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DETERMINATION OF SOLUBILITY PARAMETER VALUES FOR PURE SOLVENTS AND BINARY MIXTURES

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ABSTRACT

The estimation of the solubility parameter (δ) values for pure liquids and binary mixtures of pharmaceutical interest are considered. It is initially assumed that a previously reported relationship between solubility parameter and dielectric constant for pure polar solvents can be extended to liquid mixtures. If this expression is operative for pure liquids and binary blends, there remains a need to correlate derived values from an independent theoretical or experimental approach. Thus, it is submitted that the molal boiling point elevation as a colligative property might be useful in this regard. It is seen that a good correlation exists for the estimation of solubility parameters from both methods. Several simplifying and limiting assumptions are made for the second method and are considered.

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INTRODUCTION

The Hildebrand solubility theory has proved to be quite useful as an aid in predicting and interpreting solubility phenomena (1, 2), heats of mixing (3) and partitioning processes (4). The solubility parameter is a significant quantity since it directly reflects the intermolecular interactions involved for a pure solvent, pure solute or solvent-solute system. Although the theoretical justification of solubility theory rests upon dispersion forces and hence non-polar molecules (3), its use has been extended to semi-polar and polar systems (2).

PAST WORK

The extension of solubility parameters to liquids where hydrogen bonding or dipole–dipole forces prevail does not, however, lessen their importance with regard to understanding and interpreting intermolecular interactions. Often, the most difficult problem encountered when using solubility parameters is the calculation of the quantity itself because of the lack of necessary literature values or experimental data. The purpose of this paper is to present methods which allow for the estimation of solubility parameters for pure solvents or miscible solvent blends.

The solubility parameter (3) is defined as the square root of the cohesive energy densities and may be quantitatively stated as

$$\delta = \left(\frac{-E}{V_l}\right)^{\frac{1}{2}} \qquad \text{Eq. 1}$$

where $-E$ is the cohesive energy of the liquid, V_l is the molal volume and δ is the solubility parameter which has the units of (cal./ml.)$^{\frac{1}{2}}$. A widely used method of evaluating $-E$ is by the relationship

$$= Ev = \Delta H_v - RT \qquad \text{Eq. 2}$$

where ΔH_v is the heat of vaporization (calories/mole), R is 1.987 calories/mole and T is degree Kelvin and E_v is the energy of vaporization.

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Means of estimating ΔH_v include Trouton's and Hildebrand's rules (5), both of which rely on the boiling point of the liquid and are generally applicable only to non-polar solvents.

Other methods of evaluating the solubility parameter have been discussed (5) and include estimation from internal pressures, from equations of state and critical constants, and from surface tensions, optical and solubility data. A system proposed by Small (6) and recently evaluated (7) involves molar attraction constants which are said to be additive. A general criticism of each of the above methods would be that they are usually inappropriate for relatively polar liquids.

For binary solvent blends, Hildebrand (3) has proposed the equation:

$$\delta_m = \frac{\delta_1 \phi_1 + \delta_2 \phi_2}{\phi_1 + \phi_2} \qquad \text{Eq. 3}$$

where ϕ_1 and ϕ_2 are the respective volume fractions for the pure liquids and it is assumed that δ_1 and δ_2 are known. Equation 3 embodies the geometric mean assumption which strictly speaking is only valid for systems where association or solvation are not anticipated and as such does not apply to polar liquids. Further, it is difficult to estimate reasonable values for the volume fraction terms when solution expansion or contraction occurs subsequent to mixing of the pure solvent species.

A reported empirical relationship (8) between the solubility parameter and dielectric constant (ε) is:

$$\delta = 0.2\varepsilon + 7.5 \qquad \text{Eq. 4}$$

This expression is useful for semi-polar and polar liquids or liquid blends, but deviates at the nonpolar end of the polarity spectrum. Values of ε for pure solvents and many binary systems are currently available in the literature (9-11), which makes equation 4 useful from a practical standpoint.

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PROPOSED METHOD

The proposed method involves the molal boiling point equation (12) which may be stated quantitatively as:

$$Kb = \frac{RTb^2}{1000\ hv} \qquad \text{Eq. 5}$$

where Kb = molal boiling point elevation value, R is 1.987 cal./mole, Tb is boiling point °K and h_v is the heat of vaporization (cal./gm.)

Equation 5 is derived from a Raoult's law consideration which states that the vapor pressure lowering of a pure solvent by the addition of a nonvolitile solute is related to the mole fraction of solute concentration. A consequence of the vapor pressure lowering is an increase in the boiling point temperature. The change in temperature, ΔT is also related to the Kb value by

$$Kb = \Delta T/X_2 \qquad \text{Eq 6}$$

where X_2 is the mole fraction of solute present.

