

Solubilities of Nonvolatile Solutes in Polymers from Molecular Thermodynamics

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Because there is no simple, general method for measuring solubilities of nonvolatile solutes in a polymer, this work presents a thermodynamic framework for estimating such solubilities from infinite-dilution distribution-coefficient data for aqueous solutions of the solute in equilibrium with the polymer. The experimental infinite-dilution distribution coefficient is related to that calculated from a molecular-thermodynamic model (Flory–Huggins). The three binary Flory parameters are obtained from water–solute and water–polymer data, and from the solute’s distribution coefficient. Solubilities of 19 nonvolatile aromatic solutes were estimated in three polymers: ethyl-vinyl acetate copolymer (EVAc) with 33 (EVAc33), 45 (EVAc45) wt. % vinyl acetate content, and poly(vinyl acetate) (PVAc) at 25°C, where most of the solutes are solids. For some of these systems, predicted solubilities are compared with new experimental results. The calculations reported here may be useful for various applications, including the design of membrane processes or drug-delivery systems, and for packaging technology for foods, chemicals, and pharmaceuticals.

Introduction

The literature is rich in both experimental and theoretical studies concerning the solubilities of volatile substances in polymeric materials (for example, Wohlfarth, 1994; Hao et al., 1992; Bonner, 1975). However, little is known about solubilities of nonvolatile liquid and solid solutes in polymers, despite a need for this information in a variety of applications, including controlled-release systems where the drug solubility in the supporting polymer plays an essential role in determining load capacity and diffusion rate into the physiological environment (Langer and Peppas, 1983). In packaging technology for foods and pharmaceuticals, sorption from the contained product may alter essential properties of both the product and the polymeric container, or release of oligomers or processing additives from the polymer may contaminate the stored product (Vergnaud, 1998; Jenke et al., 1991; Hayward et al., 1990; Hayward and Jenke, 1990).

Heavy organic solutes tend to be solids near room temperature. Because equilibration of the solid–polymer interface is extremely slow, there is no simple, inexpensive way to measure a solid solute’s solubility in a polymer. However, when the solute is dissolved in a solvent that does not dissolve the polymer, infinite-dilution distribution coefficient data can be obtained more easily. Coupled with a molecular-thermodynamic model and other experimental data, it is then possible to estimate the desired solubility.

In this work, we use the Flory–Huggins model (Flory, 1953) to estimate the solubilities of nineteen nonvolatile organic solutes in three polymers: two ethyl-vinyl acetate copolymers with 33 and 45 weight percent vinyl acetate (VAc) and poly(vinyl acetate) at 25°C. We have recently measured infinite-dilution distribution coefficients for these solutes between water and polymer (Fornasiero et al., 2002). To validate our calculations, we compare the predicted solubilities with new experimental data for some of these solutes.

Table 1 presents the most relevant solute properties: molecular weights, densities, and melting points. For solutes that are solid at 25°C, the densities in Table 1 are those of the liquid at a temperature just above the melting point. In

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Table 1. Solute Properties

Solute	<i>M</i>	ρ_s	T_f	ΔH_f	Δc_p
1-Naphthol	114	1.113*	95.0 [†]	23,470 [†]	—
2-Naphthol	114	1.078*	120.4 [†]	18,790 [†]	—
2-Nitroaniline	138	1.280*	69.3 [†]	16,110 [†]	—
3-Nitroaniline	138	1.210*	113.8 [†]	23,690 [†]	—
4-Nitroaniline	138	1.050*	147.5 [†]	21,150 [†]	—
2-Nitrophenol	139	1.294*	44.8 [†]	17,450 [†]	—
3-Nitrophenol	139	1.280*	96.8 ^{††}	19,200 ^{††}	86.1 ^{††}
4-Nitrophenol	139	1.281*	113.8 [†]	18,250 [†]	85.0 ^{††}
2-Nitrotoluene	137	1.163**	−3.8 ^{††}	—	—
3-Nitrotoluene	137	1.157**	16.0 ^{††}	—	—
4-Nitrotoluene	137	1.123	51.6 [†]	16,810 [†]	—
Acetophenone	120	1.055**	19.6 [‡]	—	—
Benzoic acid	122	1.084*	112.3 [†]	18,060 [†]	—
Benzonitrile	103	1.010**	−12.8 [†]	—	—
Benzophenone	182	1.098*	47.8 [†]	18,190 [†]	55.5 [†]
Benzyl alcohol	108	1.045**	−15.5 [†]	—	—
Nicotine	162	1.010**	−80.0 ^{‡‡}	—	—
Nitrobenzene	123	1.196**	5.7 [†]	—	—
Pyridine	79.1	0.978**	−41.6 [†]	—	—

Molecular weight *M* (g/mol), density ρ_s (g/cm³), melting point T_f (°C), molar enthalpy of fusion ΔH_f (J/mol), and molar heat-capacity difference between liquid and solid-state Δc_p (J/mol K).

*Density of the liquid just above the melting point (Beilstein, 1995–1998).

**All liquid solute densities are at 20°C (Nguyen, 1999).

[†]Domalski and Hearing (1996).

^{††}Domalski and Hearing (1990).

[‡]Benes and Dohnal (1999).

^{‡‡}International Chemical Safety Card (1993).

addition, Table 1 gives molar enthalpies of fusion and differences in the liquid and solid molar heat capacity.

For each of the three polymers, Table 2 shows the average molecular weight, density at 25°C, VAc content, and glass-transition temperature.

