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Solubility Determination and Correlation of Warfarin Sodium 2-Propanol Solvate in Pure, Binary, and Ternary Solvent Mixtures

Mery Vet George De la Rosa^{†,‡}, Roberto Santiago^{‡,§}, Joseph Malavé Romero^{‡,||}, Jorge Duconge[†], Jean-Christophe Monbaliu[⊥], Vilmalí López-Mejías^{*,‡,#}, Torsten Stelzer^{*,†,‡}

[†]Department of Pharmaceutical Sciences, University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico 00936, United States

[‡]Crystallization Design Institute, Molecular Sciences Research Center, University of Puerto Rico, San Juan, Puerto Rico 00926, United States

[§]Department of Mathematics, University of Puerto Rico, Río Piedras Campus, San Juan, Puerto Rico 00931, United States

[#]Department of Chemistry, University of Puerto Rico, Río Piedras Campus, San Juan, Puerto Rico 00931, United States

^{||}Department of Biology, University of Puerto Rico, Bayamón Campus, Bayamón, Puerto Rico 00959, United States

[⊥]Center for Integrated Technology and Organic Synthesis, RU MolSys, University of Liège, B-4000 Liège, Sart Tilman, Belgium

Abstract

The solubility of warfarin sodium isopropanol solvate (WS-IPA), a widely used anticoagulant, was determined at temperatures ranging from 278.15 to 333.15 K in four pure solvents (acetone, ethanol, IPA, and water), five binary solvent mixtures (IPA + acetone, IPA + ethanol, IPA + water, IPA + heptane, and IPA + hexane), and five ternary solvent mixtures (IPA + acetone + heptane, IPA + acetone + hexane, IPA + ethanol + heptane, IPA + ethanol + hexane, and IPA + water + heptane) using the polythermal method. It was demonstrated that the solubility of WS-IPA increases with increasing temperature in the pure solvents and at constant solvent composition in the solvent mixtures. In addition, the solubility of WS-IPA in IPA increases with increasing content of acetone, ethanol, and water, which act as cosolvents, and decreases with increasing content of heptane and hexane, which act as antisolvents. The experimental solubility data of

*Corresponding Authors vilma.lopez@upr.edu (V.L.-M.), torsten.stelzer@upr.edu (T.S.).

ASSOCIATED CONTENT

Supporting Information

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Detailed experimental procedure for the solubility curves of WS-IPA in pure solvents and binary and ternary solvent mixtures, calculated surface plots of WS-IPA in binary and ternary solvent mixtures using the λh model equation, Raman spectra, powder X-ray diffractograms, and DSC and TGA thermographs (PDF)

Notes

The authors declare no competing financial interest.

WS-IPA in pure solvents and binary and ternary solvent mixtures were correlated using the modified Apelblat and λ h model equations. The correlated solubility data agree with the experimental data based on the relative deviation and the average relative deviation (ARD %) values. Thus, the correlated and experimentally derived solubility data of WS-IPA provide a pathway to engineer advanced pharmaceutical crystallization processes for WS-IPA.

Graphical Abstract

INTRODUCTION

Warfarin (Figure 1a), an essential medicine¹ prone to drug shortages,^{2–5} is the most commonly prescribed oral anticoagulant (~80 M prescriptions in 2014)⁶ for the treatment of thromboembolic complications related to cardiovascular diseases, which are the number one cause of mortality in the United States (>600 000 deaths/year).⁷ To address manufacturing-related drug shortages that often arise for pharmaceutical compounds, such as warfarin, continuous manufacturing has evolved as an area of recent research interest both in academia and industry.^{8–11} Consequently, the flow synthesis of warfarin has been developed in recent years.¹¹ This represents the first step toward the development of an end-to-end continuous manufacturing process for warfarin and other pharmaceutical products of high demand.^{8–11} Integrated continuous manufacturing, a key aspect of process intensification,^{8,9,12–14} would require the crystallization of warfarin (i) to obtain a pure product and (ii) to produce the crystalline form needed in the solid dosage formulation.¹⁵ In spite of the very low aqueous solubility of warfarin alone, its salt, warfarin sodium¹⁶ (WS, Figure 1b), shows high solubility in water and is thus grouped in the Biopharmaceutical Classification System as a class 1 compound.¹⁷ WS is formulated as a solvate,^{18–20} also known as clathrate,^{20–23} in which isopropanol (IPA) is entrapped into the crystalline lattice at a ratio of WS to IPA of 2:1 (Figure 1c).^{15,18,24} In order to advance in the development of a continuous crystallization process leading to the desired solid form (WS-IPA) for formulation,^{15,25} solubility of this compound in various solvents and solvent mixtures^{26,27} needs to be understood.

Upon reviewing the available literature, very limited solubility data for WS-IPA in various solvents have been reported.^{24,28} The solubility of WS-IPA has not been previously reported in any of the pure solvents or solvent mixtures employed in the present work.²⁹ Moreover, there is no account correlating WS-IPA solubility and solvent composition, which are

fundamental parameters needed to engineer an antisolvent cooling crystallization process for this or other compounds.³⁰ The selection of the crystallization solvent also affects nucleation and growth kinetics, crystal morphology, and structure^{31–34} that in turn influence the physicochemical properties of the active pharmaceutical ingredient and its performance.^{35,36} Hence, the present study focuses on the determination of the solubility of WS-IPA in four pure solvents (acetone, ethanol, IPA, and water), five binary mixtures (IPA + acetone, IPA + ethanol, IPA + water, IPA + heptane, and IPA + hexane), and five ternary mixtures (IPA + acetone + heptane, IPA + acetone + hexane, IPA + ethanol + heptane, IPA + ethanol + hexane, and IPA + water + heptane) at temperatures ranging from 278.15 to 333.15 K using the polythermal method³⁷ in a Crystal16 multiple reactor system.^{9,27,30,38–40} The solvents are categorized as class 3 by the Food and Drug Administration (less toxic and lower risks to human health) except hexane, which is a class 2 solvent.⁴¹ However, hexane is commonly used as an antisolvent in pharmaceutical crystallization processes.^{8,9,42} The experimental solubility data were correlated employing the modified Apelblat and λh model equations, which enable the interpolation and extrapolation of the determined solubility, providing a better understanding of the solubility profile for WS-IPA. Collectively, the experimental and correlated solubility data presented in this study pave the way to engineer a continuous antisolvent cooling crystallization process for this compound.

EXPERIMENTAL SECTION

Materials.

Table 1 shows the CAS number, commercial source, purity (determined by chemical supplier), analysis method, and solvent classification of the materials employed in this study. Nanopurified water (18.23 MOhm/cm, pH = 5.29, and mV = 76.8) was utilized as-obtained from a water purification system Aries Filter (Gemini). All materials were used “as-received” without further purification.

Solubility Measurements.