The limiting assumptions governing both equations 5 and 6, are that Kb will only remain constant for dilute solutions and for ideal solution behavior.

Of interest with respect to equation 5 is the method offered for the calculation of the heat of vaporization which was previously shown to be related to the solubility parameter. If Kb and Tb are known or experimentally determined, h_v may be calculated. Multiplication of h_v (calories/gm.) by the density (gm./ml.) yields calories/ml. The square root of this quantity then becomes the then becomes the solubility parameter.

The underlying assumption involving this calculation is h_v or ΔH_v at the boiling point is approximately equal to (ΔH_v-RT) at room temperature. This relationship holds quite well for many liquids of pharmaceutical importance. The solubility parameter equation now becomes:

$$\delta = (\Delta H_v\ (\text{boiling point})/V_1)^{\frac{1}{2}} \qquad \text{Eq. 7}$$

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or

$$\delta = (h_v \text{ (boiling point)}(\rho))^{1/2} \qquad \text{Eq. 7A}$$

where ρ is the density.

To test the validity of the relationship shown in equation 7, the solubility parameters for several polar and non-polar liquids were calculated using heat of vaporization (boiling point) values. The calculated values, as shown in Table 1, compare very favorably with literature values as well as the solubility parameters generated using equation 4. Butanol and pentanol values calculated from equation 7 deviate most from the literature solubility parameters which suggests that the assumptions underlying equations 7 and 7a are not universally applicable.

Also shown in Table I are solubility parameters calculated from the dielectric constant relationship. These calculated values appear to correlate very well in most cases with those taken from the literature.

The usefulness of equations 5-7A may be extended to include binary solvent mixtures where

$$Kb_m = \frac{RTbm^2}{1000\ h_{vm}} \qquad \text{Eq. 8}$$

and it is assumed that Eq. 9

$$Evm \text{ (room temperature)} = \Delta H_{vm} \text{ (boiling temperature)}$$

The quantities K_{bm}, T_{bm}, E_{vm}, h_{vm} have been previously defined except that they now are the values for the mixture rather than the pure solvent. Equation 9 is assumed valid if expressions 5 and 7, 7A hold for each pure solvent species. The solubility parameter expression for the mixture now becomes:

$$\delta_m = (h_{vm}\ \rho m)^{1/2} \qquad \text{Eq. 10}$$

where m is the density of the mixture and h_{vm} is calculated from

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TABLE I - COMPARISON OF CALCULATED SOLUBILITY PARAMETERS WITH LITERATURE VALUES

Pure Solvent	Hv (b.p.) cal/mole[a]	calculated equation[7]	dielectric constant[b]	calculated equation[4]	literature[c]
water	9718	23.2	78.5	23.2	23.4
methanol	8437	14.4	32.6	14.0	14.5
ethanol	9304	12.5	24.3	12.4	12.7
1-propanol	9675	11.4	20.1	11.5	11.9
1-butanol	10474	10.6	17.8	11.1	11.4
1-pentanol	10630	9.8	13.9	10.3	10.9
acetone	7092	9.8	10.7	11.6	10.0
ethyl acetate	7713	8.8	6.02	8.7	9.1
chloroform	7020	9.3	4.81	8.5	9.3
benzene	7353	9.1	2.27	8.0	9.2
p-dioxane	8550	10.0	2.21	7.9	9.9
carbon tetrachloride	7161	8.6	2.23	8.0	8.6
hexane	6896	7.2	1.89	7.9	7.3

[a] Weissberger, A., Organic Solvents Physical Properties and Methods of Purification, 2nd ed., New York, Interscience Publishers, Ltd., 1955.

[b] Reference 9

[c] Burrell, H., Interchemical Review, 14, 3 (1955)

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equation 8 given the values of Tbm and Kbm. Although Kbm might be experimentally evaluated, it should be useful to attempt its approximation by

$$K_{bm} = Kb_1X_1 + Kb_2X_2 \qquad \text{Eq. 11}$$

where X_1 and X_2 are the mole fractions of the pure solvents. Because Kb is a colligative property, it would seem that the additive nature is a reasonable assumption. The Tbm and density ρ_m values may also be experimentally determined, but fortunately are usually available in the literature. Chu (13) has documented Tbm values for many solvent blends and Nagata (14) has discussed equations which allow the calculation of Tbm with a very high degree of accuracy.