Essentials of the Estimation Method

Solubility is an equilibrium property. When a solid solute is brought into contact with a polymer film, equilibration of the solid–polymer interface is prohibitively slow. To attain equilibrium in a long (but reasonable) time, it is helpful to dissolve the solute in a liquid that is nearly immiscible with the polymer. In this work, the solvent is water. If the polymer absorbs a nonnegligible amount of solvent, the polymer phase is a ternary system. Therefore, in addition to pure-component properties, the molecular-thermodynamic model contains three unknown binary Flory parameters: one for the water–solute binary χ_{ws} , one for the water–polymer binary χ_{wp} , and one for the solute–polymer binary χ_{sp} . We need

Table 2. Polymer Properties

Polymer	<i>M</i>	ρ_s	VAc wt. %	T_{g0}
PVAc	500,000	1.189	100	39.7 (±1.5)*
EVAc45	250,000	0.952	45	−80**
EVAc33	150,000	0.936	33	−95**

Average molecular weight *M* (g/mol), density ρ_s (g/cm³), Composition (comonomer wt. %), glass-transition temperatures T_{g0} (°C).

*Measured by modulated differential scanning calorimetry (DSC 2920, Modulated DSC TA Instrument) at a heating rate of 3°C/min, with modulation amplitude of ±1°C and period of 60 s.

**Estimated using Eq. 1 and T_g (PVAc) = 32°C, T_g (PE) = −125°C (Brandrup et al., 1999).

experimental information to evaluate each binary coefficient. We seek χ_{sp} because that enables us to calculate the solubility of the solute in the dry polymer.

The desired solubility of a solute in a dry polymer is obtained in two steps. First, we measure the distribution coefficient K_s for the solute between the polymer and the solute's aqueous solution; we also measure the (small) solubility of solute-free water in the polymer, as explained elsewhere (Fornasiero et al., 2002). We also require that the organic solute be soluble in water. (If the solute is completely miscible in water, we use vapor–liquid equilibrium data for the binary solute–water mixture.) Water–solute data that give Flory parameter χ_{ws} are often available in the literature. The Flory parameter χ_{wp} (water–polymer) is obtained from water–polymer data. After these have been determined, the remaining (and desired) Flory parameter χ_{sp} is obtained from the measured distribution coefficient K_s .

Second, knowing solute–polymer Flory parameter χ_{sp} , we calculate the desired solubility of the solute in the dry polymer using the Flory–Huggins model.

Calculation of χ_{ws} and χ_{wp}

For a binary solution of solute *i* (the larger molecule) in solvent *j* (the smaller molecule), the activities of components *i* and *j* are

$$\ln a_i = \ln (1 - \Phi_j) + \left(1 - \frac{r_i}{r_j}\right) \cdot \Phi_j + \chi_{ji} \cdot \frac{r_i}{r_j} \cdot \Phi_j^2 \quad (1a)$$

$$\ln a_j = \ln (\Phi_j) + \left(1 - \frac{r_j}{r_i}\right) \cdot (1 - \Phi_j) + \chi_{ji} \cdot (1 - \Phi_j)^2 \quad (1b)$$

where χ_{ji} is the Flory interaction parameter and Φ_j represents the volume fraction of *j* defined by

$$\Phi_j = \frac{n_j r_j}{n_i r_i + n_j r_j} \quad (2)$$

where n_j is the number of molecules of type *j* and r_j is the number of segments in molecule *j*. In the Flory–Huggins model, the number of segments per molecule appears only as a ratio set equal to the ratio of (liquid) molar volumes of the two components

$$\frac{r_i}{r_j} = \frac{v_i}{v_j} \quad (3)$$

For solid solutes at 25°C, molar volumes are those of the hypothetical liquid at 25°C. We approximate these densities with the densities of the liquids that are slightly above the melting point.

First, consider the binary water(w)-solute(s) system. If *s* is a solid, the solubility of *s* in water is given by

$$f_{\text{pure } s}^S = \Gamma_{s,w} \Phi_{s,w} f_{\text{pure } s}^L \quad (4)$$

where $f_{\text{pure } s}^L$ is the fugacity of pure liquid *s*; $f_{\text{pure } s}^S$ is the fugacity of the pure solid; $\Phi_{s,w}$ is the measured aqueous solubility; and $\Gamma_{s,w} = a_{s,w} / \Phi_{s,w}$ is the volume-fraction activity coefficient of the solute in water. Equation 4 assumes that there

is negligible solubility of w in s . Equation 4 is rewritten

$$\left(\frac{f^S}{f^L}\right)_{\text{pure } s} = \Gamma_{s,w} \Phi_{s,w} \quad (5)$$

where the superscript S stands for solid and superscript L stands for (subcooled) liquid. The ratio of the two pure-component fugacities is found from the melting temperature, the enthalpy of fusion, and the heat capacities of the pure solid and pure liquid, as discussed in standard textbooks (for example, Prausnitz et al., 1999).

If solute s is a liquid, the solubility of s in water is given by

$$f_s^L = \Gamma_{s,w} \Phi_{s,w} f_{\text{pure } s}^L \quad (6a)$$

where f_s^L is the fugacity of s in the liquid phase that is in equilibrium with the aqueous phase. If the solubility of water in that phase is negligible, $f_s^L \rightarrow f_{\text{pure } s}^L$, and the solubility of s in water becomes

$$\Phi_{s,w} = \frac{1}{\Gamma_{s,w}} \quad (6b)$$

Equation 6b is a reasonable approximation for liquid solutes that are sparingly soluble in water; therefore, we used Eq. 6b for benzonitrile, nitrobenzene, and 2- and 3-nitrotoluene (Benes and Dohnal, 1999).

