Modeling the Entrainer Effects on Solubility of Solutes in Supercritical Carbon Dioxide

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Applicability of a previously published equation for calculating the solubility of solutes in supercritical carbon dioxide was extended to calculate the solubility in entrained supercritical carbon dioxide employing 42 experimental data sets collected from the literature. The accuracy of the proposed model was evaluated by calculating both the average absolute relative deviation and the individual absolute relative deviation. The proposed model showed superiority to a previously published similar model, from both correlation and prediction points of view.

Key words solubility; supercritical carbon dioxide; entrainer; calculation

Supercritical fluids (SCF) have been employed in the pharmaceutical industry for production of fine drug particles with narrow size distribution, separation of active ingredients and preparation of microemulsions and sustained drug delivery systems.[1)] Supercritical carbon dioxide (SC-CO2) is a very popular fluid for pharmaceutical applications, as it is non-toxic, non-flammable and of low cost. Furthermore, because of its low critical temperature and pressure, SC-CO2 is ideal for thermal-liable compounds. In addition to the pharmaceutical applications, supercritical fluids are very important solvents in many other industrial processes, including decaffeination of coffee, extraction of hops, spices and seed oils, as well as decontamination of environmental wastes. However, the solubility of most pharmaceutical/chemical compounds is very low in SC-CO2 and an entrainer is usually added to enhance the solubility.

Solubility data are required for designing SCF processes but experimental measurement of solubility is time-consuming and costly. Only a limited number of reports has been published on the solubility of pharmaceutical/chemical compounds in entrained supercritical fluids. Mathematical modelling of solubility data in SC-CO2+entrainer could provide useful information for pharmaceutical/chemical engineers to speed up the process. Thermodynamic models employing equations of state, lattice gas equations or expanded liquid models have been used for modelling such data. These methods require complicated computations and a number of physico-chemical properties which are often unavailable. The aim of this study was to present a simple and easy to use empirical model to calculate the solubility in SC-CO2+entrainer with respect to the concentration of the entrainer, pressure, temperature and density of pure SC-CO2. The accuracy of the proposed model is evaluated employing published experimental data sets and compared with that of a model from the literature. Reported experimental data sets containing solubility data of pharmaceutical/chemical compounds at different temperatures, pressures and entrainer concentrations were included in this study. Data sets containing the solubility at only one temperature, pressure or entrainer concentration, as well as data sets with data points numbering less than 30 (five points for each independent variable) were excluded from this study.

Computational Methods

An empirical equation has been reported[2)] to correlate the mole fraction solubility (y_2) of a solute in pure SC-CO2 with respect to the density of pure SC-CO2 (ρ), pressure (P) and temperature (T):

$$\ln y_2 = K_0 + K_1\rho + K_2P^2 + K_3PT + \frac{K_4T}{P} + K_5\ln\rho \tag{1}$$

where K_0—K_5 are the model constants computed using a least squares analysis.[2)] The accuracy of Eq. 1 has been evaluated employing 23 data sets and a mean correlation error (±S.D.) of 12.6 (±7.4)% was obtained. The model is applicable for calculating the solubility in the absence of an entrainer, and the introduction of one more term representing the concentration (in mole, weight and/or volume fraction) of the entrainer (X) enables it to compute the solubility in SC-CO2+entrainer. The proposed model is:

$$\ln y_2 = M_0 + M_1X + M_2\rho + M_3P^2 + M_4PT + \frac{M_5T}{P} + M_6\ln\rho \tag{2}$$

where M_0—M_6 are the model constants and the numerical value of ρ is calculated by Eq. 3.[3)]

$$\ln\rho = -27.091 + 0.609\sqrt{T} + \frac{2966.170}{T} - \frac{3.445P}{T} + 0.401\sqrt{P} \tag{3}$$

The M_0—M_6 terms should be computed using a least squares method by employing experimental data of entrained SC-CO2; one cannot use the numerical values of K_0—K_5 terms from pure SC-CO2 solubility data. The next limitation of Eq. 2 is that it could be used to predict the solubility data with an interpolation technique.

