and solubility modeling of rebamipide in twelve solvents at different temperatures. *J. Mol. Liq.* **2019**, *288*, 111041. [CrossRef]
140. Hatefi, A.; Jouyban, A.; Mohammadian, E.; Acree, W.E.; Rahimpour, E. Prediction of paracetamol solubility in cosolvency systems at different temperatures. *J. Mol. Liq.* **2019**, *273*, 282–291. [CrossRef]
141. He, Q.; Zheng, M.; Zhao, H. Baicalin solubility in aqueous co-solvent mixtures of methanol, ethanol, isopropanol and n-propanol revisited: Solvent–solvent and solvent–solute interactions and IKBI preferential solvation analysis. *Phys. Chem. Liq.* **2019**, *58*, 820–832. [CrossRef]
142. Hellstén, S.; Qu, H.; Louhi-Kultanen, M. Screening of Binary Solvent Mixtures and Solvate Formation of Indomethacin. *Chem. Eng. Technol.* **2011**, *34*, 1667–1674. [CrossRef]
143. Heryanto, R.; Hasan, M.; Abdullah, E.C.; Kumoro, A.C. Solubility of Stearic Acid in Various Organic Solvents and Its Prediction using Non-ideal Solution Models. *ScienceAsia* **2007**, *33*, 469–472. Available online: https://www.scienceasia.org/2007.33.n4/v33_469_472.pdf (accessed on 30 December 2023).
144. Hu, W.; Shang, Z.; Wei, N.; Hou, B.; Gong, J.; Wang, Y. Solubility of benorilate in twelve monosolvents: Determination, correlation and COSMO-RS analysis. *J. Chem. Thermodyn.* **2021**, *152*, 106272. [CrossRef]
145. Hu, X.; Gong, Y.; Cao, Z.; Huang, Z.; Sha, J.; Li, Y.; Li, T.; Ren, B. Solubility, Hansen solubility parameter and thermodynamic properties of etodolac in twelve organic pure solvents at different temperatures. *J. Mol. Liq.* **2020**, *316*, 113779. [CrossRef]
146. Hu, X.; Tian, Y.; Cao, Z.; Sha, J.; Huang, Z.; Li, Y.; Li, T.; Ren, B. Solubility measurement, Hansen solubility parameter and thermodynamic modeling of etodolac in four binary solvents from 278.15 K to 323.15 K. *J. Mol. Liq.* **2020**, *318*, 114155. [CrossRef]
147. Imran, S.; Hossain, A.; Mahali, K.; Guin, P.S.; Datta, A.; Roy, S. Solubility and peculiar thermodynamical behaviour of 2-aminobenzoic acid in aqueous binary solvent mixtures at 288.15 to 308.15 K. *J. Mol. Liq.* **2020**, *302*, 112566. [CrossRef]
148. Ivanov, E.V.; Batov, D.V. Enthalpy-related parameters of interaction of simplest α-amino acids with the pharmaceutical mebicar (N-tetramethylglycoluril) in water at 298.15 K. *J. Chem. Thermodyn.* **2019**, *128*, 159–163. [CrossRef]
149. Jia, L.; Yang, J.; Cui, P.; Wu, D.; Wang, S.; Hou, B.; Zhou, L.; Yin, Q. Uncovering solubility behavior of Prednisolone form II in eleven pure solvents by thermodynamic analysis and molecular simulation. *J. Mol. Liq.* **2021**, *342*, 117376. [CrossRef]
150. Jiménez Cruz, J.M.; Vlaar, C.P.; López-Mejías, V.; Stelzer, T. Solubility Measurements and Correlation of MBQ-167 in Neat and Binary Solvent Mixtures. *J. Chem. Eng. Data* **2021**, *66*, 832–839. [CrossRef]
151. Jiménez, D.M.; Cárdenas, Z.J.; Martínez, F. Solubility and solution thermodynamics of sulfadiazine in polyethylene glycol 400 + water mixtures. *J. Mol. Liq.* **2016**, *216*, 239–245. [CrossRef]
152. Jouyban, A.; Acree, W.E.; Martínez, F. Dissolution thermodynamics and preferential solvation of ketoconazole in some {ethanol (1) + water (2)} mixtures. *J. Mol. Liq.* **2020**, *313*, 113579. [CrossRef]
153. Jouyban, A.; Mazaher Haji Agha, E.; Rahimpour, E.; Acree, W.E., Jr. Further computation and some comments on "Stearic acid solubility in mixed solvents of (water + ethanol) and (ethanol + ethyl acetate): Experimental data and comparison among different thermodynamic models". *J. Mol. Liq.* **2020**, *310*, 113228. [CrossRef]
154. Jouyban, K.; Mazaher Haji Agha, E.; Hemmati, S.; Martinez, F.; Kuentz, M.; Jouyban, A. Solubility of 5-aminosalicylic acid in N-methyl-2-pyrrolidone + water mixtures at various temperatures. *J. Mol. Liq.* **2020**, *310*, 113143. [CrossRef]
155. Jouyban-Gharamaleki, V.; Jouyban, A.; Kuentz, M.; Hemmati, S.; Martinez, F.; Rahimpour, E. A laser monitoring technique for determination of mesalazine solubility in propylene glycol and ethanol mixtures at various temperatures. *J. Mol. Liq.* **2020**, *304*, 112714. [CrossRef]
156. Jouyban-Gharamaleki, V.; Jouyban, A.; Martinez, F.; Zhao, H.; Rahimpour, E. A laser monitoring technique for solubility study of ketoconazole in propylene glycol and 2-propanol mixtures at various temperatures. *J. Mol. Liq.* **2020**, *320*, 114444. [CrossRef]
157. Kalam, M.A.; Alshehri, S.; Alshamsan, A.; Haque, A.; Shakeel, F. Solid liquid equilibrium of an antifungal drug itraconazole in different neat solvents: Determination and correlation. *J. Mol. Liq.* **2017**, *234*, 81–87. [CrossRef]
158. Kandi, S.; Charles, A.L. Measurement, correlation, and thermodynamic properties for solubilities of bioactive compound (−)-epicatechin in different pure solvents at 298.15 K to 338.15 K. *J. Mol. Liq.* **2018**, *264*, 269–274. [CrossRef]
159. Karpiuk, I.; Wilczura-Wachnik, H.; Myśliński, A. α-Tocopherol/AOT/alkane/water system. *J. Therm. Anal. Calorim.* **2017**, *131*, 2885–2892. [CrossRef]

160. Khajir, S.; Shayanfar, A.; Acree, W.E.; Jouyban, A. Effects of N-methylpyrrolidone and temperature on phenytoin solubility. *J. Mol. Liq.* **2019**, *285*, 58–61. [CrossRef]