Benzyl alcohol and acetophenone show appreciable mutual solubility with water at 25°C. For these solutes, we calculated the Flory solute–water parameter χ_{ws} from

$$\Gamma_{s,w} \Phi_{s,w} = \Gamma_{s,s} \Phi_{s,s} \quad (6c)$$

where $\Phi_{s,w}$ and $\Phi_{s,s}$ are the experimental volume fractions of solutes s in the water-rich phase and in the solute-rich phase, respectively. Activity coefficients $\Gamma_{s,w}$ and $\Gamma_{s,s}$ are given by the Flory–Huggins equation. Experimental data are from Sorensen and Arlt (1979) and Solimo and Gramajo de Doz (1995).

Pyridine and nicotine are liquids at 25°C, and they are completely miscible in water. The equation of equilibrium for component j now is

$$\varphi_j y_j P = \Gamma_j \Phi_j f_{\text{pure } j}^L \quad (7)$$

where y_j is the vapor-phase mole fraction, P is the total pressure, and φ_j is the vapor-phase fugacity coefficient. Vapor–liquid equilibrium data (Gmehling et al., 1988), and gas–liquid chromatography data (Gmehling et al., 1994), for the binary solute–water mixture are used to find Flory parameter χ_{ws} for pyridine and nicotine in water.

Table 3 gives aqueous solubilities at 25°C for all solutes, infinite-dilution activity coefficients, and Flory solute–water parameters, together with sources of experimental data. For benzyl alcohol and acetophenone, Table 3 also gives mutual solubility data with water at 25°C. For nitrobenzene and the three isomers of nitrotoluene and nitrophenol, the aqueous solubility at 25°C has been calculated by linear interpolation of the experimental data (Benes and Dohnal, 1999), using

Table 3. Properties of Aqueous Solutions for 19 Solutes

Solute	$\Phi_{s,w}$	$\Gamma_{s,w}^\infty$	χ_{ws}
1-Naphthol	7.78*	215	1.61
2-Naphthol	7.01*	230	1.60
2-Nitroaniline	7.95**	550	1.89
3-Nitroaniline	6.10**	185	1.67
4-Nitroaniline	5.00**	168	1.57
2-Nitrophenol	12.8†	517	1.88
3-Nitrophenol	99.2†	32.7	1.41
4-Nitrophenol	113 †	27.2	1.38
2-Nitrotoluene	5.59†	1,810	2.00
3-Nitrotoluene	4.41†	2,289	2.03
4-Nitrotoluene	2.49†	2,317	2.00
Acetophenone	64.3††	156	1.64
Benzoic acid	31.4*	63.9	1.51
Benzonitrile	19.8*	522	1.93
Benzophenone	1.25*	4,854	1.82
Benzyl alcohol	426 ††	22.7	1.37
Nicotine	c.m.‡	1.38‡	0.92
Nitrobenzene	16.6†	619	1.95
Pyridine	c.m.	3.92‡‡	1.08

Aqueous solubility $\Phi_{s,w}$ (10^4 volume fraction) at 25°C, infinite-dilution activity coefficient and solute–water Flory parameter.

*Howard and Meylan (1997).

**Beilstein (1995–1998).

†Benes and Dohnal (1999).

††The corresponding equilibrium volume fractions of water in the solute-rich phase are $153 \cdot 10^{-4}$ (Sorensen and Arlt, 1979) for acetophenone and $969 \cdot 10^{-4}$ (Solimo and Gramajo de Doz, 1995) for benzyl alcohol.

‡Gmehling et al. (1994).

‡‡Gmehling et al. (1988).

‡c.m. = complete miscibility.

van't Hoff coordinates ($\ln(x_1)$ vs. $1/T$, where x_1 is the solubility in the mole fraction).

In a similar manner, assuming the negligible solubility of the polymer in water, we obtain χ_{wp} from the measured solubility of solute-free water in the polymer. Table 4 shows measured water solubilities in the three polymers and calculated Flory water–polymer parameters.

In general, Flory parameters vary with the solution composition. However, because the solubility of water in the polymer is small, final results (Table 7) are not sensitive to the coefficient χ_{wp} for EVAc copolymers, and they vary little for PVAc.

Calculation of Flory parameter χ_{sp} from distribution-coefficient data

For the ternary mixture containing water, solute, and polymer, the distribution coefficient for the solute at infinite dilution, K_s^∞ , is defined by

$$K_s^\infty = \lim_{\Phi_{s,p} \rightarrow 0} \frac{\Phi_{s,p}}{\Phi_{s,w}} = \frac{\Gamma_{s,p}^\infty}{\Gamma_{s,w}^\infty} \quad (8)$$

where $\Phi_{s,p}$ and $\Gamma_{s,p}^\infty$ refer to the wet polymer. Subscripts p and w stand for, respectively, the polymer phase and for the

Table 4. Water Content in the Saturated Polymers (wt. %) and Polymer–Water Flory Parameter at 25°C

	EVAc33	EVAc45	PVAc
Water content	~ 0	0.43 (± 0.04)	7.0 (± 0.3)
χ_{wp}	Large	4.54 (± 0.09)	1.88 (± 0.03)

Table 5. Distribution Coefficients K_s Between Water and Polymers and Infinite-Dilution Activity Coefficients $\Gamma_{s,p}^\infty$ in Three Polymers for 19 Nonvolatile Solutes at 25°C