Gonzalez and co-workers[4)] extended the mass action law-based Chrastil model to correlate the solubility data in entrained SC-CO2. Their model could be rewritten as:

$$\ln S = a + \frac{b}{T} + c\ln X + d\ln\rho \tag{4}$$

where S is the solubility of a solute (g/l), and a, b, c and d are the model constants. The authors noticed that a is equal to $[q - d\ln(M_c) - d\ln(c) - d\ln(M_e) + \ln(M_s + dM_c + cM_e)]$=constant, in which M_s, M_c and M_e are the molecular weights of the solute, carbon dioxide and entrainer, respectively, q is a constant, $b = \Delta H_{total}/R$ in which ΔH_{total} is the total reaction enthalpy and R the molar gas constant, c the association number of entrainer and d the association number of carbon dioxide. Although the Chrastil model was originally proposed to correlate solubility (in grams per liter) with density and temperature, the model was employed to correlate the mole fraction solubilities as well.[5,6)] In addition, it has been shown that for Eq. 4 replacing g/l solubility with mole fraction solubility provides more accurate calculations.[3)] Therefore, the logarithm of mole fraction solubility ($\ln y_2$) was used as a dependent variable of the Chrastil model in this work. The main limitation of Eq. 4 is that it is not applicable to pure SC-CO2 since ln(0) is not a defined value.

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A global fitness test for the multiple regression model was evaluated using the F value, found by splitting the total variations of the response variable into one part due to the regression and one part due to the residual, or error. The numerical value of F is the ratio of the mean squares due to regression to that of the residuals, and the higher the F value is, the more significant the correlation. The significance level (s.l.) of the F value (with degrees of freedom (df) related to the number of independent variables (V) and number of data points in each set (N), *i.e.* df$=N-V-1$) is provided by statistical software such as SPSS (Statistical Package for Social Sciences). A significant F value means that not all the model constants (*i.e.*, M_0—M_6 in this work) are zero although some of them might be, depending on the data set.

In order to provide a reliable accuracy criterion to compare the models possessing different numbers of curve-fitting parameters, the average absolute relative deviations (AARD) were used, and were calculated by:

$$\mathrm{AARD}=\frac{100}{(N-Z)}\sum\frac{|y_2^{\mathrm{calculated}}-y_2^{\mathrm{observed}}|}{y_2^{\mathrm{observed}}} \tag{5}$$

where N is the number of data points in each set and Z the number of curve-fitting parameters for each model (Z is equal to 7 and 4 for Eqs. 2 and 4, respectively). To test the prediction capability of the models after training using a minimum number of experimental data points, the individual absolute relative deviations (IARD) of predicted solubilities from observed values were calculated by:

$$\mathrm{IARD}=100\left(\frac{|y_2^{\mathrm{calculated}}-y_2^{\mathrm{observed}}|}{y_2^{\mathrm{observed}}}\right) \tag{6}$$

Since the aim of the present study was to compare the proposed equation with a previously published model, and because the number of curve-fitting parameters was not equal in the two models, AARD values were preferred over the IARD. It is obvious that the mean IARD values were less than the corresponding AARDs.

Results and Discussion

Table 1 shows details of the systems studied, the references, the number of data points in each set and the AARDs for correlation studies. The minimum AARD (3.8) is observed for perylene in SC-CO2+methanol and the maximum AARD (24.2) for naproxen in SC-CO2+1-propanol whereas the mean (±S.D.) of AARD is 10.9±5.4%. The corresponding minimum and maximum values of AARD for Eq. 4 are 4.0% for perylene in SC-CO2+methanol and 44.8% for

Table 1. Details of Systems Studied, Number of Correlated Data Points in Each Set (N) and Average Absolute Relative Deviation (AARD) for Eqs. 2 and 4 Using Correlative Study