Solubility measuring techniques can be grouped into isothermal^{43–45} and polythermal methods.^{37,40,46–48} The isothermal method measures the solubility at predetermined temperatures of unknown concentrations by adding excess of crystalline material into the solvent to measure the concentration after an extended period of stirring (often 24 h). The polythermal method determines the solubility at unknown temperatures of solutions with predetermined concentrations at specified heating rates. Consequently, the isothermal method allows for solubility measurements at the same temperature interval,^{49,50} whereas the polythermal method determines the solubility at different temperature intervals in between the data points of a particular solubility curve. In this study, the solubility of WS-IPA was determined applying the polythermal method^{37–40,48} by using a Crystal16 multiple reactor system (Technobis Crystallization Systems), leading to unevenly distributed data points within the reported temperature range.^{9,27,38–40} Sealed glass vials with an internal volume of 2 mL (Fisher Scientific) were employed to prepare the samples with different concentrations using a microbalance (XP26, Mettler Toledo, uncertainty ± 0.002 mg) to weigh the solute and an analytical balance (MS104S, Mettler Toledo, uncertainty ± 0.1 mg) to weigh the pure solvents and solvent mixtures. The resulting suspensions were

vigorously agitated using a magnetic stir bar (rare earth) at 700 rpm while being heated from 278.15 to 333.15 K at 0.3 K/min.^{40,51,52} Owing to the boiling point restriction of acetone (329.15 K),⁵³ the temperature range needed to be adjusted to 278.15–323.15 K for the pure solvent and all solvent mixtures containing this solvent. Assuming that the dissolution kinetics can be neglected,³⁹ the transmission of light through the suspension can be used to determine the saturation temperature at its maximum using the software CrystalClear (v 1.0.1.614).^{9,27,38–40,48,54} Each concentration was measured at least twice to ensure accuracy.⁵⁹ The uncertainty of each saturated temperature was within ± 0.1 K. The mole fraction solubility (x_i) of WS-IPA was calculated using eq 1

$$x_i = \frac{m_i/M_i}{\sum_{i=1}^n m_i/M_i} \quad (1)$$

where m_i and M_i represent the mass (g) and molecular weight (g/mol) of WS-IPA (MW = 360.36 g/mol)^{18,21,24} and the solvents employed, respectively.

The isothermal method was performed to validate the reliability of the polythermal method in providing accurate molar solubility measurements for the systems presented within this work for which the polythermal method was employed. Isothermal measurements were performed as follows: an excess of WS-IPA (1) was added to 1.5 mL of the binary solvent system IPA (2) + ethanol (3) with a mass fraction of ethanol, $w_3 = 0.304$ in sealed glass vials with an internal volume of 2 mL (Fisher Scientific). The excess amount (~ 10 mg above solubility) was calculated for each selected temperature based on the solubility of WS-IPA (1) previously determined by the polythermal method. The samples were kept at the following selected temperatures, 293.15, 303.15, 313.15, and 323.15 K in a Crystal16 multiple reactor system (Technobis Crystallization Systems) for 24 h. The resulting suspensions were vigorously agitated using a magnetic stir bar (rare earth) at 700 rpm for 20 h and left to settle for 4 h without stirring. Approximately 1 mL of the clear supernatant of each sample was filtered through a 0.2 μm syringe filter (PTFE, 25 mm, Fischer Scientific) and diluted with the binary IPA + ethanol ($w_3 = 0.304$) solvent mixture to a target concentration for absorbance measurement using UV–vis spectroscopy. The λ_{max} of absorption for WS-IPA in the binary solvent mixture occurs at 305 nm. A linear calibration curve ($R^2 = 0.9997$) was obtained by measuring serial dilutions of WS-IPA in the binary solvent mixture (IPA + ethanol with $w_3 = 0.304$).

Raman Spectroscopy.

Raman spectra were recorded at room temperature using a Thermo Scientific DXR2 Raman microscope equipped with 532 nm laser, 400 lines/mm grating, and a 25 μm slit. The spectra were collected over the range of 600–3400 cm^{-1} , averaging 20 scans with 10 s exposure time per scan. The spectra obtained were analyzed using the OMNIC for Dispersive Raman software (version 9.2.0). Before the solubility measurements, the commercial sample was analyzed by Raman microscopy and the solid-state was confirmed as the WS-IPA solvate (Supporting Information).⁵⁷ The resulting suspensions were measured by Raman microscopy after the experiments were completed to confirm that the yielded material was WS IPA (Supporting Information). For the ternary solvent system IPA + acetone + hexane, a

solid material could only be recovered for the hexane mass fractions (w_4) of 0.086 and 0.174.

Powder X-ray Diffraction.

Powder X-ray diffractograms were collected for all samples using a Rigaku XtaLAB SuperNova single microfocus Cu K α radiation ($\lambda = 1.5417 \text{ \AA}$) source equipped with a HyPix3000 X-ray detector in the transmission mode, operating at 50 kV and 1 mA (Supporting Information). Powder diffractograms were collected at 300 K over an angular 2θ range between 7 and 40° with a step of 0.01° using the Gandolfi move experiment for powders (90 s exposures). Before the solubility measurements, the commercial sample was analyzed by Powder X-ray diffraction (PXRD) and the solid-state was confirmed as the WS-IPA solvate (Supporting Information).¹⁹ The resulting suspensions were measured by PXRD after the experiments were completed to confirm that the yielded material was WS-IPA (Supporting Information). For the ternary solvent system IPA + acetone + hexane, a solid material could only be recovered for the hexane mass fractions (w_4) of 0.086 and 0.174.

Differential Scanning Calorimetry.

The melting temperature, T_m , and enthalpy of fusion, $_{\text{fus}}H$, of WS were determined in a differential scanning calorimetry (DSC) Q2000 (TA Instruments Inc.) equipped with a RCS40 single-stage refrigeration system. The calibration of the instrument was made with an indium standard ($T_m = 429.75 \text{ K}$ and $_{\text{fus}}H = 28.54 \text{ J/g}$). Samples ($\sim 2.200 \text{ mg}$) were weighed using a microbalance (XP26, Mettler Toledo, uncertainty $\pm 0.002 \text{ mg}$) and placed on hermetically sealed pans with a pinhole, which is the preferred method when studying solvates.^{58–61} The samples were equilibrated at 298.15 K for 10 min before heating to 523.15 K under a N_2 atmosphere (50 mL/min) at a rate of 5.0 K/min and a temperature accuracy of 0.1 K. The thermograms were analyzed using the software, TA Universal Analysis 2000 (version 4.5A). The measurements were conducted five times ($n = 5$), and the average result of the peak temperatures was taken to ensure accuracy (Supporting Information). The standard uncertainty, u , for the experimental temperature measured with DSC was estimated to be $u(T_m) = 0.5 \text{ K}$.

Thermogravimetric Analysis.

The desolvation and degradation of WS-IPA was recorded in a thermogravimetric analysis (TGA) Q500 (TA Instruments Inc.) calibrated with calcium oxalate monohydrate. Samples (5–10 mg) were equilibrated at 298.15 K for 10 min before heating to 523.15 K under a N_2 atmosphere (60 mL/min) at a rate of 5.0 K/min and a temperature accuracy of 0.1 K. The data were analyzed with TA Universal Analysis software v 4.5A.

THERMODYNAMIC MODELS

To facilitate a broader understanding of the solution behavior of WS-IPA in the various solvents and solvent mixtures, the experimental solubility of WS-IPA in pure solvents and binary and ternary solvent mixtures was correlated by using the modified Apelblat and λh

model equations. The modeling allows for a more general quantification of the solubility profile of WS-IPA and enables the interpolation of solubility data.

Modified Apelblat Equation.

The modified Apelblat eq 2 is a commonly used semiempirical model that correlates the solubility of a solute as a function of the absolute temperature^{40,48,54–56}

$$\ln x_1 = A + \frac{B}{T} + C \ln T \quad (2)$$

In eq 2, x_1 represents the mole fraction solubility of WS-IPA, T is the absolute temperature in kelvin (K), and A , B , and C are empirical model parameters. The values of A and B depict the variation in the solution activity coefficient, and C reflects the effect of temperature on the fusion enthalpy.^{48,62}

λh Equation.

The λh equation, eq 3, was proposed by Buchowski et al.⁶³ to correlate solubility and temperature of solid–liquid equilibrium systems.^{40,48,54–56}

$$\ln \left[1 + \lambda \frac{1 - x_1}{x_1} \right] = \lambda h \left(\frac{1}{T} - \frac{1}{T_m} \right) \quad (3)$$

In eq 3, x_1 represents the mole fraction solubility of WS-IPA, T and T_m are the experimental and normal melting temperatures of WS in kelvin (K), respectively, whereas λ and h are parameters that model the nonideal properties of the solution system and the excess mixture enthalpy of solution, respectively.