Solute	K_s			$\Gamma_{s,p}^\infty$		
	EVAc33	EVAc45	PVAc	EVAc33	EVAc45	PVAc
1-Naphthol	599	623	2,203	0.36	0.35	0.10
2-Naphthol	372	743	1,693	0.62	0.31	0.14
2-Nitroaniline	66.3	140	350	8.30	3.93	1.57
3-Nitroaniline	36.5	80.1	264	5.06	2.31	0.70
4-Nitroaniline	25.2	65.9	322	6.67	2.55	0.52
2-Nitrophenol	93.7	122	185	5.52	4.24	2.80
3-Nitrophenol	44.1	94.2	313.6	0.74	0.35	0.10
4-Nitrophenol	33.9	87.3	374.2	0.80	0.31	0.07
2-Nitrotoluene	336	483	435	5.39	3.75	4.16
3-Nitrotoluene	105	249	386	21.80	9.19	5.93
4-Nitrotoluene	345	471	423	6.72	4.92	5.48
Acetophenone	38.7	41.5	55.7	4.04	3.76	2.80
Benzoic acid	5.18	13.9	53.4	12.33	4.59	1.20
Benzonitrile	43.9	54.5	77.1	11.90	9.59	6.78
Benzophenone	1,356	2,231	1,782	3.58	2.18	2.72
Benzyl alcohol	2.79	10.8	23.4	8.13	2.10	0.97
Nicotine	1.42	22	46	0.97	0.06	0.03
Nitrobenzene	91.5	145	172	6.76	4.27	3.60
Pyridine	1.09	2.65	5.32	3.59	1.48	0.74

aqueous phase; Γ^∞ stands for the volume-fraction-based activity coefficient at the infinite dilution; and $\Gamma_{s,w}^\infty$ is obtained from the experimental data for the solute–water binary, as discussed above. For 19 solutes, Table 5 shows the distribution coefficients and the corresponding infinite-dilution activity coefficients in three polymers, as calculated from Eq. 8.

The activity coefficient of the solute in the wet-polymer phase ($\Gamma_{s,p}$) is given by the Flory–Huggins equation for a ternary system

$$\ln \Gamma_{s,p} = (1 - \Phi_s) - \Phi_w \frac{r_s}{r_w} - \Phi_p \frac{r_s}{r_p} + \left(\chi_{ws} \frac{r_s}{r_w} \cdot \Phi_w + \chi_{sp} \Phi_p \right) (\Phi_w + \Phi_p) - \chi_{wp} \frac{r_s}{r_w} \Phi_w \Phi_p \quad (9a)$$

where all volume fractions are in the wet-polymer phase (subscript p has been omitted). At infinite dilution, $\Phi_s \rightarrow 0$, Eq. 9a becomes

$$\ln \Gamma_{s,p}^\infty = 1 - \Phi_w \frac{r_s}{r_w} - \Phi_p \frac{r_s}{r_p} + \chi_{ws} \frac{r_s}{r_w} \cdot \Phi_w + \chi_{sp} \Phi_p - \chi_{wp} \frac{r_s}{r_w} \Phi_w \Phi_p \quad (9b)$$

Because Flory parameters χ_{ws} (for EVAc45 and PVAc) and χ_{wp} have been previously determined, Eq. 9b gives the desired Flory parameter, χ_{sp} . In Eq. 9b, Φ_w is set equal to the experimental solubility of solute-free water in the polymer. Because water solubility in EVAc33 is negligible, the terms containing Φ_w vanish. Because the unknown Flory parameter for water–EVAc33 binary multiplies Φ_w in Eq. 9b, it does not affect our calculation of χ_{sp} . Table 6 shows calculated solute–polymer Flory parameters.

Table 6. Polymer–Solute Interaction Parameters χ_{sp} and Activities $(f^S/f^L)_{\text{pure } s}$ of Pure Solid Solutes in Three Polymers at 25°C

Solute	χ_{sp}			$(f^S/f^L)_{\text{pure } s}$
	EVAc33	EVAc45	PVAc	
1-Naphthol	−2.02	−1.98	−3.06	0.165
2-Naphthol	−1.48	−2.09	−2.68	0.159
2-Nitroaniline	1.12	0.46	−0.15	0.431
3-Nitroaniline	0.62	−0.07	−0.88	0.112
4-Nitroaniline	0.90	0.06	−1.04	0.083
2-Nitrophenol	0.71	0.54	0.48	0.645
3-Nitrophenol	−1.30	−1.96	−2.85	0.288
4-Nitrophenol	−1.22	−2.07	−3.23	0.270
2-Nitrotoluene	0.69	0.42	0.89	—
3-Nitrotoluene	2.08	1.32	1.26	—
4-Nitrotoluene	0.91	0.69	1.20	0.574
Acetophenone	0.40	0.43	0.64	—
Benzoic acid	1.51	0.63	−0.21	0.192
Benzonitrile	1.48	1.35	1.40	—
Benzophenone	0.28	−0.08	0.75	0.605
Benzyl alcohol	1.10	−0.16	−0.48	—
Nicotine	−1.03	−3.65	−4.27	—
Nitrobenzene	0.91	0.54	0.70	—
Pyridine	0.28	−0.56	−1.47	—