161. Kuhs, M.; Svärd, M.; Rasmuson, Å.C. Thermodynamics of fenoxycarb in solution. *J. Chem. Thermodyn.* **2013**, *66*, 50–58. [CrossRef]
162. Kumari, A.; Kadakanchi, S.; Tangirala, R.; Thella, P.K.; Satyavathi, B. Measurement and modeling of solid–liquid equilibrium of para-tert-butylbenzoic acid in acetic acid/methanol+ water and acetic acid+ para-tert-butyltoluene binary systems at various temperatures. *J. Chem. Eng. Data* **2016**, *62*, 87–95. [CrossRef]
163. Lange, L.; Heisel, S.; Sadowski, G. Predicting the Solubility of Pharmaceutical Cocrystals in Solvent/Anti-Solvent Mixtures. *Molecules* **2016**, *21*, 593. [CrossRef] [PubMed]
164. Lee, S.-K.; Sim, W.-Y.; Ha, E.-S.; Park, H.; Kim, J.-S.; Jeong, J.-S.; Kim, M.-S. Solubility of bisacodyl in fourteen mono solvents and N-methyl-2-pyrrolidone + water mixed solvents at different temperatures, and its application for nanosuspension formation using liquid antisolvent precipitation. *J. Mol. Liq.* **2020**, *310*, 113264. [CrossRef]
165. Li, A.; Si, Z.; Yan, Y.; Zhang, X. Solubility and thermodynamic properties of hydrate lenalidomide in phosphoric acid solution. *J. Mol. Liq.* **2021**, *330*, 115446. [CrossRef]
166. Li, M.; Liu, S.; Li, S.; Yang, Y.; Cui, Y.; Gong, J. Determination and Correlation of Dipyridamole p-Toluene Sulfonate Solubility in Seven Alcohol Solvents and Three Binary Solvents. *J. Chem. Eng. Data* **2017**, *63*, 208–216. [CrossRef]
167. Li, R.; Fu, L.; Zhang, J.; Wang, W.; Chen, X.; Zhao, J.; Han, D. Solid-liquid equilibrium and thermodynamic properties of dipyridamole form II in pure solvents and mixture of (*N*-methyl pyrrolidone + isopropanol). *J. Chem. Thermodyn.* **2020**, *142*, 105981. [CrossRef]
168. Li, R.; Jin, Y.; Yu, B.; Xu, Q.; Chen, X.; Han, D. Solubility determination and thermodynamic properties calculation of macitentan in mixtures of ethyl acetate and alcohols. *J. Chem. Thermodyn.* **2021**, *156*, 106344. [CrossRef]
169. Li, R.; Liu, L.; Khan, A.; Li, C.; He, Z.; Zhao, J.; Han, D. Effect of Cosolvents on the Solubility of Lenalidomide and Thermodynamic Model Correlation of Data. *J. Chem. Eng. Data* **2019**, *64*, 4272–4279. [CrossRef]
170. Li, R.; Yan, H.; Wang, Z.; Gong, J. Correlation of Solubility and Prediction of the Mixing Properties of Ginsenoside Compound K in Various Solvents. *Ind. Eng. Chem. Res.* **2012**, *51*, 8141–8148. [CrossRef]
171. Li, R.; Yin, X.; Jin, Y.; Chen, X.; Zhao, B.; Wang, W.; Zhong, S.; Han, D. The solubility profile and dissolution thermodynamic properties of minocycline hydrochloride in some pure and mixed solvents at several temperatures. *J. Chem. Thermodyn.* **2021**, *157*, 106399. [CrossRef]
172. Li, R.; Zhao, B.; Chen, X.; Zhang, J.; Liu, Z.; Zhu, X.; Han, D. Solubility and apparent thermodynamic analysis of pomalidomide in (acetone + ethanol/isopropanol) and (ethyl acetate + ethanol/isopropanol) and its correlation with thermodynamic model. *J. Chem. Thermodyn.* **2021**, *154*, 106345. [CrossRef]
173. Li, W.; Yuan, J.; Wang, X.; Shi, W.; Zhao, H.; Xing, R.; Jouyban, A.; Acree, W.E. Bifonazole dissolved in numerous aqueous alcohol mixtures: Solvent effect, enthalpy–entropy compensation, extended Hildebrand solubility parameter approach and preferential solvation. *J. Mol. Liq.* **2021**, *338*, 116671. [CrossRef]
174. Li, X.; Du, C.; Cong, Y.; Zhao, H. Solubility determination and thermodynamic modelling of 3-amino-1,2,4-triazole in ten organic solvents from T = 283.15 K to T = 318.15 K and mixing properties of solutions. *J. Chem. Thermodyn.* **2017**, *104*, 189–200. [CrossRef]
175. Li, X.; Ma, M.; Du, C.; Zhao, H. Solubility of cetilistat in neat solvents and preferential solvation in (acetone, isopropanol or acetonitrile) + water co-solvent mixtures. *J. Mol. Liq.* **2017**, *242*, 618–624. [CrossRef]
176. Li, X.; Wang, M.; Du, C.; Cong, Y.; Zhao, H. Preferential solvation of rosmarinic acid in binary solvent mixtures of ethanol + water and methanol + water according to the inverse Kirkwood–Buff integrals method. *J. Mol. Liq.* **2017**, *240*, 56–64. [CrossRef]
177. Li, Y.; Wang, Y.; Ning, Z.; Cui, J.; Wu, Q.; Wang, X. Solubilities of Adipic Acid and Succinic Acid in a Glutaric Acid + Acetone or *n*-Butanol Mixture. *J. Chem. Eng. Data* **2014**, *59*, 4062–4069. [CrossRef]
178. Lin, L.; Zhao, K.; Yu, B.; Wang, H.; Chen, M.; Gong, J. Measurement and Correlation of Solubility of Cefathiamidine in Water + (Acetone, Ethanol, or 2-Propanol) from (278.15 to 308.15) K. *J. Chem. Eng. Data* **2015**, *61*, 412–419. [CrossRef]
179. Liu, J.-Q.; Wang, Y.; Tang, H.; Wu, S.; Li, Y.-Y.; Zhang, L.-Y.; Bai, Q.-Y.; Liu, X. Experimental Measurements and Modeling of the Solubility of Aceclofenac in Six Pure Solvents from (293.35 to 338.25) K. *J. Chem. Eng. Data* **2014**, *59*, 1588–1592. [CrossRef]
180. Liu, W.; Bao, Z.; Shen, Y.; Yao, T.; Bai, H.; Jin, X. Solubility measurement and thermodynamic modeling of carbamazepine (form III) in five pure solvents at various temperatures. *Chin. J. Chem. Eng.* **2021**, *33*, 231–235. [CrossRef]
