Contents lists available at ScienceDirect

Journal of Saudi Chemical Society

journal homepage: www.ksu.edu.sa

Deducing solute differential heat capacity from experimental solubilities. An exemplified treatment of ascorbic acid to improve solubility prediction

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ARTICLE INFO

Keywords:
General solubility equation
Activity coefficient model
Prediction accuracy
Heat capacity assumptions

ABSTRACT

Context: Solubility prediction based on the general solubility equation (GSE) rests on reliable values for the isobaric heat capacity difference $\Delta C_{p,1}$ of the solid solute. Usually, this value is estimated with either zero or the melting entropy $\Delta S_1(T_{m,1})$ or, in few cases, is extrapolated from data of thermally stable melts of the solute. This causes uncertainties in the prediction.

Objective: To improve prediction accuracy a simple regression method is proposed that determines $\Delta C_{p,1}$ from measured solubilities.

Materials and methods: Published experimental solubilities in neat organic solvents at 298 K of a model compound (L-(+)-ascorbic acid (LAA)) have been regressed using the GSE together with the Hansen parameter model for the activity coefficient.

Results and discussion: Regression yielded $\Delta C_{p,1} = 238$ J•mol^{-1}•K^{-1} which agrees well with cross-validation results and is consistent with estimates from various group contribution methods. It was found that prediction accuracy improved in the order of increasing $\Delta C_{p,1}$, that is, from 0, via 91 ($=\Delta S_1(T_{m,1})$) to 238 J•mol^{-1}•K^{-1}. It could be shown that mole fraction solubility of LAA can be forecast this way with an accuracy within current inter-laboratory variation.

Conclusion: The proposed method shows a general way to improve prediction accuracy of activity coefficient based solubility models by determining $\Delta C_{p,1}$ without resorting to common assumptions. The method is universally applicable and easy to implement.

1. Introduction

The solubility of solid compounds in pure solvents or solvent mixtures is a property relevant to numerous industrial processes in, e.g., chemical, pharmaceutical, and food industries. Predictive methods for solubility can contribute to more systematic solvent selection, to finding more optimal solvents, and not the least to improving business economy by reducing the need for costly measurements and by shortening product development times. Prediction in the framework of thermodynamics can be performed by formulating phase equilibrium conditions involving thermophysical properties of the constituents of the solution and state variables such as temperature and phase composition. Relating, as is common practice, the thermodynamic states of the solid solute and the supercooled solute melt, and applying the usual assumptions to a binary solute–solvent system the activity, a_1 of the solid phase at a temperature T/K is given by:

$$\ln(a_1) = \ln(\gamma_1 \cdot x_1) = \frac{\Delta H_1}{R} \cdot \left(\frac{1}{T_{m,1}} - \frac{1}{T}\right) + \frac{1}{RT} \cdot \int_T^{T_{m,1}} \Delta C_{p,1}(T)dT - \frac{1}{R} \cdot \int_T^{T_{m,1}} \frac{\Delta C_{p,1}(T)}{T} dT \quad (1)$$

where γ_1 the activity coefficient, x_1 the mole fraction solubility, ΔH_1/J·mol^{-1} the melting enthalpy, $T_{m,1}$/K the melting temperature of the pure solute (subscripted 1), and R the universal gas constant [1,2]. The right-hand side of Eq. (1) corresponds to the difference in the Gibbs energies of the two states of the solute. The summands reflect that the thermodynamic path from the solid crystalline to the liquid supercooled state can be represented as a three-step cycle (heating of the solid from T to $T_{m,1}$, phase transition by melting, cooling of the melt back to T) and thus the Gibbs energy difference can be calculated approximately. A detailed derivation is given by, for example, Ref. [2]. The quantity $\Delta C_{p,1}(T) = (C_{p,liq}(T) - C_{p,solid}(T))$/J·mol^{-1}•K^{-1} is a principally unknown function of temperature and stands for the isobaric molar heat capacity difference of the (hypothetical) supercooled liquid and the crystalline