Solubilities in the dry polymers

For solute s in the dry polymer p , activity coefficient $\Gamma_{s,p}$ is related to the desired solubility $\Phi_{s,p}$ and to χ_{sp} by Eq. 1b for the binary system solute–(dry) polymer. For solutes that are solids, once χ_{sp} is known, and assuming that the polymer solubility in the solid solute is negligible, the desired solubility $\Phi_{s,p}$ is calculated from the equilibrium equation

$$\Gamma_{s,p} \Phi_{s,p} = \left(\frac{f^S}{f^L} \right)_{\text{pure } s} \quad (10)$$

The assumption of a negligible solubility of polymer in the solute is reasonable only for solid solutes. If pure s is a solid at 25°C, the ratio $(f^S/f^L)_{\text{pure } s}$ is obtained from pure-component properties, as indicated earlier. However, if pure s is a liquid at 25°C, both components (solute and polymer) exhibit some mutual solubility. The solute chemical potential $\mu_{s,\alpha}$ and the polymer chemical potential $\mu_{p,\alpha}$ in phase α are, respectively

$$\begin{aligned} \frac{\mu_{s,\alpha}}{RT} &= \ln (\Phi_{s,\alpha}) + (1 - \Phi_{s,\alpha}) \cdot \left(1 - \frac{r_s}{r_p} \right) \\ &\quad + \chi_{s,p} \cdot (1 - \Phi_{s,\alpha})^2 + \frac{\mu_{s,\alpha}^0}{RT} \\ \frac{\mu_{p,\alpha}}{RT} &= \ln (1 - \Phi_{s,\alpha}) + \Phi_{s,\alpha} \left(1 - \frac{r_p}{r_s} \right) + \chi_{s,p} \cdot \frac{r_p}{r_s} \cdot \Phi_{s,\alpha}^2 + \frac{\mu_{p,\alpha}^0}{RT} \end{aligned} \quad (11)$$

where superscript 0 indicates the standard state. Similar relations hold for the chemical potentials in phase β . The equations of equilibrium are now $\mu_{s,\alpha} = \mu_{s,\beta}$ and $\mu_{p,\alpha} = \mu_{p,\beta}$. With $\mu_{s,\alpha}^0 = \mu_{s,\beta}^0$ and $\mu_{p,\alpha}^0 = \mu_{p,\beta}^0$, the equilibrium composi-

tions of both phases can be calculated. However, it is well known (Flory, 1953) that polymer and solute are completely miscible if the solute–polymer Flory parameter is less than $1/2[1 + (1/\sqrt{r_p/r_s})]^2$. Because $r_p \gg r_s$, the critical Flory parameter is 0.5. Therefore, we apply the phase-equilibrium equations only if $\chi_{sp} > 0.5$. In this calculation, χ_{sp} is assumed to be independent of the composition and equal to its infinite-dilution value.

Experimental Studies

To test solubility predictions, we determine experimentally the solubilities for some solutes in EVAc33. For liquid solutes, solubility can be determined gravimetrically if the polymer film does not dissolve after contact with the liquid solute. For solutes sparingly soluble in water (in particular, for solid solutes), solubility can be obtained experimentally in two steps. In the first step, a polymer film is allowed to equilibrate in a beaker with a saturated aqueous solution of a solute, continuously stirred. The saturated solution is prepared in a second beaker where an excess of solute is present, and recirculated through a filter (Whatman 42 filter paper) to the beaker containing the polymer film. Therefore, the polymer is simultaneously in contact with a saturated aqueous solution of the solute and a solute-rich phase. At equilibrium, the polymer film contains an amount of solute equal to its solubility in the polymer if two conditions are satisfied:

- (1) The solute-rich phase is pure solute;
- (2) The polymer does not absorb water.

These conditions are met for EVAc33 with our solid solutes.

In the second step, after the polymer has been saturated with the solute, we completely extract the absorbed solute with ultrapure water (Barnstead NANOpure system) in several desorption steps. By measuring the amount of water used for extraction and its solute concentration by UV-spectroscopy, we determine the solubility of the solute in the polymer. When the solution concentration becomes too small for an accurate UV measurement, or when the time for a complete desorption of the solute is too long, residual solute content in the polymer can be estimated from the solute distribution coefficient between water and polymer, assuming equilibrium. The time required for equilibration in the sorption and desorption steps can be estimated from the diffusion coefficient of the solute in the polymer (assumed constant) and the distribution coefficient between polymer and water (Fornasiero et al., 2002), using a suitable diffusion model (Crank, 1975).

The use of a solvent as a medium to contact the pure solute with the polymer film avoids the extremely long time required for equilibration at the solid–solute/polymer interface. However, this experimental procedure (saturation followed by back-extraction) to determine the solubility of a solid in a polymer is time-consuming and can be applied only when the two conditions stated earlier are reasonably satisfied.

Results and Discussion

Table 4 shows calculated water–polymer interaction parameters. Because water solubility in EVAc33 is negligible, χ_{wp} is large. Although we cannot precisely determine χ_{wp} ,

Table 7. Calculated Solubilities $\Phi_{s,p}$ (volume fraction) for 19 Nonvolatile Solute in Three Polymers at 25°C