181. Liu, Y.; Wang, Y.; Liu, Y.; Xu, S.; Chen, M.; Du, S.; Gong, J. Solubility of L-histidine in different aqueous binary solvent mixtures from 283.15 K to 318.15 K with experimental measurement and thermodynamic modelling. *J. Chem. Thermodyn.* **2017**, *105*, 1–14. [CrossRef]
182. Lou, Y.; Wang, Y.; Li, Y.; He, M.; Su, N.; Xu, R.; Meng, X.; Hou, B.; Xie, C. Thermodynamic equilibrium and cosolvency of florfenicol in binary solvent system. *J. Mol. Liq.* **2018**, *251*, 83–91. [CrossRef]
183. Mabhoot, A.; Jouyban, A. Solubility of Sodium Phenytoin in Propylene Glycol + Water Mixtures in the Presence of Β-Cyclodextrin. *Pharm. Sci.* **2015**, *21*, 152–156. [CrossRef]
184. Mahali, K.; Guin, P.S.; Roy, S.; Dolui, B.K. Solubility and solute–solvent interaction phenomenon of succinic acid in aqueous ethanol mixtures. *J. Mol. Liq.* **2017**, *229*, 172–177. [CrossRef]
185. Marcus, Y. The use of chemical probes for the characterization of solvent mixtures. Part 2. Aqueous mixtures. *J. Chem. Soc. Perkin Trans.* **1994**, *2*, 1751. [CrossRef]

186. Marcus, Y. Use of chemical probes for the characterization of solvent mixtures. Part 1. Completely non-aqueous mixtures. *J. Chem. Soc. Perkin Trans.* **1994**, *2*, 1015. [CrossRef]
187. Matsuda, H.; Kaburagi, K.; Matsumoto, S.; Kurihara, K.; Tochigi, K.; Tomono, K. Solubilities of Salicylic Acid in Pure Solvents and Binary Mixtures Containing Cosolvent. *J. Chem. Eng. Data* **2008**, *54*, 480–484. [CrossRef]
188. McHedlov-Petrosyan, N.O. Book review: Christian Reichardt and Thomas Welton, Solvents and Solvent Effects in Organic Chemistry (Fourth Edition, Updated and Enlarged; Wiley-VCH Verlag & Co. KGaA, Weinheim, 2011; 718 p. Hardcover). *Russ. J. Phys. Chem. A* **2011**, *85*, 1482. [CrossRef]
189. Mealey, D.; Svärd, M.; Rasmuson, Å.C. Thermodynamics of risperidone and solubility in pure organic solvents. *Fluid Phase Equilibria* **2014**, *375*, 73–79. [CrossRef]
190. Mirmehrabi, M.; Rohani, S. Measurement and Prediction of the Solubility of Stearic Acid Polymorphs by the UNIQUAC Equation. *Can. J. Chem. Eng.* **2004**, *82*, 335–342. [CrossRef]
191. Mo, F.; Ma, J.; Zhang, P.; Zhang, D.; Fan, H.; Yang, X.; Zhi, L.; Zhang, J. Solubility and thermodynamic properties of baicalein in water and ethanol mixtures from 283.15 to 328.15 K. *Chem. Eng. Commun.* **2019**, *208*, 183–196. [CrossRef]
192. Mohamadian, E.; Hamidi, S.; Martínez, F.; Jouyban, A. Solubility prediction of deferiprone in N-methyl-2-pyrrolidone+ ethanol mixtures at various temperatures using a minimum number of experimental data. *Phys. Chem. Liq.* **2017**, *55*, 805–816. [CrossRef]
193. Mohammadian, E.; Jouyban, A.; Barzegar-Jalali, M.; Acree, W.E.; Rahimpour, E. Solubilization of naproxen: Experimental data and computational tools. *J. Mol. Liq.* **2019**, *288*, 110985. [CrossRef]
194. Mohammadzade, M.; Barzegar-Jalali, M.; Jouyban, A. Solubility of naproxen in 2-propanol+water mixtures at various temperatures. *J. Mol. Liq.* **2015**, *206*, 110–113. [CrossRef]
195. Moodley, K.; Rarey, J.; Ramjugernath, D. Experimental solubility of diosgenin and estriol in various solvents between T = (293.2–328.2)K. *J. Chem. Thermodyn.* **2017**, *106*, 199–207. [CrossRef]
196. Moodley, K.; Rarey, J.; Ramjugernath, D. Experimental solubility data for prednisolone and hydrocortisone in various solvents between (293.2 and 328.2) K by employing combined DTA/TGA. *J. Mol. Liq.* **2017**, *240*, 303–312. [CrossRef]
197. Mora, C.P.; Martínez, F. Solubility of naproxen in several organic solvents at different temperatures. *Fluid Phase Equilibria* **2007**, *255*, 70–77. [CrossRef]
198. Moradi, M.; Mazaher Haji Agha, E.; Hemmati, S.; Martinez, F.; Kuentz, M.; Jouyban, A. Solubility of 5-aminosalicylic acid in {N-methyl-2-pyrrolidone + ethanol} mixtures at T = (293.2 to 313.2) K. *J. Mol. Liq.* **2020**, *306*, 112774. [CrossRef]
199. Ning, L.; Gong, X.; Li, P.; Chen, X.; Wang, H.; Xu, J. Measurement and correlation of the solubility of estradiol and estradiol-urea co-crystal in fourteen pure solvents at temperatures from 273.15 K to 318.15 K. *J. Mol. Liq.* **2020**, *304*, 112599. [CrossRef]
200. Noda, K.; Aono, Y.; Ishida, K. Viscosity and Density of Ethanol-Acetic Acid-Water Mixtures. *Kagaku Kogaku Ronbunshu* **1983**, *9*, 237–240. [CrossRef]
201. Noda, K.; Ohashi, M.; Ishida, K. Viscosities and densities at 298.15 K for mixtures of methanol, acetone, and water. *J. Chem. Eng. Data* **1982**, *27*, 326–328. [CrossRef]
202. Noubigh, A. Stearic acid solubility in mixed solvents of (water + ethanol) and (ethanol + ethyl acetate): Experimental data and comparison among different thermodynamic models. *J. Mol. Liq.* **2019**, *296*, 112101. [CrossRef]
203. Oliveira, G.; Bonassoli, A.B.G.; Rolemberg, M.P.; Mota, M.A.; Basso, R.C.; Soares, R.d.P.; Igarashi-Mafra, L.; Mafra, M.R. Water Effect on Solubilities of Lauric and Palmitic Acids in Ethanol and 2-Propanol Determined by Differential Scanning Calorimetry. *J. Chem. Eng. Data* **2021**, *66*, 2366–2373. [CrossRef]
204. Ortiz, C.P.; Cardenas-Torres, R.E.; Martínez, F.; Delgado, D.R. Solubility of Sulfamethazine in the Binary Mixture of Acetonitrile + Methanol from 278.15 to 318.15 K: Measurement, Dissolution Thermodynamics, Preferential Solvation, and Correlation. *Molecules* **2021**, *26*, 7588. [CrossRef]