Origin (OriginLab Corporation, version B95.0.193) was used to model the modified Apelblat and λh model equations using the Levenberg–Marquardt algorithm to solve the nonlinear curve-fitting problem. The relative deviation (RD) and average relative deviation (ARD %) were determined using eqs 4 and 5, respectively, to evaluate the correlation between the experimental and calculated solubility data.

$$RD_i = \frac{x_{1,i}^{\text{exp}} - x_{1,i}^{\text{cal}}}{x_{1,i}^{\text{exp}}} \quad (4)$$

$$\text{ARD \%} = \frac{100}{N} \sum_{i=1}^N \left| \frac{x_{1,i}^{\text{exp}} - x_{1,i}^{\text{cal}}}{x_{1,i}^{\text{exp}}} \right| \quad (5)$$

In eqs 4 and 5, $x_{1,i}^{\text{exp}}$ and $x_{1,i}^{\text{cal}}$ are the i th experimental and correlated mole fraction solubility, respectively, and N is the total number of experimental values.

RESULTS AND DISCUSSION

Validation of Experimental Technique.

To confirm the accuracy of the results obtained employing the polythermal method, the solubility of WS-IPA (1) was measured in a binary solvent system composed of IPA (2) + ethanol (3) with $w_3 = 0.304$, using the isothermal method. The molar solubilities determined at 293.15, 303.15, 313.15, and 323.15 K were used as reference to calculate the ARD % of the solubility data determined by the polythermal method. For comparison, the data for the polythermal method were derived by calculating the respective concentrations at the target temperatures using the modified Apelblat and λh model equations with the optimized parameter values for the WS-IPA (1) + IPA (2) + ethanol (3) with $w_3 = 0.304$ system determined within this work. The solubility data for the isothermal and polythermal methods are listed in Table 2 and graphically compared in Figure 2. It can be observed that the isothermal and polythermal data are closely correlated. Moreover, the low ARD % values of 4.30 and 4.27 for the isothermal method with respect to the polythermal method derived from the modified Apelblat and the λh model equations, respectively, prove the reliability of the polythermal method in providing accurate molar solubility measurements for the systems presented within this work.

DSC & TGA Results.

The peak melting temperature (T_m) for WS was reported previously by Gao and Maurin²⁸ (460.15 K) using an open pan but was redetermined experimentally within this study using hermetically sealed pans with a pinhole, which is the preferred method when studying solvates.^{58–61} It could be confirmed that WS-IPA loses its IPA content (~8%) at ~393.15 K²⁸ without further chemical degradation before the melting of the desolvated form, WS (Supporting Information). The average peak value of $T_m = 468.87$ K obtained in this study was used to calculate the correlated mole fraction solubility (x_1^{cal}) employing the λh model equation.

Solubility Data.

The experimentally measured mole fraction solubility data of WS-IPA in the pure solvents and solvent mixtures as well as the RD between the experimental and correlated solubility are presented in Tables 3–13. The mole fraction solubility of WS-IPA in the four pure solvents (acetone, ethanol, IPA, and water) is listed in Table 3, whereas the mole fraction solubility data for the binary solvent systems (IPA + acetone, IPA + ethanol, IPA + water, IPA + heptane, and IPA + hexane) and ternary mixtures (IPA + acetone + heptane, IPA + acetone + hexane, IPA + ethanol + heptane, IPA + ethanol + hexane, and IPA + water + heptane) are shown in Tables 4–8 and Tables 9–13, respectively.

The modified Apelblat and λh model equations were used to correlate the experimental solubility data. Origin was employed to obtain the optimized values for both equations, which allows for direct calculation of the solubility of WS-IPA at a specific temperature in the pure solvents and solvent mixtures studied. The correlation parameters for the Apelblat and λh model equations along with the ARD % for the solubility of WS-IPA in the pure solvents and solvent mixtures studied are listed in Table 14. The low RD and ARD % values

demonstrate that the correlated solubility data obtained from the two model equations agree well with the experimental solubility data obtained by employing the polythermal method, with the exception of the pure solvent, water that shows a relatively high ARD % (32.0817) when correlated with the λh model equation. The latter is in strong contrast with the correlated data for the Apelblat model equation, which presents a much lower ARD % (3.6525). In general, the Apelblat model equation was found to give better correlation results for pure solvents as well as binary and ternary solvent mixtures compared to the λh model equation. Unlike the Apelblat model equation, the λh model equation depends on the accurate determination of the T_m of the solute, as a parameter to accurately correlate the experimental solubility data. Owing to the desolvation of WS-IPA upon heating, the T_m determined here and used to correlate the experimental solubility data in the λh model equation corresponds to the desolvated form of WS-IPA, and thus, WS. On this account, it can be concluded that the Apelblat model equation represents the better model to calculate the solubility behavior of WS-IPA, when compared to the λh model equation.

On the basis of Figure 3, it can be concluded that the solubility of WS-IPA increases with increasing temperature in all pure solvents employed in this study. The solubility of WS-IPA in the pure solvents ranks as follows: ethanol > acetone > water > IPA below 310 K, and ethanol > water > acetone > IPA above 310 K. The solubility of WS-IPA in heptane and hexanes is extremely low, <0.2 mg/mL, in the temperature range studied (278.15–333.15 K). Therefore, the solubility of WS-IPA could not be determined in these two pure solvents; instead, heptane and hexanes were used as antisolvents in some of the binary and all ternary solvent mixtures.

The experimental and correlated mole fraction solubility of WS-IPA based on the modified Apelblat equation in the binary and ternary solvent mixtures are shown as surface plots in Figures 4 and 5, respectively. Figures presenting the experimental and correlated mole fraction solubility of WS-IPA using the λh model equation can be found in the Supporting Information. Figure 4a–c shows that the solubility of WS-IPA increases with increasing the weight fraction of acetone, ethanol, and water in these binary solvent mixtures and that these exceed the solubility of WS-IPA in pure IPA. This demonstrates that all three solvents (acetone, ethanol, and water) can be utilized as cosolvents to increase the solubility of WS-IPA in IPA.^{64–66} Figures 4d,e and 5a–e show that in both binary and ternary solvent mixtures, the solubility of WS-IPA decreases with increasing content of hexane and heptane because of the extremely low solubility of WS-IPA in these two pure solvents. Thus, hexane and heptane can be employed as antisolvents when developing an antisolvent cooling crystallization method for WS-IPA.

CONCLUSIONS

The solubility of WS-IPA in four pure solvents and five binary and five ternary solvent mixtures was experimentally measured from 278.15 to 333.15 K using the polythermal method enabled by the use of a Crystal16 multiple reactor system. The experimental data were correlated using the modified Apelblat and λh model equations to provide a general quantification of the solubility profiles for this highly prescribed pharmaceutical compound. The low RD and ARD % values obtained indicate that the correlated solubility data obtained

employing the two model equations agree well with the experimental solubility data. Even though both the modified Apelblat and λh model equations do not take into consideration the solvent composition and require separate parameters for each solvent, they provide a direct approach to calculate the solubility of WS-IPA in various solvents and solvent mixtures. The presence of IPA in all binary and ternary solvent systems ensured that the crystalline phase of recovered material corresponded to the active form, WS-IPA, used in pharmaceutical formulations of this drug. Based on the correlated and experimentally derived solubility data, the selected solvent mixtures are potential candidates to be employed as cosolvents and antisolvents when developing enhanced pharmaceutical crystallization processes for the WS-IPA clathrate.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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NOMENCLATURE

<i>A, B, C</i>	empirical model parameters for Apelblat equation
ARD %	average relative deviation
DSC	differential scanning calorimetry
<i>h</i>	model parameter for λh equation representing excess
IPA	isopropanol
<i>m</i>	mass (g)
<i>M</i>	molecular mass (g mol^{-1})
PXRD	powder X-ray diffraction
RD	relative deviation
<i>T</i>	absolute temperature (K)
<i>T_m</i>	melting temperature of WS (K)
<i>u</i>	standard uncertainty

u_r	relative standard uncertainty
w	solvent mixture compositions
WS	warfarin sodium
WS·IPA	warfarin sodium isopropanol solvate
x_1	mole fraction solubility of WS-IPA (mol)
x_1^{cal}	correlated mole fraction solubility of WS-IPA (mol)
x_1^{exp}	experimental mole fraction solubility of WS-IPA (mol)

GREEK SYMBOLS

$_{\text{fus}}H$	molar fusion enthalpy
λ	model parameter for λh equation representing non-ideal properties of the system
λ_{max}	maximum wavelength of absorption in UV–vis measurements

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Figure 1.
Molecular structure of (a) warfarin, (b) WS, and (c) WSIPA.