Therefore, if Kbm is approximated and Tbm is known, then the hvm value may be calculated. Knowledge of hvm and the density of the mixture shows the calculation of δm from equation 10.

Equation (4) may be rewritten to include its use for a mixture also, and as such is expressed by $\delta m = 0.2\ \varepsilon m + 7.5$ Eq. 12
As a test situations, equations 3, 10 and 12 were used to generate δm values for an ethanol-water system. The calculated values are shown in Table II and a high degree of correlation is evident for each method with all mixtures tested.

From the data in Table II, there is no evidence to suggest that one method is most recommended for a binary mixture of polar components. It would seem that when applying a method, the limitint factor becomes the availability of the necessary data. The method chosen must also be consistent with the governing limitations regarding its use. For the molal boiling point equation, the h_v values at the boiling point must be approximately equal to the values at room temperature. The dielectric constant - solubility parameter relationship should be limited to solvent blends in the dielectric range of about 10-78. As mentioned previously, equation (3) suffers from the fact that the calculation of the volume fractions does not include the effect of solution expan-

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TABLE II - CALCULATION OF SOLUBILITY PARAMETERS FOR ETHANOL - WATER MIXTURES

% Ethanol (w/w)	Equation 10[*]	Equation 12	Equation 3
3	22.5	22.6	22.7
10	21.8	22.1	22.1
15	21.3	21.5	21.4
20	20.8	21.0	20.8
25	20.3	20.4	20.2
30	19.9	19.8	19.6
35	19.4	19.2	19.1
40	18.9	18.6	18.5
45	18.4	17.9	18.0
50	17.9	17.3	17.4
55	17.4	16.6	16.9
60	16.9	16.1	16.4
65	16.4	15.5	15.9
70	15.9	15.0	15.4
75	15.4	14.4	14.9
80	14.8	14.0	14.5
85	14.3	13.6	14.0
90	13.7	13.3	13.6
95	13.2	12.8	13.1

[*] Tbm values taken from reference 13.

[*] Kb values for water and ethanol taken from reference 12.

[•] Density values taken from *The United States Pharmacopeia*, Seventeenth Revision.

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sion on contraction. Solution contraction may become a very significant factor for alcohol-water systems where hydrogen bonding occurs.

From equation 10, it is seen that any error or variation that is introduced into the solubility parameter of the mixture is due to the heat of vaporization value. Therefore, it should be of interest to test the sensitivity of δm with respect to changes in h_{vm} Equation 10 may be rewritten in general form as:

$$\delta m = (X)^{\frac{1}{2}} \qquad \text{Eq. 13}$$

where X = hvm. m The ratio of dδm/dx then becomes

$$\frac{d\delta m}{dx} = \frac{1}{2(X)^{\frac{1}{2}}} = \frac{1}{2\,\delta m} \qquad \text{Eq. 14}$$

If the quantity X is allowed to assume a variation of 5%, then

$$dx = .05 . X = .05\ \delta m^2 \qquad \text{Eq. 15}$$

and

$$d\delta m = \frac{1}{2\delta m}\ (.05 \cdot \delta m^2) \qquad \text{Eq. 16.}$$

The δm values calculated from equation 10 for the ethanol-water mixtures were used to generate values of dδm. These data are presented in Table III which shows that dδm decreases with decreasing values of δm. As expected, the percent error, in this case defined as (dδm/δm) · 100, is constant for each solvent blend. Given the conditions of equation 16, it would seem that a variation in δm of 2.5% is acceptable.

The data in Tables I and II suggests that both the molal boiling point and dielectric constant equations may be used to reasonably estimate the solubility parameters of pure solvents and miscible solvent blends. Neither equation is proposed as an absolute method, but each may be very useful depending upon the literature values and/or laboratory equipment available.

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TABLE III - VALUES OF $d\delta_m$ GENERATED FROM EQUATION (16) FOR THE ETHANOL-WATER MIXTURES

% Ethanol (w/w)	(equation 10) δ_m	$d\delta_m$	$d\delta_m/\delta_m \cdot 100$
5	22.5	.56	2.5
10	21.8	.54	2.5
15	21.3	.53	2.5
20	20.8	.52	2.5
25	20.3	.51	2.5
30	19.9	.49	2.5
35	19.4	.48	2.5
40	18.9	.47	2.5
45	18.4	.46	2.5
50	17.9	.45	2.5
55	17.4	.44	2.5
60	16.9	.42	2.5
65	16.4	.41	2.5
70	15.9	.40	2.5
75	15.4	.38	2.5
80	14.8	.37	2.5
85	14.3	.36	2.5
90	13.7	.34	2.5
95	13.2	.33	2.5

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