205. Osorio, I.P.; Martínez, F.; Peña, M.A.; Jouyban, A.; Acree, W.E. Solubility, dissolution thermodynamics and preferential solvation of sulfadiazine in (*N*-methyl-2-pyrrolidone + water) mixtures. *J. Mol. Liq.* **2021**, *330*, 115693. [CrossRef]
206. Pabba, S.; Kumari, A.; Ravuri, M.G.; Thella, P.K.; Satyavathi, B.; Shah, K.; Kundu, S.; Bhargava, S.K. Experimental determination and modelling of the co-solvent and antisolvent behaviour of binary systems on the dissolution of pharma drug; L-aspartic acid and thermodynamic correlations. *J. Mol. Liq.* **2020**, *314*, 113657. [CrossRef]
207. Pacheco, D.P.; Martínez, F. Thermodynamic analysis of the solubility of naproxen in ethanol + water cosolvent mixtures. *Phys. Chem. Liq.* **2007**, *45*, 581–595. [CrossRef]
208. Padervand, M.; Naseri, S.; Boroujeni, H.C. Preferential solvation of pomalidomide, an anticancer compound, in some binary mixed solvents at 298.15 K. *Chin. J. Chem. Eng.* **2020**, *28*, 2626–2633. [CrossRef]
209. Pasham, F.; Jabbari, M.; Farajtabar, A. Solvatochromic Measurement of KAT Parameters and Modeling Preferential Solvation in Green Potential Binary Mixtures of *N*-Formylmorpholine with Water, Alcohols, and Ethyl Acetate. *J. Chem. Eng. Data* **2020**, *65*, 5458–5466. [CrossRef]
210. Patel, A.; Vaghasiya, A.; Gajera, R.; Baluja, S. Solubility of 5-Amino Salicylic Acid in Different Solvents at Various Temperatures. *J. Chem. Eng. Data* **2010**, *55*, 1453–1455. [CrossRef]
211. Przybyłek, M.; Miernicka, A.; Nowak, M.; Cysewski, P. New Screening Protocol for Effective Green Solvents Selection of Benzamide, Salicylamide and Ethenzamide. *Molecules* **2022**, *27*, 3323. [CrossRef]

212. Qiu, J.; Huang, H.; He, H.; Liu, H.; Hu, S.; Han, J.; Guo, Y.; Wang, P. Measurement and Correlation of *trans*-4-Hydroxyl-proline Solubility in Sixteen Individual Solvents and a Water + Acetonitrile Binary Solvent System. *J. Chem. Eng. Data* **2020**, *66*, 575–587. [CrossRef]
213. Radmand, S.; Rezaei, H.; Zhao, H.; Rahimpour, E.; Jouyban, A. Solubility and thermodynamic study of deferiprone in propylene glycol and ethanol mixture. *BMC Chem* **2023**, *17*, 37. [CrossRef]
214. Ràfols, C.; Rosés, M.; Bosch, E. Solute–solvent and solvent–solvent interactions in binary solvent mixtures. Part 5. Preferential solvation of solvatochromic indicators in mixtures of propan-2-ol with hexane, benzene, ethanol and methanol. *J. Chem. Soc. Perkin Trans.* **1997**, *2*, 243–248. [CrossRef]
215. Rani, R.S.; Rao, G.N. Stability of binary complexes of L-aspartic acid in dioxan–water mixtures. *Bull. Chem. Soc. Ethiop.* **2013**, *27*, 367–376. [CrossRef]
216. Rashid, A.; White, E.T.; Howes, T.; Litster, J.D.; Marziano, I. Effect of Solvent Composition and Temperature on the Solubility of Ibuprofen in Aqueous Ethanol. *J. Chem. Eng. Data* **2014**, *59*, 2699–2703. [CrossRef]
217. Rathi, P.B.; Kale, M.; Soleymani, J.; Jouyban, A. Solubility of Etoricoxib in Aqueous Solutions of Glycerin, Methanol, Polyethylene Glycols 200, 400, 600, and Propylene Glycol at 298.2 K. *J. Chem. Eng. Data* **2018**, *63*, 321–330. [CrossRef]
218. Ren, J.; Chen, D.; Yu, Y.; Li, H. Solubility of dicarbohydrazide bis[3-(5-nitroimino-1,2,4-triazole)] in common pure solvents and binary solvents at different temperatures. *R. Soc. Open Sci.* **2019**, *6*, 190728. [CrossRef]
219. Rezaei, H.; Rahimpour, E.; Martinez, F.; Jouyban, A. Measurement and correlation of solubility data for deferiprone in propylene glycol and 2-propanol at different temperatures. *Heliyon* **2023**, *9*, e17402. [CrossRef]
220. Rezaei, H.; Rezaei, H.; Rahimpour, E.; Martinez, F.; Jouyban, A. Solubility profile of phenytoin in the mixture of 1-propanol and water at different temperatures. *J. Mol. Liq.* **2021**, *334*, 115936. [CrossRef]
221. Rodríguez, A.; Trigo, M.; Aubourg, S.P.; Medina, I. Optimisation of Low-Toxicity Solvent Employment for Total Lipid and Tocopherol Compound Extraction from Patagonian Squid By-Products. *Foods* **2023**, *12*, 504. [CrossRef] [PubMed]
222. Rosales-García, T.; Rosete-Barreto, J.M.; Pimentel-Rodas, A.; Davila-Ortiz, G.; Galicia-Luna, L.A. Solubility of Squalene and Fatty Acids in Carbon Dioxide at Supercritical Conditions: Binary and Ternary Systems. *J. Chem. Eng. Data* **2017**, *63*, 69–76. [CrossRef]
223. Roses, M.; Ortega, J.; Bosch, E. Variation ofE T(30) polarity and the Kamlet-Taft solvatochromic parameters with composition in alcohol-alcohol mixtures. *J. Solut. Chem.* **1995**, *24*, 51–63. [CrossRef]
224. Ruidiaz, M.A.; Delgado, D.R.; Martínez, F. Indomethacin solubility estimation in 1,4-dioxane + water mixtures by the extended hildebrand solubility approach. *Química Nova* **2011**, *34*, 1569–1574. [CrossRef]
225. Sajedi-Amin, S.; Barzegar-Jalali, M.; Fathi-Azarbayjani, A.; Kebriaeezadeh, A.; Martínez, F.; Jouyban, A. Solubilization of bosentan using ethanol as a pharmaceutical cosolvent. *J. Mol. Liq.* **2017**, *232*, 152–158. [CrossRef]