Figure 2.

Comparison between experimental solubility data (isothermal method) of WS-IPA (1) in the binary solvent system IPA (2) + ethanol (3) with $w_3 = 0.304$ determined by employing the isothermal method (□) with that of the polythermal method derived using the modified Apelblat (Δ) and the λh (⊙) model equation, respectively, with the optimized parameter values determined within this work.

Figure 3. Experimental and correlated solubility data of WS-IPA in pure solvents; $\diamond$, ethanol; $\square$, acetone; $\circ$, water; and $\triangle$, IPA; —, calculated using the modified Apelblat equation. x_1 represents the mole fraction solubility of WS-IPA, and T is the temperature in kelvin (K).

Figure 4.

Surface plots for the solubility of WS-IPA (1) in binary solvent systems, (a) IPA (2) + acetone (3), (b) IPA (2) + ethanol (3), (c) IPA (2) + water (3), (d) IPA (2) + heptane (3), and (e) IPA (2) + hexane (3) correlated with the modified Apelblat equation. x_1 represents the mole fraction solubility of WS-IPA, and T is the temperature in kelvin (K).

Figure 5.

Surface plots for the solubility of WS-IPA (1) in ternary solvent systems, (a) IPA (2) + acetone (3) with $w_3 = 0.095$ + heptane (4), (b) IPA (2) + acetone (3) with $w_3 = 0.095$ + hexane (4), (c) IPA (2) + ethanol (3) with $w_3 = 0.198$ + heptane (4), (d) IPA (2) + ethanol (3) with $w_3 = 0.198$ + hexane (4), and (e) IPA (2) + water (3) with $w_3 = 0.013$ + heptane (4) correlated with the modified Apelblat equation. x_1 represents the mole fraction solubility of WS-IPA, and T is the temperature in kelvin (K).

Table 1.
Sources and Mass Fraction Purity of Materials with Corresponding Analysis Method

chemical name	CAS registry number	source	percentage purity (%) ^a	purification method	analysis method	solvent classification ^{d1}
acetone	67-64-1	VWR	99.5	none	GC ^b	class 3
ethanol	64-17-5	Pharmco Aaper	99.9	none	GC ^b	class 3
heptane	142-82-5	VWR	99.9	none	GC ^b	class 3
hexane	110-54-3	VWR	98.5	none	GC ^b	class 2
IPA	67-63-0	VWR	99.5	none	GC ^b	class 3
warfarin	81-81-2	Ningbo Samreal	99.25	none	HPLC ^c	
WS-IPA	67430-45-9	Ningbo Samreal	97.0	none	HPLC ^c	

^a Provided by the supplier.

^b Gas chromatography.

^c High-performance liquid chromatography.

Table 2.

Solubility of WS-IPA (x_1) in Binary Solvent Mixture of IPA (2) + Ethanol (3) with $w_3 = 0.304$ at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa^a

T/K	$10^3 x_1^{\text{exp}}$	$10^3 x_A$	$10^3 x_\lambda$
293.2	5.15	5.56	5.57
303.2	7.27	7.06	7.06
313.2	8.19	8.87	8.86
323.2	10.48	11.04	11.03
ARD %		4.30	4.27

^aStandard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_T are $u_T(p) = 0.1$, $u_T(x_1) = 0.01$, and $u_T(w_3) = 0.001$. x_1^{exp} refers to the experimental mole fraction solubility measured with the isothermal method. x_A and x_λ represent the derived solubility using the modified Apelblat and the λh model equation, respectively, with the optimized parameter values for the WS-IPA (1) + IPA (2) + ethanol (3) with $w_3 = 0.304$ system determined within this work. w_3 is the mass fraction of ethanol (3) in a binary IPA (2) + ethanol (3) mixture.

Table 3.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in Pure Solvents Acetone, Ethanol, IPA, and Water at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	T/K	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	10^2 RD
acetone												
278.9	5.77	5.93	-2.72	6.05	-4.85	278.8	23.99	24.38	-1.62	23.75	1.00	
283.6	7.31	7.08	3.06	7.16	1.98	284.9	27.27	26.88	1.43	26.66	2.23	
297.8	11.28	11.61	-2.97	11.56	-2.47	293.4	31.00	30.91	0.28	31.16	-0.50	
304.0	14.35	14.15	1.35	14.06	1.98	306.4	38.76	38.61	0.39	39.18	-1.09	
307.4	16.10	15.71	2.42	15.61	3.00	312.3	42.76	42.81	-0.13	43.34	-1.35	
315.3	19.25	19.78	-2.79	19.76	-2.65	321.3	49.69	50.27	-1.16	50.39	-1.41	
320.8	23.25	23.03	0.93	23.15	0.45	324.6	53.53	53.35	0.33	53.21	0.59	
IPA												
water												
280.5	0.63	0.67	-6.14	0.62	0.75	282.4	1.33	1.22	8.64	2.57	-93.12	
283.7	0.76	0.73	4.05	0.70	8.24	288.1	2.26	2.35	-4.04	3.85	-70.47	
302.2	1.32	1.29	2.32	1.32	0.09	303.2	7.39	9.68	-31.00	10.37	-40.34	
312.9	1.79	1.80	-0.54	1.84	-2.60	317.9	25.59	25.99	-1.56	24.69	3.53	
315.6	1.94	1.97	-1.23	2.00	-2.85	320.2	32.08	29.42	8.29	28.04	12.56	
326.4	2.80	2.79	0.36	2.74	1.93	329.8	44.53	45.53	-2.25	46.59	-4.65	

^aStandard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_r are $u_r(p) = 0.1$, $u_r(x_1) = 0.01$. x_1^{exp} refers to the experimental mole fraction solubility, x_1^{cal} refers to the calculated solubility data using the Apelblat and λh model equations. RD represents the corresponding relative deviation.

Table 4.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Binary Solvent Mixture of IPA (2) + Acetone (3) at Different Temperatures, T , and at Pressure, $p = 101.3 \text{ kPa}$ ^a

T/K	$10^3\ x_1^{\text{exp}}$	Apelblat		λh		T/K	$10^3\ x_1^{\text{exp}}$	Apelblat		λh	
		$10^3\ x_1^{\text{cal}}$	$10^2\ \text{RD}$	$10^3\ x_1^{\text{cal}}$	$10^2\ \text{RD}$			$10^3\ x_1^{\text{cal}}$	$10^2\ \text{RD}$	$10^3\ x_1^{\text{cal}}$	$10^2\ \text{RD}$
$w_3 = 0.047$											
280.3	1.36	1.39	-2.70	1.32	2.33	281.2	1.99	2.04	-2.68	2.01	-1.05
287.1	1.53	1.56	-1.95	1.55	-1.06	283.3	2.14	2.15	-0.82	2.13	0.21
290.8	1.73	1.67	3.10	1.68	2.46	294.0	2.95	2.81	4.50	2.84	3.66
296.6	1.97	1.87	4.97	1.92	2.93	306.3	3.79	3.82	-0.97	3.87	-2.21
304.9	2.17	2.23	-2.99	2.29	-5.52	318.0	5.02	5.11	-1.97	5.12	-2.14
312.5	2.60	2.66	-2.18	2.68	-3.25	322.7	5.82	5.75	1.26	5.71	1.81
320.4	3.25	3.21	1.14	3.15	2.95						
$w_3 = 0.148$											
283.6	2.97	3.15	-6.10	3.16	-6.47						
290.2	3.85	3.65	5.26	3.65	5.18						
296.2	4.25	4.16	2.09	4.15	2.19						
307.3	5.14	5.24	-1.83	5.22	-1.59						
314.1	5.94	6.00	-1.05	5.99	-0.89						
320.5	6.75	6.79	-0.65	6.79	-0.69						
322.8	7.18	7.09	1.23	7.10	1.08						

^aStandard uncertainty, u , is $u(T) = 2 \text{ K}$. Relative standard uncertainties, u_r are $u_r(p) = 0.1$, $u_r(x_1) = 0.01$, and $u_r(w_3) = 0.001$. x_1^{cal} refers to the experimental mole fraction solubility. x_1^{exp} refers to the calculated solubility data using the Apelblat and λh model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of acetone (3) in a binary IPA (2) + acetone (3) mixture.