SN[a]	Solute	Entrainer	Reference	N	Eq. 2	Eq. 4
1	2,2′,3,4,4′,5,5′-Heptachlorobiphenyl	Butane	11	96	10.1	41.0
2	2,2′,3,4,4′,5,5′-Heptachlorobiphenyl	Methanol	11	96	10.8	37.0
3	2,2′,4,4′,5,5′-Hexachlorobiphenyl	Butane	11	96	8.6	33.6
4	2,2′,4,4′,5,5′-Hexachlorobiphenyl	Methanol	11	96	8.1	30.6
5	2,2′,4,5,5′-Pentachlorobiphenyl	Butane	11	96	9.9	39.7
6	2,2′,4,5,5′-Pentachlorobiphenyl	Methanol	11	96	9.6	35.5
7	2,4′,5-Trichlorobiphenyl	Butane	11	96	6.8	27.5
8	2,4′,5-Trichlorobiphenyl	Methanol	11	96	6.8	24.8
9	2-2′-Dichlorobiphenyl	Butane	11	96	9.3	35.2
10	2-2′-Dichlorobiphenyl	Methanol	11	96	9.2	32.9
11	2-Monochlorobiphenyl	Butane	11	96	6.7	25.5
12	2-Monochlorobiphenyl	Methanol	11	96	6.6	24.1
13	3,3′,4,4′-Tetrachlorobiphenyl	Butane	11	96	10.9	44.8
14	3,3′,4,4′-Tetrachlorobiphenyl	Methanol	11	96	10.6	41.8
15	4,4′-Dichlorobiphenyl	Butane	11	96	9.0	31.4
16	4,4′-Dichlorobiphenyl	Methanol	11	96	8.6	27.7
17	4-Monochlorobiphenyl	Butane	11	96	8.5	31.9
18	4-Monochlorobiphenyl	Methanol	11	96	8.4	31.5
19	Anthracene	Butane	12, 13	164	8.7	13.7
20	Anthracene	Ethane	12, 13	172	7.7	12.4
21	Anthracene	Methanol	12, 13	99	8.7	10.0
22	Anthracene	Propane	12, 13	176	9.0	15.2
23	Behenic acid	Ethanol	14	53	19.4	18.4
24	Behenic acid	*n*-Octane	15	52	16.4	26.4
25	Behenic acid	Pentane	15	49	22.6	37.2
26	beta-Carotene	Ethanol	16	31	22.7	7.1
27	beta-Carotene	Vegetable oil	16	37	11.5	8.5
28	Naproxen	1-Propanol	17	33	24.2	12.1
29	Naproxen	2-Propanol	17	40	21.0	16.5
30	Naproxen	Acetone	17	51	17.4	17.7
31	Naproxen	Ethanol	17	42	18.8	16.0
32	Naproxen	Ethyl acetate	17	36	15.4	17.6
33	Naproxen	Methanol	17	44	18.7	21.3
34	Perylene	Methanol	12, 13	42	3.8	4.0
35	Phenanthrene	Methanol	12, 13	108	6.7	10.6
36	Phenanthrene	Methanol	12, 13	92	5.4	15.9
37	Phenanthrene	Propane	12, 13	120	5.8	7.6
38	Phenanthrene	Ethane	12, 13	128	4.6	11.0
39	Pyrene	Butane	12, 13	184	8.5	4.8
40	Pyrene	Ethane	12, 13	184	5.6	12.6
41	Pyrene	Methanol	12, 13	112	6.8	14.6
42	Pyrene	Propane	12, 13	184	8.6	10.7
					10.9±5.4[b]	22.3±11.6[b]

[a] SN is the system number. [b] The mean AARD difference of Eqs. 2 and 4 is statistically significant (paired *t*-test, s.l.<0.0005).

3, 3′, 4, 4′ tetrachlorobiphenyl in SC-CO2+butane, respectively, and the mean (±S.D.) is 22.3±11.6%. Both the mean and standard deviation of Eq. 4 are twice those of Eq. 2. The low error value for Eq. 2 could be considered as acceptable when it is compared with the relative standard deviation, which is around 15%, for repeated experiments under the same experimental conditions.[7)]

Table 2 shows the correlation coefficients (c.c.), standard error (s.e.), *F* and significance levels (s.l.) for Eqs. 2 and 4. The correlation coefficients of Eq. 2 vary between 0.974 to 0.999, showing a good correlation between the independent variable (*i.e.*, $\ln y_2$) and dependent variables (*i.e.* ρ, X, P^2, $P \cdot T$, T/P and $\ln(\rho)$) as also indicated by high *F* values, low standard errors and significance levels of <0.0005. Equation 4 in only two cases produces c.c. values greater than the corresponding c.c. values for Eq. 2, indicating that the proposed model is able to provide better correlations than the previously published Eq. 4.

The RSD values for repeated experiments using the same operating conditions in the same laboratory was reported to be relatively high, *i.e.*, 10—25% (see refs. 7—9). However, the discrepancies between solubility data for a given solute obtained under the same conditions from different laboratories were even higher (*e.g.*, differences by a factor of 10, see ref. 10 and references herein). These differences may be caused by the presence of impurities, differences in pressure or temperature calibrations, or technical variations during solubility measurements. In other words, there is no reliable solution to the use of previously collected data from another laboratory to design proper SCF technology. On the other hand, solubility measurements are costly and also time-consuming and therefore, it is not recommended that solubility be measured under all operational conditions of interest. As an alternative solution, a minimum number of experimental solubility data at pressures, temperatures and entrainer concentrations of interest could be collected. Then the data

Table 2. The Correlation Coefficients (c.c.), Standard Error (s.e.), F and Significance Levels (s.l.) for Eqs. 2 and 4 for Correlative Studies