226. Serna-Carrizales, J.C.; Zárate-Guzmán, A.I.; Aguilar-Aguilar, A.; Forgionny, A.; Bailón-García, E.; Flórez, E.; Gómez-Durán, C.F.A.; Ocampo-Pérez, R. Optimization of Binary Adsorption of Metronidazole and Sulfamethoxazole in Aqueous Solution Supported with DFT Calculations. *Processes* **2023**, *11*, 1009. [CrossRef]
227. Sha, J.; Ma, T.; Huang, Z.; Hu, X.; Zhang, R.; Cao, Z.; Wan, Y.; Sun, R.; He, H.; Jiang, G.; et al. Corrigendum to "Solubility determination, model evaluation, Hansen solubility parameter and thermodynamic properties of benorilate in six pure solvents and two binary solvent mixtures". *J. Chem. Thermodyn.* **2021**, *158*, 106365. [CrossRef]
228. Sha, J.; Yang, X.; Hu, X.; Huang, Z.; Cao, Z.; Wan, Y.; Sun, R.; Jiang, G.; He, H.; Li, Y.; et al. Solubility determination, model evaluation, Hansen solubility parameter and thermodynamic properties of benflumetol in pure alcohol and ester solvents. *J. Chem. Thermodyn.* **2021**, *154*, 106323. [CrossRef]
229. Sha, J.; Yang, X.; Ji, L.; Cao, Z.; Niu, H.; Wan, Y.; Sun, R.; He, H.; Jiang, G.; Li, Y.; et al. Solubility determination, model evaluation, Hansen solubility parameter, molecular simulation and thermodynamic properties of benflumetol in four binary solvent mixtures from 278.15 K to 323.15 K. *J. Mol. Liq.* **2021**, *333*, 115867. [CrossRef]
230. Shakeel, F.; Iqbal, M.; Ezzeldin, E.; Haq, N. Thermodynamics of solubility of ibrutinib in ethanol+water cosolvent mixtures at different temperatures. *J. Mol. Liq.* **2015**, *209*, 461–464. [CrossRef]
231. Shao, D.; Yang, Z.; Zhou, G.; Chen, J.; Zheng, S.; Lv, X.; Li, R. Improving the solubility of acipimox by cosolvents and the study of thermodynamic properties on solvation process. *J. Mol. Liq.* **2018**, *262*, 389–395. [CrossRef]
232. Sharapova, A.; Ol'khovich, M.; Blokhina, S.; Perlovich, G. Solubility and vapor pressure data of bioactive 6-(acetylamino)-*N*-(5-ethyl-1,3,4-thiadiazol-2-yl) hexanamide. *J. Chem. Thermodyn.* **2019**, *135*, 35–44. [CrossRef]
233. Shen, B.; Wang, Q.; Wang, Y.; Ye, X.; Lei, F.; Gong, X. Solubilities of Adipic Acid in Acetic Acid + Water Mixtures and Acetic Acid + Cyclohexane Mixtures. *J. Chem. Eng. Data* **2013**, *58*, 938–942. [CrossRef]
234. Sheng, X.; Luo, W.; Wang, Q. Determination and Correlation for the Solubilities of Succinic Acid in Cyclohexanol + Cyclohexanone + Cyclohexane Solvent Mixtures. *J. Chem. Eng. Data* **2018**, *63*, 801–811. [CrossRef]
235. Shi, S.; Yan, M.; Tao, B.; Luo, W. Measurement and correlation for solubilities of succinic acid, glutaric acid and adipic acid in five organic solvents. *J. Mol. Liq.* **2020**, *297*, 111735. [CrossRef]
236. Singh, S. Studies on the Interactions of Paracetamol in Water and Binary Solvent Mixtures at T = (298.15–313.15) K: Viscometric and Surface Tension Approach. *Biointerface Res. Appl. Chem.* **2021**, *12*, 2776–2786. [CrossRef]
237. Smirnov, V.I. Thermochemical investigation of L-glutamine dissolution processes in aqueous co-solvent mixtures of acetonitrile, dioxane, acetone and dimethyl sulfoxide at T = 298.15 K. *J. Chem. Thermodyn.* **2020**, *150*, 106227. [CrossRef]

238. Smirnov, V.I.; Badelin, V.G. Similarity and differences of the thermochemical characteristics of l-glutamine dissolution in aqueous solutions of some acetamides and formamides at T = 298.15 K. *J. Mol. Liq.* **2019**, *285*, 84–88. [CrossRef]
239. Soltanpour, S.; Gharagozlu, A. Piroxicam Solubility in Binary and Ternary Solvents of Polyethylene Glycols 200 or 400 with Ethanol and Water at 298.2 K: Experimental Data Report and Modeling. *J. Solut. Chem.* **2015**, *44*, 1407–1423. [CrossRef]
240. Soltanpour, S.; Jouyban, A. Solubility of Acetaminophen and Ibuprofen in Binary and Ternary Mixtures of Polyethylene Glycol 600, Ethanol and Water. *Chem. Pharm. Bull.* **2010**, *58*, 219–224. [CrossRef] [PubMed]
241. Soltanpour, S.; Nazemi, V. Solubility of Ketoconazole in Binary and Ternary Solvents of Polyethylene Glycols 200, 400 or 600 with Ethanol and Water at 298.2 K. Data Report and Analysis. *J. Solut. Chem.* **2018**, *47*, 65–79. [CrossRef]
242. Soltanpour, S.; Shekarriz, A.-H. Naproxen solubility in binary and ternary solvents of polyethylene glycols 200, 400 or 600 with ethanol and water at 298.2 K—Experimental data report and modelling. *Phys. Chem. Liq.* **2015**, *53*, 748–762. [CrossRef]
243. Solymosi, T.; Tóth, F.; Orosz, J.; Basa-Dénes, O.; Angi, R.; Jordán, T.; Ötvös, Z.; Glavinas, H. Solubility Measurements at 296 and 310 K and Physicochemical Characterization of Abiraterone and Abiraterone Acetate. *J. Chem. Eng. Data* **2018**, *12*, 4453–4458. [CrossRef]
244. Sun, H.; Liu, B.; Liu, P.; Zhang, J.; Wang, Y. Solubility of Fenofibrate in Different Binary Solvents: Experimental Data and Results of Thermodynamic Modeling. *J. Chem. Eng. Data* **2016**, *61*, 3177–3183. [CrossRef]
245. Sun, J.; Liu, X.; Fang, Z.; Mao, S.; Zhang, L.; Rohani, S.; Lu, J. Solubility Measurement and Simulation of Rivaroxaban (Form I) in Solvent Mixtures from 273.15 to 323.15 K. *J. Chem. Eng. Data* **2015**, *61*, 495–503. [CrossRef]
246. Swinerd, G.G. *Orbital Mechanics: Theory and Applications*; Logsdon, T., Ed.; John Wiley and Sons Limited: Chichester, UK, 1998. [CrossRef]