Table 5.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Binary Solvent Mixture of IPA (2) + Ethanol (3) at Different Temperatures, T , and at Pressure, $p = 101.3 \text{ kPa}$ ^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD
$w_3 = 0.099$												
282.5	1.11	1.17	-5.20	1.16	-4.18	280.6	1.48	-0.22	1.44	2.41		
285.6	1.32	1.29	2.44	1.28	3.00	287.9	1.86	0.36	1.84	1.22		
289.6	1.50	1.47	2.31	1.47	2.46	304.7	3.08	-0.09	3.11	-1.05		
303.9	2.27	2.28	-0.70	2.29	-1.21	317.6	4.48	-0.32	4.52	-1.04		
312.3	2.95	2.92	0.91	2.94	0.48	324.4	5.44	0.40	5.45	0.22		
322.4	3.85	3.90	-1.18	3.90	-1.25	330.7	6.48	-0.13	6.45	0.36		
328.2	4.60	4.58	0.52	4.57	0.75							
$w_3 = 0.304$												
284.4	4.48	4.46	0.39	4.47	0.07							
296.4	5.93	6.01	-1.23	6.01	-1.33							
307.4	7.83	7.78	0.66	7.77	0.76							
316.2	9.57	9.48	0.90	9.47	1.08							
326.4	11.67	11.82	-1.29	11.81	-1.21							
332.9	13.61	13.54	0.50	13.56	0.37							

^aStandard uncertainty, u , is $u(T) = 2 \text{ K}$. Relative standard uncertainties, u_r are $u_r(p) = 0.1$, $u_r(x_1) = 0.01$, and $u_r(w_3) = 0.001$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λh model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of ethanol (3) in a binary IPA (2) + ethanol (3) mixture.

Table 6.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Binary Solvent Mixture of IPA (2) + Water (3) at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$
	$w_3 = 0.013$			$w_3 = 0.026$			$w_3 = 0.026$			$w_3 = 0.026$		
278.9	1.13	1.28	-13.46	1.33	-17.21	283.6	3.00	2.97	0.83	2.86	4.52	
290.7	2.18	1.99	8.61	2.00	8.01	295.2	4.11	4.14	-0.73	4.13	-0.54	
305.4	3.25	3.24	0.39	3.21	1.22	308.7	6.05	6.06	-0.15	6.14	-1.50	
314.9	4.27	4.31	-1.02	4.27	-0.18	319.4	8.18	8.17	0.05	8.25	-0.92	
322.8	5.30	5.38	-1.61	5.37	-1.36	327.4	10.26	10.21	0.52	10.21	0.57	
328.9	6.40	6.33	1.06	6.37	0.50	330.7	11.14	11.19	-0.38	11.12	0.23	
	$w_3 = 0.036$			$w_3 = 0.036$			$w_3 = 0.036$			$w_3 = 0.036$		
279.6	3.94	3.96	-0.49	4.09	-3.82							
295.0	6.60	6.57	0.48	6.58	0.43							
301.9	7.99	8.07	-1.04	8.02	-0.42							
308.7	9.96	9.78	1.80	9.70	2.61							
316.6	11.91	12.05	-1.17	11.99	-0.63							
322.9	14.07	14.10	-0.23	14.12	-0.33							
325.8	15.19	15.12	0.40	15.20	-0.11							

^aStandard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_r are $u_r(p) = 0.1$, $u_r(x_1) = 0.01$, and $u_r(w_3) = 0.001$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λh model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of water (3) in a binary IPA (2) + water (3) mixture.

Table 7.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Binary Solvent Mixture of IPA (2) + Heptane (3) at Different Temperatures, T , and at Pressure, $p = 101.3 \text{ kPa}$ ^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	T/K	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	10^2 RD
$w_3 = 0.091$												
283.4	0.59	0.62	-4.95	0.64	-6.96	283.6	0.50	0.47	7.18	0.50	1.06	
285.7	0.70	0.68	2.06	0.69	0.80	291.9	0.60	0.65	-7.91	0.66	-9.94	
289.3	0.79	0.78	2.00	0.78	1.57	309.2	1.19	1.18	1.29	1.15	3.58	
300.5	1.15	1.14	0.67	1.13	1.76	321.6	1.68	1.69	-0.06	1.66	1.42	
311.7	1.60	1.61	-0.82	1.59	0.34	326.4	1.91	1.91	0.17	1.90	0.53	
324.4	2.30	2.30	0.16	2.31	-0.35	331.5	2.16	2.17	-0.18	2.19	-1.50	
$w_3 = 0.277$												
287.2	0.50	0.50	0.62	0.49	2.41	282.7	0.27	0.28	-3.75	0.28	-4.69	
296.9	0.64	0.65	-0.65	0.65	-0.74	293.2	0.41	0.40	3.52	0.40	3.39	
313.7	1.01	1.01	-0.09	1.02	-1.01	317.3	0.81	0.82	-1.25	0.82	-0.77	
323.0	1.30	1.29	0.32	1.30	-0.03	327.0	1.07	1.07	0.66	1.07	0.77	
330.4	1.56	1.56	-0.13	1.56	0.33	331.8	1.21	1.21	-0.15	1.21	-0.39	
$w_3 = 0.469$												
278.4	0.14	0.15	-2.63	0.15	-6.85							
295.2	0.28	0.28	0.38	0.28	0.04							
307.2	0.42	0.42	0.71	0.41	1.50							
316.7	0.57	0.56	1.78	0.55	2.59							
326.2	0.71	0.73	-3.97	0.73	-3.86							
330.5	0.84	0.82	2.00	0.83	1.53							

^aStandard uncertainty, u , is $u(T) = 2 \text{ K}$. Relative standard uncertainties, u_i are $u_i(p) = 0.1$, $u_i(x_1) = 0.01$, and $u_i(w_3) = 0.001$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λh model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of heptane (3) in a binary IPA (2) + heptane (3) mixture.