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https://doi.org/10.1016/j.jscs.2024.101827
Received 14 December 2023; Received in revised form 23 January 2024; Accepted 20 February 2024
Available online 24 February 2024
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state of the solute. For thermally stable compounds the heat capacity values of the melt, in principle, can be extrapolated to the application temperature $T < T_{m,1}$ to obtain an approximation for $C_{p,liq}(T)$ and thus for $\Delta C_{p,1}(T)$ [3,4]. For reasons of practicability, however, it is customary to treat $\Delta C_{p,1}(T) \equiv \Delta C_{p,1}$ as constant, which simplifies Eq. (1) and gives the following expression for the solubility x_1:

$$\ln(x_1) = \frac{\Delta H_1}{R} \bullet \left(\frac{1}{T_{m,1}} - \frac{1}{T}\right) + \frac{\Delta C_{p,1}}{R} \bullet \left[\left(\frac{T_{m,1}}{T} - 1\right) - \ln\left(\frac{T_{m,1}}{T}\right)\right] - \ln(\gamma_1) \tag{2}$$

Because in many situations the square bracketed term in Eq. (2) is close to zero the entire second summand is frequently considered negligible so that for ease of treatment $\Delta C_{p,1} = 0$ is assumed. However, a number of studies concluded that this assumption is insufficient at least at moderate temperature for compounds with higher melting points and should not be generally used [3,4–6]. A better approximation can sometimes be achieved if the entropy of fusion at the melting point is assumed equal to $\Delta C_{p,1} = \Delta S_1(T_{m,1}) = \Delta H_1(T_{m,1})/T_{m,1}$ [3,4,7]. All approximations are subject to errors and in many circumstances these were found to be substantial so that a great deal of uncertainty as to the "true" value of $\Delta C_{p,1}$ remains [1,2,4,6,8,9]. Therefore, the quality of solubility forecasts based on Eq. (2) is principally compromised by the uncertainty in $\Delta C_{p,1}$. Accordingly, to improve the accuracy of solubility forecasting, more reliable estimates of $\Delta C_{p,1}$ are required.

Activity coefficient models that account for thermodynamic non-ideal behaviour of the solid–liquid-equilibrium are generally modelled as a function of solution composition, temperature, molecular structural and interaction parameters, and for a binary solution, can be expressed as a function $\gamma_1 = \gamma_1(x_1, T)$. The equilibrium molar solubility according to Eq. (2) is then given by a function $x_1 = f(\Delta H_1,\ T_{m,1},\ \Delta C_{p,1},\ \gamma_1(x_1,T),\ T)$ and can be obtained from a self-consistent (numerical) minimization of $|x_1 - f(\Delta H_1,\ T_{m,1},\ \Delta C_{p,1},\ \gamma_1(x_1,T),\ T)|$ with respect to x_1 if the material parameters of the solute are known. For the uncertainty regarding the value of $\Delta C_{p,1}$ and for the inadequacies of the assumptions $\Delta C_{p,1} = 0$ and, resp., $\Delta C_{p,1} = \Delta S_1(T_{m,1})$, it is proposed here to derive a value for $\Delta C_{p,1}$ from a simultaneous regression with respect to $\Delta C_{p,1}$ for a number of solvents. Although such a regressed $\Delta C_{p,1}$ value is empirically fitted from solubility data and, therefore, is not independently determined, it can be expected to help provide a more reliable estimate than the usual approaches and consequently contributes to improved solubility prognosis.

In this paper, it will be shown in an exemplary fashion for the compound L-(+)-ascorbic acid (LAA) how with simple means an estimate for $\Delta C_{p,1}$ can be obtained following the approach outlined above. LAA is chosen as an example because of its economic relevance, its importance to the food and health sectors, and the lack of information on $\Delta C_{p,1}$ which owes itself to thermal instability of molten LAA [10]. In principle, any activity coefficient model can be used in the suggested procedure. Here, the early Scatchard-Hildebrand solubility parameter approach, which is still successfully used and appreciated in practice, is chosen because of its ease of concept and simple applicability [1,7]. According to Scatchard and Hildebrand, the activity coefficient at temperature T is given by $ln(\gamma_1) = V_1 \cdot \Phi_2^2 \cdot (\delta_1 - \delta_2)^2/(RT)$ which together with Eq. (2) gives:

$$\ln(x_1) = \frac{\Delta H_1}{R} \cdot \left(\frac{1}{T_{m,1}} - \frac{1}{T}\right) + \frac{\Delta C_{p,1}}{R} \cdot \left[\left(\frac{T_{m,1}}{T} - 1\right) - \ln\left(\frac{T_{m,1}}{T}\right)\right] - \frac{V_1 \cdot \Phi_2^2 \cdot (\delta_1 - \delta_2)^2}{RT} \tag{3}$$

where V_1/m^3•mol^{-1} the molar volume of the standard state of the solute, and Φ_2 the solvent (subscripted 2) volume fraction. The Hildebrand solubility parameters are denoted δ_i/(MPa)$^{0.5}$ and may be equated with the respective total Hansen solubility parameters (HSP) [11,12]. The thermophysical data needed for the regression (ΔH_1, $T_{m,1}$, V_1, V_2) are available in the literature, and the values of δ_1 and δ_2 can be calculated using established group contribution methods (GCM) [11–13]. After deriving a value for $\Delta C_{p,1}$ a full cross-validation is performed to assess the consistency and predictive quality of the approach. Next, the solubilities gained with the so derived value for $\Delta C_{p,1}$ are compared with results of the conventional approaches using $\Delta C_{p,1} = 0$ or, resp., $\Delta C_{p,1} = \Delta S_1(T_{m,1})$. Lastly, the prediction accuracy is compared with the inter-laboratory variation of experimental LAA solubilities and with predictions from studies relying on other solubility models.

2. Materials and computational methods

2.1. Solvents and experimental solubilities

All organic solvents whose experimental solubility data are accessible in the open literature were considered. The experimental solubilities $x_{1,\mathrm{exp}}$ of LAA in pure organic solvents were taken from [14–18]. The specifications of all chemicals used in those studies are compiled in Supplementary Information, Table S1. Solubilities in water and aqueous solvent mixtures were not considered in this study for several reasons. These include experimentally not fully controlled pH effects on solubility behaviour and the fact that the HSPs of water are known to vary greatly as a function of mixture composition, leading to considerable ambiguity regarding the value of δ_2 [12,19,20].

2.2. Solute

Results from a recent exhaustive study of available material data on LAA were used, which qualified the following material values and their minimum–maximum ranges: $\Delta H_1 = 42.1$ (±5) kJ•mol^{-1}, $T_{m,1} = 463.8$ (±5) K, and $V_1(298\ K) = 109.9$ (±4) cm^3•mol^{-1} [21,22]. From these data a value for the melting entropy $\Delta S_1(T_{m,1}) = \Delta H_1/T_{m,1} = 90.8$ J•mol^{-1}•K^{-1} can be calculated.

2.3. Solubility parameters

The same reference as under section 2.2 provides total HSPs as calculated by the additive GCM of Hoftyzer and van Krevelen, and puts their standard uncertainty at $u(\delta_1) = u(\delta_2) = \pm 0.5$ (MPa)$^{0.5}$ while the value of the solute is $\delta_1(298\ K) = 35.3$ (MPa)$^{0.5}$ [13,21]. All of the solvents, except acetone, are part of the Hansen "90 test set". Values for δ_2 at 298 K are compiled in the Section Results below.

2.4. Computation of $\Delta C_{p,1}$

The regression calculations were performed utilizing commercial standard application software (*Excel*, Vs. 2016, Microsoft Corp.) without the need for specific coding. Fitting of the continuous nonlinear problem was performed with the Excel Solver add-in in "GRG solution mode". No numerical constraints were imposed on $\Delta C_{p,1}$, the starting value for all iterations was set to 90 J•mol^{-1}•K^{-1}. It was ensured that variation of this value left the fitting results unaffected. Since the experimental solubilities in the neat solvents at 298 K are $x_{1,\mathrm{exp}} = 0.0108$ for methanol and smaller than 0.0038 for the others, $\Phi_2 \approx 1$ holds meaning that the solvent molar volume V_2 does not enter the calculations. The solubilities $x_{1,calc}$ were calculated analytically for iterated values of $\Delta C_{p,1}$ from Eq. (3) using the root-mean-square-relative deviation (*RMSRD*) as objective function (OF):

$$RMSRD = \sqrt{\frac{1}{N} \bullet \sum_{i=1}^{N} \left(\frac{x_{1,\mathrm{exp}(i)} - x_{1,\mathrm{calc}(i)}}{x_{1,\mathrm{exp}(i)}}\right)^2} \tag{4}$$

where N is the number of data points and $OF(\Delta C_{p,1})$ is optimised to a minimum. Convergence criterion was a relative change between successive iterations $\leq 10^{-6}$. Relative deviations were used for the *OF* because the solubilities vary by several orders of magnitude, which

could lead to a dominance of a few higher solubility solvents on the fitting results when using an unweighted approach. See Fig. 1 for a summary of the general methodology for determining $\Delta C_{p,1}$.