247. Tang, W.; Wang, Z.; Feng, Y.; Xie, C.; Wang, J.; Yang, C.; Gong, J. Experimental Determination and Computational Prediction of Androstenedione Solubility in Alcohol + Water Mixtures. *Ind. Eng. Chem. Res.* **2014**, *53*, 11538–11549. [CrossRef]
248. Tang, W.; Xie, C.; Wang, Z.; Wu, S.; Feng, Y.; Wang, X.; Wang, J.; Gong, J. Solubility of androstenedione in lower alcohols. *Fluid Phase Equilibria* **2014**, *363*, 86–96. [CrossRef]
249. Teutenberg, T.; Wiese, S.; Wagner, P.; Gmehling, J. High-temperature liquid chromatography. Part II: Determination of the viscosities of binary solvent mixtures—Implications for liquid chromatographic separations. *J. Chromatogr. A* **2009**, *1216*, 8470–8479. [CrossRef]
250. Thati, J.; Nordström, F.L.; Rasmuson, Å.C. Solubility of Benzoic Acid in Pure Solvents and Binary Mixtures. *J. Chem. Eng. Data* **2010**, *55*, 5124–5127. [CrossRef]
251. Torres, N.; Escalera, B.; Martínez, F.; Peña, M.Á. Thermodynamic Analysis of Etoricoxib in Amphiprotic and Amphiprotic: Aprotic Solvent Mixtures at Several Temperatures. *J. Solut. Chem.* **2020**, *49*, 272–288. [CrossRef]
252. Valavi, M.; Ukrainczyk, M.; Dehghani, M.R. Prediction of solubility of active pharmaceutical ingredients by semi- predictive Flory Huggins/Hansen model. *J. Mol. Liq.* **2017**, *246*, 166–172. [CrossRef]
253. Vargas-Santana, M.S.; Cruz-González, A.M.; Ortiz, C.P.; Delgado, D.R.; Martínez, F.; Peña, M.Á.; Acree, W.E.; Jouyban, A. Solubility of sulfamerazine in (ethylene glycol + water) mixtures: Measurement, correlation, dissolution thermodynamics and preferential solvation. *J. Mol. Liq.* **2021**, *337*, 116330. [CrossRef]
254. Vieira, A.W.; Molina, G.; Mageste, A.B.; Rodrigues, G.D.; de Lemos, L.R. Partitioning of salicylic and acetylsalicylic acids by aqueous two-phase systems: Mechanism aspects and optimization study. *J. Mol. Liq.* **2019**, *296*, 111775. [CrossRef]
255. Volkova, T.V.; Levshin, I.B.; Perlovich, G.L. New antifungal compound: Solubility thermodynamics and partitioning processes in biologically relevant solvents. *J. Mol. Liq.* **2020**, *310*, 113148. [CrossRef]
256. Wang, H.; Yao, G.; Zhang, H. Measurement and Correlation of the Solubility of Baicalin in Several Mixed Solvents. *J. Chem. Eng. Data* **2019**, *64*, 1281–1287. [CrossRef]
257. Wang, S.; Chen, N.; Qu, Y. Solubility of Florfenicol in Different Solvents at Temperatures from (278 to 318) K. *J. Chem. Eng. Data* **2011**, *56*, 638–641. [CrossRef]
258. Wang, S.; Chen, Y.; Gong, T.; Dong, W.; Wang, G.; Li, H.; Wu, S. Solid-liquid equilibrium behavior and thermodynamic analysis of dipyridamole in pure and binary solvents from 293.15 K to 328.15 K. *J. Mol. Liq.* **2019**, *275*, 8–17. [CrossRef]
259. Wang, S.; Li, Q.-S.; Su, M.-G. Solubility of 1*H*-1,2,4-Triazole in Ethanol, 1-Propanol, 2-Propanol, 1,2-Propanediol, Ethyl Formate, Methyl Acetate, Ethyl Acetate, and Butyl Acetate at (283 to 363) K. *J. Chem. Eng. Data* **2007**, *52*, 856–858. [CrossRef]
260. Wang, S.; Qin, L.; Zhou, Z.; Wang, J. Solubility and Solution Thermodynamics of Betaine in Different Pure Solvents and Binary Mixtures. *J. Chem. Eng. Data* **2012**, *57*, 2128–2135. [CrossRef]
261. Wang, S.; Song, Z.; Wang, J.; Dong, Y.; Wu, M. Solubilities of Ibuprofen in Different Pure Solvents. *J. Chem. Eng. Data* **2010**, *55*, 5283–5285. [CrossRef]
262. Wang, S.; Zhang, Y.; Wang, J. Solubility Measurement and Modeling for Betaine in Different Pure Solvents. *J. Chem. Eng. Data* **2014**, *59*, 2511–2516. [CrossRef]
263. Wang, X.; Zhang, D.; Liu, S.; Chen, Y.; Jia, L.; Wu, S. Thermodynamic Study of Solubility for Imatinib Mesylate in Nine Monosolvents and Two Binary Solvent Mixtures from 278.15 to 318.15 K. *J. Chem. Eng. Data* **2018**, *63*, 4114–4127. [CrossRef]
264. Wang, Z.; Xu, Z.; Xu, X.; Yang, A.; Luo, W.; Luo, Y. Solubility of benzoic acid in twelve organic solvents: Experimental measurement and thermodynamic modeling. *J. Chem. Thermodyn.* **2020**, *150*, 106234. [CrossRef]
265. Watterson, S.; Hudson, S.; Svärd, M.; Rasmuson, Å.C. Thermodynamics of fenofibrate and solubility in pure organic solvents. *Fluid Phase Equilibria* **2014**, *367*, 143–150. [CrossRef]

266. Wei, H.; Gao, N.; Dang, L. Solubility and Thermodynamic Properties of Sulfamethazine–Saccharin Cocrystal in Pure and Binary (Acetonitrile + 2-Propanol) Solvents. *Trans. Tianjin Univ.* **2020**, *27*, 460–472. [CrossRef]
267. Wu, J.; Gu, L.; Wang, H.; Tao, L.; Wang, X. Solubility of Baicalein in Different Solvents from (287 to 323) K. *Int. J. Thermophys.* **2014**, *35*, 1465–1475. [CrossRef]
268. Wu, K.; Li, Y. Solubility and solution thermodynamics of isobutyramide in 15 pure solvents at temperatures from 273.15 to 324.75 K. *J. Mol. Liq.* **2020**, *311*, 113294. [CrossRef]
269. Wu, S.; Shi, Y.; Zhang, H. Solubility Measurement and Correlation for Amrinone in Four Binary Solvent Systems at 278.15–323.15 K. *J. Chem. Eng. Data* **2020**, *65*, 4108–4115. [CrossRef]
270. Wu, Y.; Ren, M.; Zhang, X. Solubility Determination and Model Correlation of Benorilate between T = 278.18 and 318.15 K. *J. Chem. Eng. Data* **2020**, *65*, 3690–3695. [CrossRef]