Table 8.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Binary Solvent Mixture of IPA (2) + Hexane (3) at Different Temperatures, T , and at Pressure, $p = 101.3 \text{ kPa}$ ^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{exp}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	
$w_3 = 0.085$												$w_3 = 0.172$
281.0	0.56	0.56	-0.49	0.56	-0.72	283.7	0.49	0.50	-2.32	0.51	-4.58	
282.9	0.64	0.60	5.85	0.61	5.66	289.5	0.62	0.61	0.81	0.62	0.07	
291.8	0.81	0.83	-2.25	0.83	-2.28	293.7	0.70	0.71	-1.81	0.71	-1.76	
295.3	0.91	0.94	-3.23	0.94	-3.19	301.5	0.95	0.91	3.54	0.91	4.49	
307.5	1.38	1.39	-1.11	1.39	-0.96	317.4	1.44	1.46	-1.44	1.45	-0.61	
315.4	1.84	1.78	3.01	1.78	3.10	322.8	1.68	1.69	-0.57	1.69	-0.43	
322.5	2.17	2.20	-1.17	2.20	-1.26	327.0	1.89	1.88	0.77	1.89	0.17	
$w_3 = 0.267$												$w_3 = 0.361$
279.6	0.31	0.34	-10.89	0.33	-7.31	280.7	0.30	0.31	-0.65	0.29	3.17	
282.6	0.36	0.37	-2.89	0.37	-0.57	289.9	0.38	0.39	-3.47	0.39	-2.45	
291.0	0.52	0.49	4.80	0.49	4.98	298.1	0.51	0.49	4.69	0.49	4.20	
296.6	0.62	0.59	5.49	0.59	4.84	309.7	0.66	0.67	-1.61	0.68	-2.88	
313.2	1.00	0.99	0.57	1.00	-0.70	314.9	0.77	0.77	0.86	0.77	-0.25	
321.3	1.24	1.27	-2.44	1.28	-3.17	327.1	1.04	1.06	-1.70	1.06	-1.68	
327.4	1.50	1.52	-1.20	1.52	-1.21	331.3	1.19	1.18	1.04	1.17	1.64	
332.0	1.77	1.74	1.40	1.73	2.03							
$w_3 = 0.456$												
279.5	0.27	0.27	0.78	0.25	6.40							
290.0	0.32	0.33	-3.75	0.33	-3.61							
298.0	0.40	0.39	2.90	0.39	0.85							
309.0	0.49	0.49	0.87	0.50	-1.77							
321.5	0.64	0.65	-2.30	0.66	-2.63							
326.5	0.75	0.74	1.16	0.73	2.47							

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Standard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_r are $u_r(p) = 0.1$, $u_r(x_1) = 0.01$, and $u_r(w_3) = 0.001$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λ h model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of hexane (3) in a binary IPA (2) + hexane (3) mixture.

Table 9.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Ternary Solvent Mixture of IPA (2) + Acetone (3) with $w_3 = 0.095$ + Heptane (4) at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa.^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD
$w_4 = 0.088$												
281.1	1.43	1.44	-0.85	1.46	-1.95	282.3	1.10	1.12	-1.63	1.15	-4.17	
284.5	1.61	1.58	1.62	1.59	1.01	284.7	1.21	1.20	0.35	1.22	-1.24	
289.4	1.79	1.80	-0.49	1.80	-0.55	290.5	1.44	1.41	1.73	1.41	1.82	
299.3	2.29	2.31	-0.81	2.30	-0.23	297.0	1.67	1.67	0.22	1.65	1.43	
306.0	2.72	2.71	0.46	2.69	1.10	302.9	1.90	1.92	-1.08	1.89	0.49	
313.2	3.19	3.18	0.12	3.17	0.48	312.5	2.38	2.38	0.20	2.35	1.05	
322.2	3.85	3.85	-0.08	3.87	-0.56	321.1	2.82	2.82	0.03	2.85	-1.02	
$w_4 = 0.274$												
280.8	0.79	0.80	-1.50	0.80	-1.44	284.6	0.60	0.60	-0.70	0.59	2.32	
285.6	0.89	0.89	0.06	0.89	0.05	298.2	0.81	0.79	1.60	0.80	0.63	
291.2	1.02	1.01	1.21	1.01	1.16	306.7	0.94	0.95	-1.43	0.97	-2.88	
301.7	1.28	1.26	1.45	1.26	1.43	312.4	1.09	1.08	1.04	1.09	0.08	
312.6	1.54	1.57	-2.54	1.57	-2.51	319.3	1.24	1.27	-1.88	1.26	-1.57	
318.4	1.78	1.77	0.78	1.77	0.79	321.6	1.35	1.34	1.24	1.32	2.10	
321.3	1.88	1.87	0.29	1.87	0.27							
$w_4 = 0.471$												
281.2	0.36	0.36	0.98	0.37	-0.97							
286.6	0.40	0.41	-2.24	0.42	-2.88							
293.2	0.49	0.48	2.11	0.48	2.58							
300.9	0.57	0.58	-1.37	0.57	-0.26							
310.5	0.71	0.70	0.51	0.70	1.40							
321.9	0.87	0.88	-0.09	0.88	-0.79							

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Standard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_T are $u_T(\rho) = 0.1$, $u_T(x_1) = 0.01$, $u_T(w_3) = 0.001$, and $u_T(w_4) = 0.003$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λ h model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of acetone (3) in binary IPA (2) + acetone (3) mixture. w_4 is the mass fraction of heptane (4) in ternary IPA (2) + acetone (3) + heptane (4) mixture.

Table 10.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Ternary Solvent Mixture of IPA (2) + Acetone (3) with $w_3 = 0.095$ + Hexane (4) at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	T/K	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	10^2 RD
$w_4 = 0.086$												
280.1	1.52	1.54	-1.32	1.58	-4.15	279.8	1.03	1.02	0.92	1.06	-3.28	
285.8	1.81	1.78	1.49	1.79	0.86	281.0	1.07	1.06	0.67	1.10	-2.77	
291.5	2.04	2.04	0.01	2.03	0.83	285.8	1.21	1.23	-1.54	1.24	-2.43	
304.2	2.68	2.69	-0.36	2.64	1.44	296.5	1.66	1.65	0.24	1.62	2.59	
312.4	3.14	3.14	-0.01	3.12	0.89	303.7	1.96	1.97	-0.70	1.91	2.13	
320.8	3.63	3.63	0.07	3.68	-1.14	312.6	2.40	2.38	0.79	2.35	2.42	
						322.7	2.87	2.88	-0.23	2.93	-2.15	
$w_4 = 0.272$												
279.8	0.87	0.87	-0.06	0.86	1.31	279.4	0.54	0.56	-2.35	0.56	-3.51	
286.3	0.99	0.99	0.49	0.98	0.61	287.6	0.67	0.67	0.45	0.67	0.45	
293.4	1.12	1.13	-0.77	1.14	-1.38	294.5	0.80	0.78	2.96	0.77	3.52	
299.1	1.26	1.26	0.12	1.27	-0.64	311.6	1.07	1.09	-2.12	1.09	-1.59	
307.9	1.51	1.50	0.67	1.51	0.28	315.6	1.17	1.18	-0.27	1.18	-0.07	
312.6	1.64	1.65	-0.66	1.65	-0.59	321.6	1.32	1.31	0.88	1.32	0.36	
315.9	1.76	1.76	0.20	1.75	0.69							
$w_4 = 0.468$												
281.1	0.33	0.33	-0.89	0.33	-2.36							
284.3	0.36	0.36	0.73	0.36	0.14							
301.5	0.56	0.56	0.59	0.55	1.94							
311.4	0.69	0.70	-1.64	0.70	-0.99							
315.0	0.77	0.76	1.31	0.75	1.36							
318.9	0.82	0.82	-0.23	0.82	-1.01							

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Standard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_T are $u_T(\rho) = 0.1$, $u_T(x_1) = 0.01$, $u_T(w_3) = 0.001$, and $u_T(w_4) = 0.003$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λ h model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of acetone (3) in binary IPA (2) + acetone (3) mixture. w_4 is the mass fraction of hexane (4) in ternary IPA (2) + acetone (3) + hexane (4) mixture.