2.5. Cross-validation of regression results

A full cross-validation was performed to assess the predictive quality of the methodology and to provide a consistency check of the computational results. From the set of N experimental solubility data one

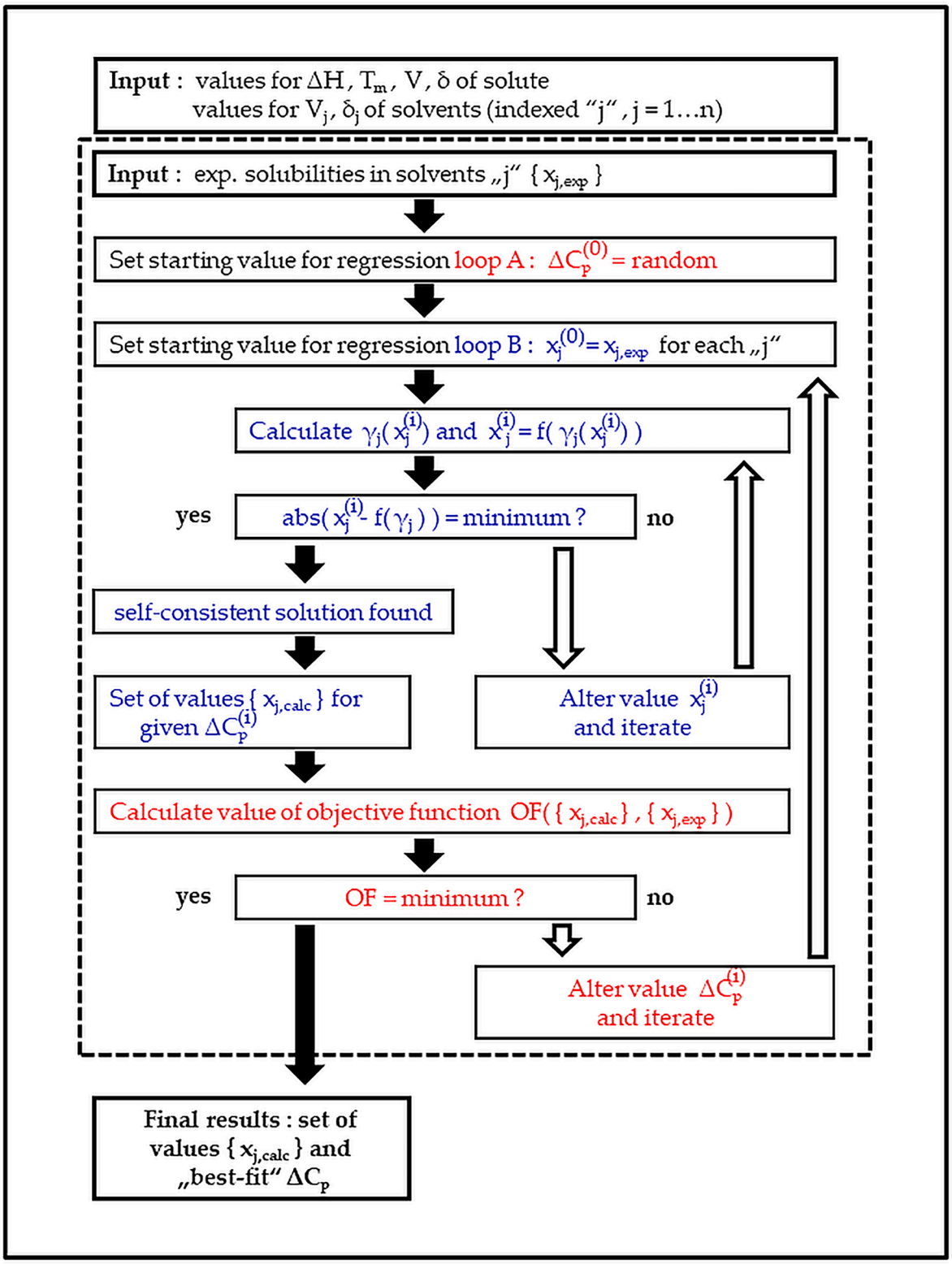

Fig. 1. General algorithm for computing $\Delta C_{p,1}$ from experimental solubilities. To simplify expressions the solute subscript "1″ was dropped so that the molar solubility of the solute in solvent "j" reads x_j and, accordingly, $\Delta C_{p,1}$ turns ΔC_p and $\gamma_{1,j}$ becomes $\underline{\gamma}_j$. Superscript "(i)" for ΔC_p and x_j denotes the iteration number in if-then-loops "A" and, resp., "B". Start of iteration is indicated as i = 0.

solvent (one data point) was excluded at a time so that a (*N-1*) subset remained. For this subset $\Delta C_{p,1}$ was computed according to Section 2.4 (calibration). Using this value the molar fraction solubility of the solvent that was excluded from the calibration was calculated. Then the squared relative deviation for this solvent was determined. This procedure was repeated *N* times until each solvent had been excluded from the calibration set once (validation). The accrued data were aggregated and summarized as validation error in terms of the *RMSRD* or, resp., *%-RMSRD* in order to later compare the accuracy of the solubility forecast with the inter-laboratory variation. In addition, the cross-validation results provide another avenue for estimating the value of $\Delta C_{p,1}$ so that the consistency with the results from Section 2.4. can be checked.

3. Results and discussion

3.1. Regression and cross-validation for T = 298 K