271. Wu, Y.; Wu, C.; Yan, S.; Hu, B. Solubility of Bisacodyl in Pure Solvent at Various Temperatures: Data Correlation and Thermodynamic Property Analysis. *J. Chem. Eng. Data* **2019**, *65*, 43–48. [CrossRef]
272. Wu, Y.; Wu, J.; Wang, J.; Gao, J. Effect of Solvent Properties and Composition on the Solubility of Ganciclovir Form I. *J. Chem. Eng. Data* **2019**, *64*, 1501–1507. [CrossRef]
273. Wüst Zibetti, A.; Aydi, A.; Claumann, C.A.; Eladeb, A.; Adberraba, M. Correlation of solubility and prediction of the mixing properties of rosmarinic acid in different pure solvents and in binary solvent mixtures of ethanol + water and methanol + water from (293.2 to 318.2) K. *J. Mol. Liq.* **2016**, *216*, 370–376. [CrossRef]
274. Xia, Q.; Chen, S.-N.; Chen, Y.-S.; Zhang, M.-S.; Zhang, F.-B.; Zhang, G.-L. Solubility of decanedioic acid in binary solvent mixtures. *Fluid Phase Equilibria* **2011**, *304*, 105–109. [CrossRef]
275. Xu, R.; Han, T.; Shen, L.; Zhao, J.; Lu, X.a. Solubility Determination and Modeling for Artesunate in Binary Solvent Mixtures of Methanol, Ethanol, Isopropanol, and Propylene Glycol + Water. *J. Chem. Eng. Data* **2019**, *64*, 755–762. [CrossRef]
276. Marcus, Y. Preferential Solvation of Drugs in Binary Solvent Mixtures. *Pharm. Anal. Acta* **2017**, *10*, 4172. [CrossRef]
277. Yan, M.; Li, X.; Tao, B.; Yang, L.; Luo, W. Solubility of succinic acid, glutaric acid and adipic acid in propionic acid + ε-caprolactone mixtures and propionic acid + cyclohexanone mixtures: Experimental measurement and thermodynamic modeling. *J. Mol. Liq.* **2018**, *272*, 106–119. [CrossRef]
278. Yang, H.; Rasmuson, Å.C. Solubility of Butyl Paraben in Methanol, Ethanol, Propanol, Ethyl Acetate, Acetone, and Acetonitrile. *J. Chem. Eng. Data* **2010**, *55*, 5091–5093. [CrossRef]
279. Yang, H.; Zhang, T.; Xu, S.; Han, D.; Liu, S.; Yang, Y.; Du, S.; Li, M.; Gong, J. Measurement and Correlation of the Solubility of Azoxystrobin in Seven Monosolvents and Two Different Binary Mixed Solvents. *J. Chem. Eng. Data* **2017**, *62*, 3967–3980. [CrossRef]
280. Yang, L.; Zhang, Y.; Cheng, J.; Yang, C. Solubility and thermodynamics of polymorphic indomethacin in binary solvent mixtures. *J. Mol. Liq.* **2019**, *295*, 111717. [CrossRef]
281. Yang, Z.; Shao, D.; Zhou, G. Analysis of solubility parameters of fenbendazole in pure and mixed solvents and evaluation of thermodynamic model. *J. Chem. Thermodyn.* **2020**, *140*, 105876. [CrossRef]
282. Yang, Z.; Shao, D.; Zhou, G. Solubility profile of imatinib in pure and mixed solvents and calculation of thermodynamic properties. *J. Chem. Thermodyn.* **2020**, *144*, 106031. [CrossRef]
283. Yang, Z.; Shao, D.; Zhou, G. Improvement of solubility and analysis thermodynamic properties of β tegafur in pure and mixed organic solvents. *J. Chem. Thermodyn.* **2020**, *146*, 106090. [CrossRef]
284. Yaws, C.L. Physical Properties—Inorganic Compounds. In *The Yaws Handbook of Physical Properties for Hydrocarbons and Chemicals*; Elsevier: Amsterdam, The Netherlands, 2015; pp. 684–810.
285. Yu, Q.; Ma, X.; Xu, L. Solubility, dissolution enthalpy and entropy of l-glutamine in mixed solvents of ethanol+water and acetone+water. *Thermochim. Acta* **2013**, *558*, 6–9. [CrossRef]
286. Zadaliasghar, S.; Jouyban, A.; Martinez, F.; Barzegar-Jalali, M.; Rahimpour, E. Solubility of ketoconazole in the binary mixtures of 2-propanol and water at different temperatures. *J. Mol. Liq.* **2020**, *300*, 112259. [CrossRef]
287. Zhang, C.-L.; Li, B.-Y.; Wang, Y. Solubilities of Sulfadiazine in Methanol, Ethanol, 1-Propanol, 2-Propanol, Acetone, and Chloroform from (294.15 to 318.15) K. *J. Chem. Eng. Data* **2010**, *55*, 2338–2339. [CrossRef]
288. Zhang, F. Commentary on the "Solubility of l-histidine in different aqueous binary solvent mixtures from 283.15 K to 318.15 K with experimental measurement and thermodynamic modelling". *J. Chem. Thermodyn.* **2018**, *124*, 98–100. [CrossRef]
289. Zhang, H.; Yin, Q.; Liu, Z.; Gong, J.; Bao, Y.; Zhang, M.; Hao, H.; Hou, B.; Xie, C. Measurement and correlation of solubility of dodecanedioic acid in different pure solvents from T = (288.15 to 323.15)K. *J. Chem. Thermodyn.* **2014**, *68*, 270–274. [CrossRef]
290. Zhang, J.; Huang, C.; Chen, J.; Xu, R. Equilibrium Solubility Determination and Modeling of Fenbendazole in Cosolvent Mixtures at (283.15–328.15) K. *J. Chem. Eng. Data* **2019**, *64*, 4095–4102. [CrossRef]
291. Zhang, J.; Huang, C.; Xu, R. Solubility of Bifonazole in Four Binary Solvent Mixtures: Experimental Measurement and Thermodynamic Modeling. *J. Chem. Eng. Data* **2019**, *64*, 2641–2648. [CrossRef]
292. Zhang, J.; Huang, C.; Xu, R. Solubility Determination and Mathematical Modeling of Nicorandil in Several Aqueous Cosolvent Systems at Temperature Ranges of 278.15–323.15 K. *J. Chem. Eng. Data* **2020**, *65*, 4063–4070. [CrossRef]
293. Zhang, J.; Song, X.; Xu, R. Solubility Determination and Modeling for Milrinone in Binary Solvent Mixtures of Ethanol, Isopropanol, Ethylene Glycol, and *N*,*N*-Dimethylformamide + Water. *J. Chem. Eng. Data* **2020**, *65*, 4100–4107. [CrossRef]