Table 11.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Ternary Solvent Mixture of IPA (2) + Ethanol (3) with $w_3 = 0.198$ + Heptane (4) at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{cal}}$	10^2 RD
$w_4 = 0.087$												
282.7	1.30	1.32	-2.29	1.31	-0.97	283.5	1.18	-4.98	1.18	-0.16		
290.7	1.72	1.69	1.68	1.69	1.86	288.9	1.44	0.75	1.40	2.85		
304.8	2.60	2.57	0.99	2.59	0.41	298.0	1.87	1.84	1.54	0.90		
315.9	3.49	3.53	-1.12	3.54	-1.50	304.8	2.35	2.23	5.00	2.27	3.42	
326.6	4.75	4.73	0.28	4.72	0.54	314.1	2.79	2.90	-3.70	2.95	-5.48	
						322.7	3.67	3.70	-0.67	3.72	-1.30	
						326.7	4.13	4.14	-0.32	4.13	-0.11	
						329.8	4.57	4.52	0.91	4.48	1.85	
$w_4 = 0.270$												
280.3	0.74	0.73	1.42	0.73	1.48	280.3	0.52	0.53	-2.44	0.53	-1.46	
284.8	0.85	0.84	0.89	0.84	0.84	286.8	0.66	0.64	2.28	0.64	2.49	
298.6	1.22	1.26	-3.12	1.26	-3.24	305.1	1.05	1.05	0.29	1.06	-0.21	
313.7	1.94	1.91	1.49	1.91	1.53	313.9	1.31	1.32	-0.63	1.33	-0.94	
322.8	2.42	2.42	-0.20	2.42	-0.12	326.1	1.80	1.80	0.15	1.79	0.38	
333.0	3.12	3.13	-0.10	3.13	-0.14							
$w_4 = 0.470$												
279.4	0.40	0.42	-5.50	0.43	-6.64							
287.4	0.55	0.52	4.81	0.52	4.47							
299.7	0.71	0.70	1.07	0.70	1.43							
314.6	0.95	0.97	-2.23	0.97	-1.72							
320.4	1.09	1.10	-0.93	1.10	-0.64							
324.4	1.22	1.19	1.93	1.19	1.98							
330.1	1.33	1.34	-0.32	1.34	-0.76							

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Standard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_T are $u_T(\rho) = 0.1$, $u_T(x_1) = 0.01$, $u_T(w_3) = 0.001$, and $u_T(w_4) = 0.003$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λ h model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of ethanol (2) + ethanol (3) mixture. w_4 is the mass fraction of heptane (4) in ternary IPA (2) + ethanol (3) + heptane (4) mixture.

Table 12.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Ternary Solvent Mixture of IPA (2) + Ethanol (3) with $w_3 = 0.198$ + Hexane (4) at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa.^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	T/K	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	10^2 RD	10^2 RD
$w_4 = 0.084$												
284.2	1.53	1.54	-0.63	1.48	3.32	282.5	1.05	1.04	0.46	1.08	-2.75	
288.7	1.74	1.73	0.08	1.70	2.03	286.0	1.16	1.18	-2.16	1.20	-3.95	
303.6	2.59	2.56	1.09	2.61	-0.61	290.4	1.38	1.37	0.89	1.38	0.61	
315.6	3.50	3.53	-0.90	3.59	-2.73	303.2	2.06	2.04	1.23	2.00	3.11	
324.8	4.54	4.52	0.26	4.55	-0.26	314.5	2.74	2.77	-0.93	2.72	0.62	
331.6	5.44	5.44	0.00	5.39	1.03	326.1	3.66	3.65	0.20	3.69	-0.74	
$w_4 = 0.268$												
284.3	0.95	0.96	-1.04	0.93	2.66	288.3	0.77	0.79	-2.11	0.77	-0.70	
294.5	1.24	1.23	0.40	1.23	0.93	296.3	0.99	0.97	2.54	0.97	2.57	
306.1	1.68	1.64	2.22	1.66	1.14	307.3	1.27	1.29	-0.85	1.29	-1.51	
313.4	1.92	1.96	-2.22	1.99	-3.47	312.9	1.50	1.48	0.91	1.49	0.35	
321.2	2.39	2.38	0.33	2.40	-0.40	320.5	1.77	1.80	-1.60	1.80	-1.67	
332.1	3.13	3.12	0.07	3.10	0.89	325.1	2.04	2.02	0.80	2.01	1.21	
$w_4 = 0.462$												
280.1	0.40	0.41	-2.17	0.40	0.54							
289.7	0.52	0.52	0.65	0.52	0.85							
300.2	0.69	0.67	1.97	0.68	0.94							
312.6	0.92	0.91	0.70	0.92	-0.25							
319.0	1.04	1.06	-2.20	1.07	-2.60							
323.6	1.18	1.19	-0.99	1.19	-0.80							
326.3	1.29	1.27	1.54	1.26	2.12							

^aStandard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_r are $u_r(p) = 0.1$, $u_r(x_1) = 0.01$, $u_r(w_3) = 0.001$, and $u_r(w_4) = 0.003$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and λh model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of ethanol (3) in binary IPA (2) + ethanol (3) mixture. w_4 is the mass fraction of hexane (4) in ternary IPA (2) + ethanol (3) + hexane (4) mixture.

Table 13.

Experimental and Correlated Mole Fraction Solubility of WS-IPA (x_1) in the Ternary Solvent Mixture of IPA (2) + Water (3) with $w_3 = 0.013$ + Heptane (4) at Different Temperatures, T , and at Pressure, $p = 101.3$ kPa^a

T/K	Apelblat			λh			Apelblat			λh		
	$10^3 x_1^{\text{exp}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{cal}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{exp}}$	10^2 RD	$10^3 x_1^{\text{cal}}$	$10^3 x_1^{\text{cal}}$	10^2 RD
$w_4 = 0.087$												
282.2	1.35	1.41	-5.09	1.45	-7.66	278.3	1.09	1.11	-1.34	1.11	-1.22	
286.1	1.61	1.62	-0.37	1.64	-1.89	280.8	1.21	1.20	0.43	1.20	0.48	
295.2	2.26	2.19	3.52	2.18	3.61	295.3	1.88	1.88	0.43	1.88	0.35	
301.7	2.71	2.67	1.57	2.65	2.33	302.4	2.32	2.30	0.75	2.31	0.71	
312.5	3.61	3.64	-0.85	3.60	0.24	315.2	3.25	3.28	-0.88	3.28	-0.85	
323.4	4.79	4.86	-1.44	4.84	-1.06	324.2	4.17	4.15	0.28	4.15	0.28	
330.2	5.80	5.75	0.80	5.79	0.20							
$w_4 = 0.275$												
281.2	1.01	1.03	-1.18	0.99	1.97	281.2	0.65	0.67	-3.76	0.68	-5.32	
289.2	1.26	1.24	1.69	1.24	2.15	288.8	0.84	0.83	0.38	0.84	-0.05	
309.7	2.04	2.06	-0.81	2.09	-2.47	296.4	1.05	1.02	3.18	1.02	3.46	
317.9	2.51	2.52	-0.61	2.55	-1.59	307.1	1.35	1.33	1.01	1.33	1.71	
323.9	2.97	2.93	1.40	2.93	1.34	315.1	1.59	1.61	-1.52	1.60	-0.97	
328.9	3.30	3.32	-0.58	3.29	0.34	322.9	1.88	1.92	-2.21	1.92	-2.22	
						326.7	2.12	2.08	1.81	2.09	1.37	
$w_4 = 0.473$												
285.1	0.58	0.58	0.40	0.58	0.64							
301.2	0.83	0.84	-0.84	0.84	-0.94							
308.2	0.98	0.98	-0.03	0.98	-0.11							
314.8	1.14	1.13	0.92	1.13	0.89							
320.6	1.27	1.27	-0.44	1.27	-0.42							
326.2	1.43	1.43	0.00	1.43	0.04							

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Standard uncertainty, u , is $u(T) = 2$ K. Relative standard uncertainties, u_T are $u_T(\rho) = 0.1$, $u_T(x_1) = 0.01$, $u_T(w_3) = 0.001$, and $u_T(w_4) = 0.003$. x_1^{exp} refers to the experimental mole fraction solubility. x_1^{cal} refers to the calculated solubility data using the Apelblat and 2h model equations. RD represents the corresponding relative deviation. w_3 is the mass fraction of water (3) in binary IPA (2) + water (3) mixture. w_4 is the mass fraction of heptane (4) in ternary IPA (2) + water (3) + heptane (4) mixture.