Solute	$\Phi_{s,p}$		
	EVAc33	EVAc45	PVAc
1-Naphthol	0.246 (± 0.005)	0.242 (± 0.017)	0.332 (± 0.023)
2-Naphthol	0.188 (± 0.004)	0.246 (± 0.006)	0.296 (± 0.014)
2-Nitroaniline	0.064 (± 0.003)	0.127 (± 0.003)	0.216 (± 0.009)
3-Nitroaniline	0.023 (± 0.001)	0.046 (± 0.001)	0.093 (± 0.004)
4-Nitroaniline	0.013 (± 0)	0.03 (± 0)	0.08 (± 0.003)
2-Nitrophenol	0.174 (± 0.013)	0.209 (± 0.007)	0.221 (± 0.014)
3-Nitrophenol	0.276 (± 0.007)	0.347 (± 0.010)	0.42 (± 0.024)
4-Nitrophenol	0.253 (± 0.003)	0.343 (± 0.020)	0.432 (± 0.027)
2-Nitrotoluene	0.614 (± 0.075)	c.m. —	0.391 (± 0.035)
3-Nitrotoluene	0.063 (± 0.003)	0.184 (± 0.004)	0.202 (± 0.009)
4-Nitrotoluene	0.117 (± 0.005)	0.148 (± 0.005)	0.084 (± 0.003)
Acetophenone	c.m.* —	c.m. —	0.675 (± 0.056)
Benzoic acid	0.017 (± 0.002)	0.041 (± 0.007)	0.092 (± 0.004)
Benzonitrile	0.144 (± 0.003)	0.175 (± 0.007)	0.162 (± 0.012)
Benzophenone	0.242 (± 0.009)	0.318 (± 0.008)	0.151 (± 0.010)
Benzyl alcohol	0.266 (± 0.014)	c.m. —	c.m. —
Nicotine	c.m. —	c.m. —	c.m. —
Nitrobenzene	0.375 (± 0.006)	0.909** (± 0.047)	0.592 (± 0.068)
Pyridine	c.m. —	c.m. —	c.m. —

*c.m. = complete miscibility.

**The calculated polymer volume fraction in the solute-rich phase is $2.63 \cdot 10^{-4}$ for nitrobenzene in EVAc45. For all other polymer–solute systems, it is negligible.

calculated solubilities in dry EVAc33 are not affected by this uncertainty because the volume fraction of water in the polymer phase is essentially zero. For EVAc45, we obtained $\chi_{wp} = 4.54$, which is very close to the 4.91 reported by Chuang et al. (2000) for EVAc copolymer with 37% VAc at 32°C. For PVAc, we determined a Flory parameter equal to 1.88 at 25°C, whereas Immergut et al. (1999) give $\chi_{wp} = 2.5$ at 40°C.

Table 6 reports solute–polymer interaction parameters, and Table 7 shows calculated solubilities in the dry polymer (for PVAc, calculated solubilities at 25°C are reliable if the saturated polymer–solute mixtures have glass-transition temperatures lower than 25°C, as discussed in Appendix A). Solubilities range from a minimum of 1.3% volume fraction for 4-nitroaniline in EVAc33 to complete miscibility for nicotine and pyridine in all three polymers.

For solid solutes, the solubility depends on the strength of polymer–solute interaction as well as on the melting properties of the pure solid. The solubilization process can be split into two steps: the first corresponds to melting the pure solute (the enthalpy required to raise the temperature of the pure solute from the experimental temperature to the triple point, and lowering it back to the experimental temperature after melting is usually negligible when compared with the enthalpy of fusion), and the second corresponds to mixing the (subcooled) liquid solute with the polymer (for solid solutes at 25°C, we use the density of the hypothetical liquid at 25°C). Solubility increases upon lowering the melting point and the enthalpy of fusion, because less energy is required for the melting transition. Solubility also increases with a decreasing Flory parameter that provides an inverse measure of solute–polymer affinity: the lower the parameter, the higher the affinity. Therefore, when we compare calculated solubilities for different solutes in the same polymer, there is no direct correlation between Flory parameter and solubility be-

cause the melting properties differ from solute to solute. On the other hand, if we compare the solubility for the same solute in our three different polymers, there is a clear trend with the Flory parameter. For liquid solutes, the solute with the smallest Flory interaction parameter has the largest solubility, since here the melting properties play no role; for $\chi_{sp} < 0.5$ we have complete miscibility.

Complete miscibility is predicted for pyridine and nicotine in all three polymers; for benzyl alcohol in EVAc45 and PVAc; for acetophenone in EVAc copolymers; and for 2-nitrotoluene with EVAc45. For these systems, we tested the prediction by preparing solutions with $\sim 50\%$ polymer weight fraction. Clear solutions were obtained at 25°C for PVAc in pyridine and nicotine. For EVAc45, clear solutions were obtained for pyridine, benzyl alcohol, acetophenone, and 2-nitrotoluene, suggesting complete miscibility for these systems. For PVAc + benzyl alcohol and EVAc45 + nicotine mixtures, some cloudiness is observed for 50% polymer weight fraction, indicating possible partial solubility or, more likely, that a long time is required to attain equilibrium. For EVAc33, results are inconclusive.

Solubility increases with VAc content in the polymer for most solutes (nitroanilines, nitrophenols, and so on). The solubility of 1-naphthol in EVAc33 is the same as that in EVAc45 within the calculational uncertainty, obtained as described in Appendix B. Only acetophenone shows the reverse trend, while nitrobenzene, 2- and 4-nitrotoluene, benzophenone, and benzonitrile have the highest solubilities in EVAc45.