The fitting results, based on the available data points at 298 K, are summarized in Table 1. For more details see the file S2 FittingData in the Supplementary Information. This file also contains the results of the cross-validation that was performed to assess the correlative quality of the approach employed here. The iterations converged rapidly and monotonously with a best-fit value of 237.8 J•mol^{-1}•K^{-1} for $\Delta C_{p,1}$ and a *%-RMSRD* of 71 % between measured and calculated solubilities.

The full cross-validation of the set of n = 16 solvents further yielded a mean for $\Delta C_{p,1}$ of 237.9 J•mol^{-1}•K^{-1} which differs less than 0.1 % from the value above. The root-mean-square error of cross-validation is ± 2.0 J•mol^{-1}•K^{-1} so that the 95 % confidence interval (CI) is (237.9 ± 1.1) J•mol^{-1}•K^{-1} with the interval limits calculated using ±t(5 %, n − 1)•(2.0 J•mol^{-1}•K^{-1})•n$^{-1/2}$. This low uncertainty supports the validity of the methodology used here.

Because of the lack of experimental values on LAA it is an obvious choice to compare the above results with estimates of $C_{p,liq}$ and $C_{p,solid}$ from GCM so that a value for their difference $\Delta C_{p,1} = (C_{p,liq} - C_{p,solid})$ can be estimated. The detailed results of seven additive GCM are compiled in Supplementary Information, Table S3. Values estimated in this way yield $\Delta C_{p,1} \approx 180$ J•mol^{-1}•K^{-1}. With typical uncertainties of 20 J•mol^{-1}•K^{-1} for each, the solid and liquid heat capacities, a combined uncertainty $u(\Delta C_{p,1}) \approx 30$ J•mol^{-1}•K^{-1} can be derived for the GCM approximations by Gaussian error addition. The fact that $\Delta C_{p,1}$ here is much larger than $\Delta S_1(T_{m,1}) = 90.8$ J•mol^{-1}•K^{-1} by a factor of ≈2 by GCM and, respectively, of ≈2.5 by regression seems surprising, but calorimetry studies show that this is the case for 20 % of the organic compounds studied, which provides support for the results presented here. See Table S3 for more details.