Table 14.

Optimized Values for the Parameters in the Apelblat and λh Model Equations, and the Resulting ARD % Employed for the Correlation of the Mole Fraction Solubility of WS-IPA (1) in All Pure Solvents and Binary and Ternary Solvent Mixtures^a

solvent	model					
	Apelblat			λh		
	A	B	C	ARD %	λ	h
acetone	40.19227	-4453.5832	-5.21225	0.1030	0.34847	8024.47622
ethanol	-98.21059	2934.77406	14.91362	0.0123	0.13573	9541.11686
IPA	-168.14598	4845.50445	25.46934	0.1951	0.03625	78 532.6849
water	793.0886	-42 237.216	-115.22091	3.6525	8.73772	660.34109
	IPA (2) + Acetone (3) ^b					
w ₃ = 0.047	-212.42314	7620.28099	31.70073	0.0858	0.0136	124 024.946
w ₃ = 0.111	-95.7517	2118.49529	14.54609	0.1155	0.03775	55 476.8042
w ₃ = 0.148	-23.30329	-803.09409	3.60796	0.1503	0.02654	60 467.0328
	IPA (2) + Ethanol (3) ^c					
w ₃ = 0.099	-49.0643	-412.16498	7.75605	0.1295	0.04747	55 929.5443
w ₃ = 0.202	-72.05357	675.82423	11.19978	0.0020	0.06172	42 751.0333
w ₃ = 0.304	-27.7247	-800.16381	4.44694	0.0121	0.0593	32 320.5083
	IPA (2) + Water (3) ^d					
w ₃ = 0.013	31.56036	-4174.5572	-4.12862	1.0052	0.07245	38 146.7916
w ₃ = 0.026	-100.15491	2075.94625	15.40812	0.0228	0.09892	25 877.8135
w ₃ = 0.036	36.26167	-4093.4908	-4.81959	0.0357	0.13913	17 670.9545
	IPA (2) + Heptane (3) ^e					
w ₃ = 0.091	50.53958	-5066.4769	-7.09047	0.1446	0.0299	92 694.4175
w ₃ = 0.176	106.29142	-7713.3439	-15.36234	0.0812	0.02344	11 8496.523
w ₃ = 0.277	-88.53187	1585.64037	13.32239	0.0129	0.01125	209 260.365
w ₃ = 0.372	-6.55071	-2408.948	1.22208	0.1943	0.01101	238 084.753
w ₃ = 0.469	28.14306	-4201.1073	-3.88435	0.2881	0.00971	293 134.792

solvent	model					
	Apelblat			λh		
	A	B	C	ARD %	λ	ARD %
$w_3 = 0.085$	-10.49662	-2360.7192	2.02504	0.0877	0.03317	0.0502
$w_3 = 0.172$	43.76406	-4715.7858	-6.15163	0.1459	0.0207	0.3790
$w_3 = 0.267$	-81.0248	878.56894	12.40759	0.6470	0.01902	0.1385
$w_3 = 0.361$	-95.26691	1870.07397	14.28232	0.1198	0.00835	0.2490
$w_3 = 0.456$	-174.43438	5826.06284	25.80672	0.0582	0.00314	0.2838
$w_4 = 0.088$	7.45879	-2444.78	-0.94003	0.0027	0.02153	0.1007
$w_4 = 0.179$	71.51033	-5320.9624	-10.53596	0.0267	0.01549	0.2327
$w_4 = 0.274$	-40.35096	-100.03658	5.95624	0.0370	0.00723	0.0360
$w_4 = 0.374$	-157.71758	5115.82168	23.4169	0.0222	0.00606	0.1133
$w_4 = 0.471$	31.45409	-3424.6109	-4.82412	0.0160	0.00365	0.1538
$w_4 = 0.086$	71.69696	-5087.9876	-10.64908	0.0203	0.01394	0.2106
$w_4 = 0.174$	119.41188	-7483.9616	-17.66924	0.0212	0.01576	0.4989
$w_4 = 0.272$	-100.48322	2701.47644	14.8711	0.0020	0.00603	0.0421
$w_4 = 0.366$	2.65773	-1985.3615	-0.54043	0.0762	0.00448	0.1394
$w_4 = 0.468$	48.96548	-4360.3244	-7.35507	0.0204	0.00491	0.1541
$w_4 = 0.087$	-58.08448	75.97897	9.06933	0.0931	0.0465	0.0683
$w_4 = 0.180$	-131.15428	3455.69773	19.8809	0.1831	0.0398	0.2455
$w_4 = 0.270$	-30.03447	-1123.4194	4.75911	0.0633	0.02235	0.0579
$w_4 = 0.376$	-54.80922	89.13291	8.33145	0.0702	0.01314	0.0534
$w_4 = 0.470$	-14.98909	-1426.7894	2.18895	0.1676	0.00554	0.2683

solvent	model						λh	
	Apelblat			ARD %	λ	h	ARD %	
	A	B	C					
$w_4 = 0.084$	-129.22928	3492.20594	19.55325	0.0181	0.03917	60 927.654	0.4628	
$w_4 = 0.173$	77.38158	-6026.0412	-11.14761	0.0525	0.03269	74 848.3745	0.5174	
$w_4 = 0.268$	-109.48199	2722.35279	16.45304	0.0394	0.01786	121 643.807	0.2920	
$w_4 = 0.359$	-89.00989	1697.60223	13.41346	0.0502	0.01462	152 936.509	0.0423	
$w_4 = 0.462$	-96.50606	2117.21059	14.40116	0.0733	0.00743	278 107.384	0.1154	
IPA (2) + Water (3) + Heptane (4) ^k								
$w_4 = 0.087$	29.09294	-3901.1315	-3.86842	0.2664	0.05081	49 968.9272	0.6028	
$w_4 = 0.178$	-26.0761	-1314.9426	4.26366	0.0532	0.03918	62 747.9646	0.0418	
$w_4 = 0.275$	-112.43256	2860.93181	16.91358	0.0153	0.01922	110 043.434	0.2888	
$w_4 = 0.386$	4.36243	-2446.9006	-0.52602	0.1576	0.01206	170 499.156	0.2884	
$w_4 = 0.473$	-47.18466	94.09656	6.9711	0.0035	0.00596	295 426.336	0.0158	

^a ARD % represents the corresponding average relative deviation.

^b w_3 is the mass fraction of acetone (3) in binary IPA (2) + acetone (3) mixture.

^c w_3 is the mass fraction of ethanol (3) in binary IPA (2) + ethanol (3) mixture.

^d w_3 is the mass fraction of water (3) in binary IPA (2) + water (3) mixture.

^e w_3 is the mass fraction of heptane (3) in binary IPA (2) + heptane (3) mixture.

^f w_3 is the mass fraction of hexane (3) in binary IPA (2) + hexane (3) mixture.

^g w_4 is the mass fraction of heptane (4) in ternary IPA (2) + acetone (3) with $w_3 = 0.095$ + heptane (4) mixture.

^h w_4 is the mass fraction of hexane (4) in ternary IPA (2) + acetone (3) with $w_3 = 0.095$ + hexane (4) mixture.

ⁱ w_4 is the mass fraction of heptane (4) in ternary IPA (2) + ethanol (3) with $w_3 = 0.198$ + heptane (4) mixture.

^j w_4 is the mass fraction of hexane (4) in ternary IPA (2) + ethanol (3) with $w_3 = 0.198$ + hexane (4) mixture.

^k w_4 is the mass fraction of heptane (4) in ternary IPA (2) + water (3) with $w_3 = 0.013$ + heptane (4) mixture.