For a copolymer AB in a solvent s , Flory interaction parameter $\chi_{s(AB)}$, is given by

$$\chi_{s(AB)} = \chi_{sA}\Phi_A + \chi_{sB}\Phi_B - \chi_{AB}\Phi_A\Phi_B \quad (12)$$

where χ_{sA} , χ_{sB} , and χ_{AB} are Flory interaction parameters for A - s , B - s , and A - B , respectively ($A = \text{VAc}$, $B = \text{ethylene}$, $s = \text{solute}$); Φ_A and Φ_B represent the volume fraction of monomer A and B in the copolymer, respectively (Stockmayer et al., 1955). Therefore, the calculated Flory parameter $\chi_{sp} = \chi_{s(AB)}$ is, in general, a nonmonotonic function of the copolymer composition, and a minimum or maximum can be found for some copolymer compositions, depending on χ_{sA} , χ_{sB} , and χ_{AB} . Equation 12 may explain the solubility maximum in EVAc45 for some of the solutes. For PVAc, all solutes with polar moieties give Flory parameters that are negative or much smaller than 0.5, probably because of the attractive specific interactions between the vinyl acetate group in the polymer chain and the polar groups in the solute molecules. The orthosubstituted phenol, 2-nitrophenol, is an exception because the nitro group in the ortho position may form attractive intramolecular interactions with the hydroxyl group, decreasing affinity with vinyl acetate. Nitrotoluenes, acetophenone, benzonitrile, benzophenone, and nitrobenzene have positive Flory parameters. We also notice that the latter are the same solutes that do not show rising solubilities with increasing VAc content in the EVAc copolymers. When solute-polymer interactions are dominated by attractive specific interactions between polar moieties and the vinyl acetate group, solubility increases monotonically with VAc con-

tent; otherwise, it presents an inverse trend or a maximum in the range 33–100% VAc content.

Our calculations rest on the validity of the Flory-Huggins theory for ternary systems. By comparing experimental equilibrium data for polymer-solvents ternary systems with the prediction of the Flory-Huggins model, Favre et al. (1996) showed that fairly good agreement can be achieved for sorption of apolar liquids in elastomers. However, the application of the Flory-Huggins theory to ternary systems leads to large deviations for polar liquids in both homopolymers and copolymers, and for semicrystalline polymers. The observed discrepancies are probably due to nonconstancy of the polymer-solvent Flory parameter.

In our calculations the solute-polymer Flory parameter χ_{sp} is assumed independent of the composition; this approximation is reasonable if the predicted solubility in the polymer is small. However, Table 7 shows that for most solutes the solubility is quite large (20–60% volume fraction). This is not consistent with the approximation, which reduces confidence in these calculations. We expect, therefore, that uncertainties in calculated solubilities may be significantly larger than those estimated from uncertainties in the experimental data shown in Table 7.

We test our solubility calculations for two solid solutes (4-nitroaniline and 4-nitrotoluene) by applying the sorption-desorption procedure described earlier and for two liquid solutes (benzonitrile and 3-nitrotoluene) by gravimetric measurements. For 4-nitroaniline, the experimental solubility in EVAc33 is 1.3% volume fraction, which is in excellent agreement with our prediction. This experimental result has been reproduced in a separate experiment. Solubility of 4-nitrotoluene in EVAc33 is 5.6% volume fraction, roughly half of the predicted value. For 4-nitrotoluene, we measured a water solubility equal to $1.65 \cdot 10^{-4}$ volume fraction, whereas the literature value used in the calculation is $2.49 \cdot 10^{-4}$ volume fraction. If we use the new experimental water solubility, the predicted solubility in EVAc33 for 4-nitrotoluene drops to 7.4% (± 0.3) volume fraction, much closer to the measured solubility. For benzonitrile and 3-nitrotoluene in EVAc33, we obtained solubilities equal to 74.6 and 75.7% volume fraction, respectively. The prediction for these systems is poor. While a more extensive comparison is needed for conclusive results, our test indicates that our thermodynamic procedure to predict solubilities in polymers gives reasonable results for solid solutes when solubilities are small. However, for liquid solutes, when solubilities are large, calculated solubilities are not reliable.

For liquid solutes, the calculated polymer volume fractions in the solute-rich phase $\Phi_{p,s}$ are negligible when $\chi_{sp} > 0.6$. For EVAc45 in nitrobenzene, $\Phi_{p,s}$ reaches the maximum value $2.63 \cdot 10^{-4}$, with $\chi_{sp} = 0.54$, and decreases rapidly with rising χ_{sp} . The Flory-Huggins model predicts that the solute-rich phase is nearly pure solute. However, because we calculated the Flory parameters at the infinite dilution of solute, calculated results in the solute-concentrated phase may be unreliable.

Conclusion

Because there is no simple and fast method to experimentally determine the solubility of a solid or nonvolatile liquid

in a polymer, a simple method based on the Flory–Huggins model is proposed to calculate that solubility. This method requires infinite-dilution distribution-coefficient data for the solute's distribution between the polymer and a liquid solvent that does not dissolve the polymer. Additional required data includes the solubility of the solute in the solvent and the solubility of the solvent in the polymer. From these data we determine the Flory parameter for the solute-(dry) polymer system; that parameter gives us the desired solubility of the solute in the (dry) polymer.

This thermodynamic framework is applied to nineteen aromatic nonvolatile solutes in ethylene-vinyl acetate with 33% or 45% vinyl acetate content, and poly(vinyl acetate). For solid solutes, solubility depends on the strength of polymer-solute interaction as well as on the melting properties of the pure solute, whereas for liquid solutes it depends only on the former. Solubility increases monotonically with VAc content in the polymer for those solutes where attractive specific interactions between polar moieties in the solute molecules and the vinyl acetate group in the polymer dominate the solute–polymer interaction.