Table 1
Comparison of experimental and calculated mole fraction solubility x_1 of ascorbic acid in various solvents at $T = 298$ K. Calculated values were obtained in the course of fitting $\Delta C_{p,1}$.*

Solvent			Mole fraction solubility		Square rel. deviation
Name	Ref.	Solubility parameter δ_2/(MPa)$^{0.5}$	exp. $x_{1,exp}$ •10^4	calc. $x_{1,calc}$•10^4	$[(x_{1,exp} - x_{1,calc})/x_{1,exp}]^2$
Ethyl acetate	[14]	18.15	1.300	0.001311	0.9980
	[17]		1.060		0.9975
Tetrahydrofuran	[14]	19.46	6.700	0.008866	0.9974
	[17]		4.100		0.9957
Acetone	[14]	19.94	3.200	0.01708	0.9894
	[17]		2.980		0.9885
Propan-2-ol	[14]	23.58	6.300	1.353	0.6166
	[17]		5.000		0.5320
Acetonitrile	[14]	24.40	2.400	3.090·	0.0826
	[17]		2.900		0.0043
Propan-1-ol	[15]	24.60	21.827	3.735	0.6871
Ethanol	[14]	26.52	27.400	19.700	0.0789
	[15]		37.500		0.2252
	[17]		24.060		0.0328
Methanol	[14]	29.41	108.300	128.500	0.0348
	[17]		108.800		0.0328
				RMSRD	0.7101 (71.0 %)
				Fitted $\Delta C_{p,1}$	237.8 J•mol^{-1}•K^{-1}

* Fitting objective function was *RMSRD* (root-mean-square-relative-deviation). According to the referenced studies experimental solubilities were measured at ambient pressure and standard uncertainty $u(T) = 0.1$ K, $u(P) =$ unspecified.

3.2. Comparison of prediction accuracy for different assumptions on value of $\Delta C_{p,1}$

The solubilities were calculated analytically with the aforementioned three different values for $\Delta C_{p,1}$. The values 0 and 90.8 J•mol^{-1}•K^{-1} correspond to the two usual assumptions for $\Delta C_{p,1}$. The value 238 J•mol^{-1}•K^{-1}, on the other hand, was derived empirically from experimental solubilities by regression. Fig. 2 shows how the predicted solubilities correspond better to the measured values when one goes from 0 to 91 to 238 J•mol^{-1}•K^{-1}. It shall be noted that the value of 238 J•mol^{-1}•K^{-1} minimises the *RMSRD* between measured and predicted values, so that a further increase above this value no longer improves the prediction quality, but rather reduces it again.

Quantifying the predictive accuracy in terms of *%-RMSRD* gives 97 %, 88 % and 52 % for $\Delta C_{p,1} = 0$, 91, and 238 J•mol^{-1}•K^{-1}, respectively. While there is some difference between the two conventional assumptions, the value of 238 J•mol^{-1}•K^{-1} gives a significantly better accuracy. For numerical details see Table S4. Clearly, the solubility model used here provides the experimentally observed tendency for the solubility to increase as the solvent δ_2 approaches the solute δ_1. But Fig. 2 shows that, regardless of the value of $\Delta C_{p,1}$, ethyl acetate (2 hydrogen bond acceptors Ac) and THF (1 Ac) show poorer prediction accuracy than EtOH and MeOH (1 Ac and 1 Dn each). However, all four compounds have very similar dipole moments between about 1.6 and 1.8 Debye, making it unlikely that differences in polar interaction lead to the discrepancies in prediction quality between different solvents. With regard to the polyalcohol ascorbic acid (6 Ac, 4 Dn), one could argue

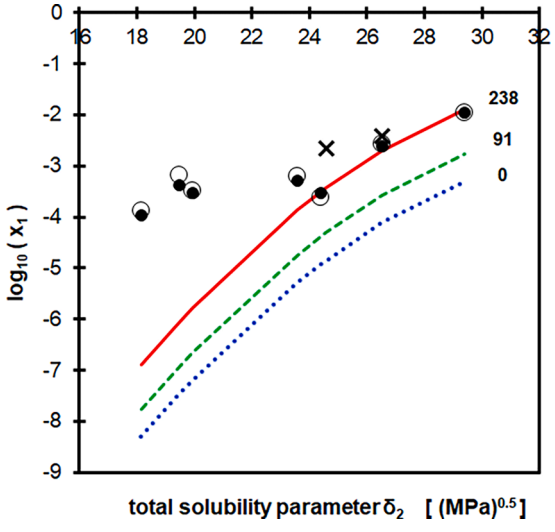

Fig. 2. Molar solubility x_1 of ascorbic acid at 298 K from experimental studies: Ref. [14] (circle o), Ref. [15] (cross x), Ref. [18] (black disk ●), and prediction (lines). Calculations were carried out with values for $\Delta C_{p,1} = 0$ (dotted), 91 (dashed), and 238 J•mol^{-1}•K^{-1} (continuous).

that insufficient consideration of hydrogen bonding is the cause of the discrepancies. However, it is EtOH and MeOH with probably the strongest hydrogen-bond interaction with the solute that are best predicted. The exact cause of this and a conclusive explanation for this behaviour cannot be offered at this point.