294. Zhang, J.; Zhang, H.; Xu, R. Solubility Determination and Modeling for Tirofiban in Several Mixed Solvents at 278.15–323.15 K. *J. Chem. Eng. Data* **2020**, *65*, 4071–4078. [CrossRef]
295. Zhang, N.; Li, S.; Yang, H.; Li, M.; Yang, Y.; Tang, W. Measurement and Correlation of the Solubility of Tetramethylpyrazine in Nine Monosolvents and Two Binary Solvent Systems. *J. Chem. Eng. Data* **2019**, *64*, 995–1006. [CrossRef]
296. Zhang, P.; Sha, J.; Wan, Y.; Zhang, C.; Li, T.; Ren, B. Apparent thermodynamic analysis and the dissolution behavior of levamisole hydrochloride in three binary solvent mixtures. *Thermochim. Acta* **2019**, *681*, 178375. [CrossRef]
297. Zhang, P.; Wan, Y.; Zhang, C.; Zhao, R.; Sha, J.; Li, Y.; Li, T.; Ren, B. Solubility and mixing thermodynamic properties of levamisole hydrochloride in twelve pure solvents at various temperatures. *J. Chem. Thermodyn.* **2019**, *139*, 105882. [CrossRef]
298. Zhang, P.; Zhang, C.; Zhao, R.; Wan, Y.; Yang, Z.; He, R.; Chen, Q.; Li, T.; Ren, B. Measurement and Correlation of the Solubility of Florfenicol Form A in Several Pure and Binary Solvents. *J. Chem. Eng. Data* **2018**, *63*, 2046–2055. [CrossRef]
299. Zhang, X.; Chen, J.; Hu, J.; Liu, M.; Cai, Z.; Xu, Y.; Sun, B. The solubilities of benzoic acid and its nitro-derivatives, 3-nitro and 3,5-dinitrobenzoic acids. *J. Chem. Res.* **2021**, *45*, 1100–1106. [CrossRef]
300. Zhang, X.; Cui, P.; Yin, Q.; Zhou, L. Measurement and Correlation of the Solubility of Florfenicol in Four Binary Solvent Mixtures from T = (278.15 to 318.15) K. *Crystals* **2022**, *12*, 1176. [CrossRef]
301. Zhu, Y.; Yang, H.; Si, Z.; Zhang, X. Solubility and thermodynamics of l-hydroxyproline in water and (methanol, ethanol, n-propanol) binary solvent mixtures. *J. Mol. Liq.* **2020**, *298*, 112043. [CrossRef]
302. Zorrilla-Veloz, R.I.; Stelzer, T.; López-Mejías, V. Measurement and Correlation of the Solubility of 5-Fluorouracil in Pure and Binary Solvents. *J. Chem. Eng. Data* **2018**, *63*, 3809–3817. [CrossRef]
303. Milescu, R.A.; Zhenova, A.; Vastano, M.; Gammons, R.; Lin, S.; Lau, C.H.; Clark, J.H.; McElroy, C.R.; Pellis, A. Polymer Chemistry Applications of Cyrene and its Derivative Cygnet 0.0 as Safer Replacements for Polar Aprotic Solvents. *ChemSusChem* **2021**, *14*, 3367–3381. [CrossRef]
304. Glass, M.; Aigner, M.; Viell, J.; Jupke, A.; Mitsos, A. Liquid-liquid equilibrium of 2-methyltetrahydrofuran/water over wide temperature range: Measurements and rigorous regression. *Fluid Phase Equilibria* **2017**, *433*, 212–225. [CrossRef]
305. Dargo, G.; Kis, D.; Gede, M.; Kumar, S.; Kupai, J.; Szekely, G. MeSesamol, a bio-based and versatile polar aprotic solvent for organic synthesis and depolymerization. *Chem. Eng. J.* **2023**, *471*, 144365. [CrossRef]
306. Komarova, A.O.; Dick, G.R.; Luterbacher, J.S. Diformylxylose as a new polar aprotic solvent produced from renewable biomass. *Green Chem.* **2021**, *23*, 4790–4799. [CrossRef]
307. Kamlet, M.J.; Abboud, J.L.M.; Abraham, M.H.; Taft, R.W. Linear solvation energy relationships. 23. A comprehensive collection of the solvatochromic parameters,. pi.*,. alpha., and. beta., and some methods for simplifying the generalized solvatochromic equation. *J. Org. Chem.* **1983**, *48*, 2877–2887. [CrossRef]
308. Abraham, M.H. Scales of solute hydrogen-bonding: Their construction and application to physicochemical and biochemical processes. *Chem. Soc. Rev.* **1993**, *22*, 73–83. [CrossRef]
309. Liu, X.; Acree, W.E.; Abraham, M.H. Descriptors for some compounds with pharmacological activity; calculation of properties. *Int. J. Pharm.* **2022**, *617*, 121597. [CrossRef]
310. Vitha, M.; Carr, P.W. The chemical interpretation and practice of linear solvation energy relationships in chromatography. *J. Chromatogr. A* **2006**, *1126*, 143–194. [CrossRef]
311. West, C.; Lesellier, E. Characterisation of stationary phases in subcritical fluid chromatography with the solvation parameter model: III. Polar stationary phases. *J. Chromatogr. A* **2006**, *1110*, 200–213. [CrossRef]
312. Efimov, I.; Povarov, V.G.; Rudko, V.A. Comparison of UNIFAC and LSER Models for Calculating Partition Coefficients in the Hexane–Acetonitrile System Using Middle Distillate Petroleum Products as an Example. *Ind. Eng. Chem. Res.* **2022**, *61*, 9575–9585. [CrossRef]
313. EPA. CompTox Chemicals Dashboard v2.3.0. 2023. Available online: https://comptox.epa.gov/dashboard/ (accessed on 31 December 2023).
314. Hou, P.; Jolliet, O.; Zhu, J.; Xu, M. Estimate ecotoxicity characterization factors for chemicals in life cycle assessment using machine learning models. *Environ. Int.* **2020**, *135*, 105393. [CrossRef]
315. Wojeicchowski, J.P.; Abranches, D.O.; Ferreira, A.M.; Mafra, M.R.; Coutinho, J.A.P. Using COSMO-RS to Predict Solvatochromic Parameters for Deep Eutectic Solvents. *ACS Sustain. Chem. Eng.* **2021**, *9*, 10240–10249. [CrossRef]
316. Wojeicchowski, J.P.; Ferreira, A.M.; Okura, T.; Pinheiro Rolemberg, M.; Mafra, M.R.; Coutinho, J.A.P. Using COSMO-RS to Predict Hansen Solubility Parameters. *Ind. Eng. Chem. Res.* **2022**, *61*, 15631–15638. [CrossRef]