The procedure described here rests on the validity of the Flory–Huggins model for ternary (solute–solvent–polymer) systems. Therefore, there is some uncertainty in the accuracy of the solubilities presented here. While further studies are needed to assess the validity of our approach, a comparison with some experimental solubility data shows that reliable predictions are obtained for solid solutes when solubilities are small, whereas, for liquid solutes, when solubilities are large, predictions are unrealistic. Nevertheless, our calculations may be useful for process and product design whenever polymers are used as membranes, as matrices for drug-delivery systems, or as packaging materials for foods, chemicals, or pharmaceuticals.

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Appendix A: Effect of Glass-Transition Temperature

The Flory–Huggins model applies only to mixtures where the polymer is rubbery. While ethylene-vinyl acetate copolymers EVAc33 and EVAc45 are rubbery at room tempera-

ture, pure poly(vinyl acetate) is glassy; its glass-transition temperature T_{g0} is 39.7°C. However, sorption of a solute lowers the glass-transition temperature; this reduction is often called plasticization. The plasticization effect of a solute can be estimated using Chow's equation (Chow, 1980)

$$\ln \left(\frac{T_g}{T_{g0}} \right) = \zeta [(1 - \theta) \ln(1 - \theta) + \theta \ln \theta] \quad (\text{A1})$$

where T_g is the glass-transition temperature of the polymer-solute mixture, and T_{g0} is the glass-transition temperature of the solute-free polymer; ζ is a physically significant constant; and θ is a measure of solute concentration defined by

$$\zeta = \frac{zR}{M_{\text{mon}} \Delta C_p}$$

$$\theta = \frac{M_{\text{mon}} \rho_s}{z M_w \rho_p} \frac{\Phi_{s,p}}{1 - \Phi_{s,p}} \quad (\text{A2})$$

where z is the lattice coordination number, R is the gas constant, ΔC_p is the variation of the isobaric specific heat at the glass transition, ρ_s and ρ_p are solute and polymer densities, and M_{mon} and M_w are monomer and solute molecular weights. We used $z = 2$ as suggested by Chow, $\Delta C_p = 0.5$ kJ/kg·K (Brandrup et al., 1999), and $M_{\text{mon}} = 86.1$ g/mol.

In our solubility calculations, we assume that the solute-polymer mixture is rubbery. We consider the calculated solubilities to be reliable, if they are larger than the solute volume fraction required to depress T_g to 25°C (Φ_{25}). For all solutes studied here, this condition is verified, except 4-nitroaniline, for which Φ_{25} is 8.9%. At saturation, the calculated glass-transition temperature for its mixtures with PVAc is 26.2°C; therefore, the calculated solubility at 25°C should be viewed with caution. For water, Bair et al. (1981) showed that the Φ_{25} required to lower T_g to 25°C is approximately equal to 2.5%, which is lower than the measured water solubility in PVAc (7 wt %). Therefore, we can determine with confidence the water-polymer Flory interaction parameter from the water-solubility data.

Appendix B: Uncertainties in the Solubility Predictions

The uncertainties σ_ϕ in the solubility predictions of the solutes in the water-free polymer (Table 7) are estimated

using

$$\sigma_\phi = \sqrt{\left(\frac{\partial \phi_s}{\partial \chi_{sp}} \right)^2 \sigma_\chi^2 + \left(\frac{\partial \phi_s}{\partial \ln a_s} \right)^2 \sigma_{\ln a}^2} \quad (\text{B1})$$

where σ_χ and $\sigma_{\ln a}$ are the uncertainties in χ_{sp} and solute activity, respectively.

For pure solid solutes, the uncertainties in the solute activity depend on the (unknown) accuracy of the melting properties for solid solutes. For liquid solutes, it can be neglected if the polymer solution is in equilibrium with a nearly pure solute (high binary parameter), since the solute activity is very close to unity. When $\chi_{sp} + \sigma_\chi < 0.5$, complete miscibility is predicted by the Flory model without uncertainty. We assumed negligible uncertainties in a_s for all solutes.

The functional relationship between $\ln a_s$, χ_{sp} , and ϕ_s is given by Eq. 1b in the text. Equation 1b cannot be solved analytically for ϕ_s ; however, $\chi_{sp} = f(\ln a_s, \phi_s)$ and $\partial \phi_s / \partial \chi_{sp}$ (the only nonzero term in Eq. B1) are easily obtained. A direct relation between σ_χ and the solubility uncertainty σ_ϕ is derived from Eq. B1:

$$\sigma_\phi = \frac{(1 - \phi_s)^2 \cdot \sigma_\chi}{\left| 1 - \frac{r_s}{r_p} + 2 \frac{\ln(\phi_s)}{1 - \phi_s} + \frac{1}{\phi_s} \right|} \quad (\text{B2})$$

The main source of uncertainty for χ_{sp} is the experimental error in the distribution coefficients. Additional uncertainties in χ_{sp} derive from uncertainties in the other binary parameters χ_{ws} and χ_{wp} , and in the water solubility in the polymer ϕ_{wp} . The first one is strictly related to the accuracy of the published aqueous solubilities, LLE or VLE experimental data used to determine χ_{ws} . Since this accuracy is unknown, we assumed negligible uncertainties for χ_{ws} . Uncertainties in χ_{wp} are estimated from the experimental uncertainties of water solubilities in the polymers, reported in Table 4. The contributions of χ_{wp} and ϕ_{wp} uncertainties to χ_{sp} uncertainty are unimportant for EVAc copolymers, but they are nonnegligible for PVAc.

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