3.3. Comparison of prediction accuracy with experimental inter-lab variability

Experimental solubilities from different laboratories are reported in [14–18]. There, values of $x_{1,\mathrm{exp}}$ for the same solvent differ on average by a factor of 1.87 while the corresponding inter-laboratory *RMSRD* accounts to 160 % (See Supplementary Information, Table S5). The *RMSRD* of 71 % obtained here with the best-fit value $\Delta C_{p,1} = 238$ J•mol^{-1}•K^{-1} compares favourably with this inter-laboratory spread.

The literature solubility data show the trend that the discrepancy between results from different laboratories increases as the experimental solubility falls. It seems obvious to use the difference in purity as an explanation for the discrepancy present, but also the measurement protocols differ in several respects even though all studies except one used the same gravimetric shake-flask method. In view of the instability of LAA to oxygen (especially in dilute solutions), to light and to traces of metal cations (catalyse auto-oxidation), it is quite possible that factors other than solute purity may have influenced the measurements. This might be an indication of still persisting challenges in measuring solubility of LAA [19,23–26].

Although the regressed $\Delta C_{p,1}$ value can probably not be considered exact, it can be used in conjunction with the chosen solubility model and the available thermophysical literature data as an additional, empirically adjusted parameter yielding solubility predictions for LAA whose relative deviations, on average, are smaller than the discrepancy between different laboratories. This shows that the Scatchard-Hildebrand approach can provide useful correlations in this way, given the quality of the experimental data currently available.

3.4. Comparison of prediction accuracy with other study

Some authors have used different approaches in conjunction with Eq. (2) to predict the solubility of LAA in water [19,23,24] and in organic solvents [25]. To the best knowledge of the author reference [25] is the only one publication that aims to predict solubilities of ascorbic acid in organic solvents. The $\Delta C_{p,1}$ value this study had based its computations on was 81.4 J•mol^{-1}•K^{-1} without providing information on how this value was perceived [25]. The value for $\Delta C_{p,1}$ derived here is larger by a factor of 3 compared to this number, meaning that the other study, had it used the value of this work, would have predicted systematically higher solubilities.

Mota et al. [25] used, in contrast to this work, an equation of state method and have not explicitly published their predicted solubility values. However, they quote absolute percentage deviations (*AD%*) in comparison with experimental literature values for 7 solvents, which come from a single literature source [14]. These solubility values were also used for fitting in the present work, so that, on this basis, a comparison of the prediction quality of the two studies is feasible. For this purpose, the corresponding $AD\% = \mathrm{abs}(x_{1,exp} - x_{1,calc})/x_{1,exp}\bullet 100$ % for this study have been calculated from the solubility data in [14]. The values range from 24.0 % to 99.9 % (average 66 %). See also Fig. 3.

Ref. [25] only provides *AD%* values that, for each solvent, were averaged over solubilities at different temperatures between 293 and 323 K. In this respect, and to be precise on this point, their deviation values actually relate to average absolute deviations (*AAD%*). These aggregated values range from 44.4 % to 99.9 % (average 87 %). With due caution, it might be stated that the approach presented here, despite its relative simplicity, performs at least equally well in terms of the AD% criterion.

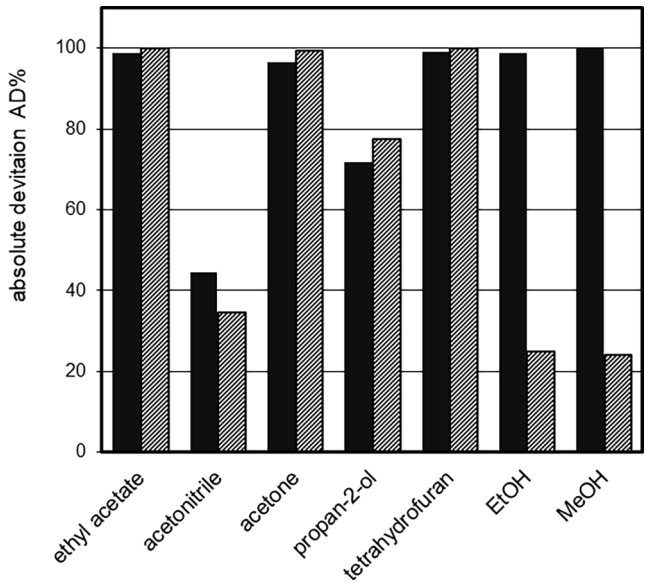

Fig. 3. Absolute deviation of solubility forecasts for ascorbic acid in various solvents. Study by Mota et al. [25] (black bars) and this study (striped grey bars) with $AD\% = \mathrm{abs}(x_{1,\mathrm{exp}} - x_{1,\mathrm{calc}})/x_{1,\mathrm{exp}}\bullet 100$ %.

4. Conclusions

It has been shown in an exemplary way that experimental solubility data can readily be analyzed to arrive at an estimate of the heat capacity difference $\Delta C_{p,1} = 238$ J•mol^{-1}•K^{-1} for the solute LAA. Comparisons with group contribution estimates arriving at an approximate value of $\Delta C_{p,1} \approx 180$ J•mol^{-1}•K^{-1} show reasonable agreement with this regression result. Based on the general solubility equation and the Scatchard-Hildebrand activity coefficient model, the mole fraction solubilities of LAA in 8 organic solvents were calculated to assess how the solubility prediction accuracy depends on the value of $\Delta C_{p,1}$. In terms of the root-mean-square-relative-deviation (*RMSRD*), the accuracy was shown to increase in the order "0" < "91" < "238" (all in units of J•mol^{-1}•K^{-1}).The first two numbers represent the commonly assumed values where 91 J•mol^{-1}•K^{-1} is the melting entropy of LAA.

Comparison of the calculated solubilities (using $\Delta C_{p,1} = 238$ J•mol^{-1}•K^{-1}) with experimental solubilities from different laboratories showed that prediction accuracy (*RMSRD = 71 %*) compared favourably with the inter-laboratory deviation (*RMSRD = 160 %*). Comparison with the only other predictive study [25] on LAA in organic solvents was only feasible by the *AD%* criterion (absolute percentage deviation). It was found that the approach presented here (average *AD%* = 66 %) performs at least equally well compared to reference 25 (average *AD%*=87 %).

The disadvantage of the proposed method generally is that the estimation of $\Delta C_{p,1}$ from solubility data is correlative by nature and thus merely provides an additional parameter adjusted within the same model (GSE, γ, solute molecule). Nevertheless, the method as such is universally applicable to all solid solutes, is independent of the chosen approach for the activity coefficient and, here, shows self-consistent behaviour as well as providing more precise predictions than the usual assumptions $\Delta C_{p,1} = 0$ and, resp., $\Delta C_{p,1} = \Delta S_1(T_{m,1})$. In all, this in connection with using the GSE and the Scatchard-Hildebrand approach for γ makes a simple-concept, simple-to-implement-and-use, and as was shown for ascorbic acid, fairly-well-performing method. It may not be for theorists, but it is of value to practitioners in industry who deal with solubility problems and need quick, useful and workable results.

Clearly, it would be desirable to obtain the value for $\Delta C_{p,1}$ in an independent manner, most preferably, directly from experiment. This seems to be difficult to achieve in principle, e.g. with calorimetric measurements of the heat capacity of rapidly cooled melts, because

thermodynamic non-equilibrium systems are present. As such, their properties are always a function of the material history and the exact manufacturing process. For solutes that are thermally unstable above the melting point, such as LAA, even this route is fundamentally inaccessible, so that alternative approaches are needed. The work outlined in this paper is intended to contribute to this.

CRediT authorship contribution statement

Ralph J. Lehnert: Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Visualization, Validation, Formal anaylsis, Methodology, Software.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The article processing charge is funded by Reutlingen University.

Appendix A. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.jscs.2024.101827.

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