SN[a)]	Eq. 2				Eq. 4			
	c.c.	s.e.	F	s.l.	c.c.	s.e.	F	s.l.
1	0.991	0.2634	42.564	<0.0005	0.963	0.4965	18.899	<0.0005
2	0.991	0.2581	41.344	<0.0005	0.964	0.4783	17.981	<0.0005
3	0.992	0.2177	31.741	<0.0005	0.951	0.4881	13.634	<0.001
4	0.990	0.2330	30.743	<0.0005	0.957	0.4486	13.046	<0.001
5	0.991	0.2663	44.798	<0.0005	0.965	0.4858	19.112	<0.0005
6	0.991	0.2711	45.355	<0.0005	0.965	0.4943	19.827	<0.0005
7	0.989	0.1808	15.815	<0.0005	0.950	0.3416	6.482	<0.001
8	0.989	0.1777	15.682	<0.0005	0.948	0.3481	6.402	<0.001
9	0.991	0.2342	35.033	<0.0005	0.961	0.4571	15.086	<0.0005
10	0.991	0.2346	35.014	<0.0005	0.959	0.4675	15.126	<0.001
11	0.990	0.1787	17.619	<0.0005	0.957	0.3300	7.108	<0.001
12	0.992	0.1665	18.037	<0.0005	0.955	0.3462	7.502	<0.001
13	0.991	0.3042	55.875	<0.0005	0.964	0.5651	24.852	<0.0005
14	0.991	0.2982	56.433	<0.0005	0.963	0.5776	25.502	<0.0005
15	0.989	0.1757	15.329	<0.0005	0.937	0.3670	5.864	<0.002
16	0.991	0.1632	15.585	<0.0005	0.942	0.3621	6.230	<0.001
17	0.991	0.2301	32.574	<0.0005	0.966	0.3983	13.328	<0.0005
18	0.990	0.2434	33.241	<0.0005	0.961	0.4373	14.025	<0.0005
19	0.991	0.1502	13.995	<0.0005	0.966	0.2926	9.622	<0.0005
20	0.998	0.0806	16.737	<0.0005	0.960	0.3595	12.138	<0.0005
21	0.980	0.2064	8.421	<0.0005	0.953	0.2359	2.777	<0.005
22	0.998	0.0797	15.324	<0.0005	0.964	0.3201	10.836	<0.0005
23	0.986	0.2274	38.368	<0.0005	0.983	0.1931	17.847	<0.0005
24	0.982	0.2300	27.059	<0.0005	0.950	0.3680	17.588	<0.0005
25	0.986	0.2405	37.170	<0.0005	0.917	0.4963	18.280	<0.0005
26	0.974	0.2561	18.523	<0.0005	0.984	0.0877	2.117	<0.0005
27	0.995	0.0939	11.106	<0.0005	0.989	0.0635	1.597	<0.0005
28	0.991	0.2517	23.196	<0.0005	0.993	0.1645	6.121	<0.001
29	0.989	0.2580	24.773	<0.0005	0.981	0.2669	7.425	<0.003
30	0.987	0.1821	13.375	<0.0005	0.959	0.2644	5.645	<0.0005
31	0.991	0.2257	21.413	<0.0005	0.983	0.2480	7.015	<0.002
32	0.985	0.2126	10.110	<0.0005	0.980	0.2595	4.954	<0.008
33	0.989	0.2426	27.354	<0.0005	0.967	0.3464	10.438	<0.001
34	0.997	0.0555	2.247	<0.0005	0.987	0.0858	1.417	<0.0005
35	0.996	0.1254	21.116	<0.0005	0.993	0.1543	13.440	<0.0005
36	0.996	0.1240	15.111	<0.0005	0.981	0.2454	7.702	<0.001
37	0.996	0.1088	16.305	<0.0005	0.990	0.1460	8.627	<0.0005
38	0.999	0.0570	19.719	<0.0005	0.978	0.2617	12.192	<0.0005
39	0.976	0.2737	16.414	<0.0005	0.995	0.0989	7.802	<0.0005
40	0.999	0.0574	19.131	<0.0005	0.971	0.2933	10.071	<0.0005
41	0.997	0.1303	17.666	<0.0005	0.978	0.3128	8.684	<0.003
42	0.985	0.2151	17.964	<0.0005	0.988	0.1600	9.618	<0.0005

a) SN is the system number and the details are the same as in Table 1.

could be used to train the proposed model and after successful training, the solubility data at any pressure, temperature and entrainer concentration could be predicted using the interpolation technique within the range studied.

In order to test the prediction capability of the proposed model, a minimum number of experimental data points was used to train the models and the solubility at other data points was predicted using trained models. The training data points included the experimental solubility data at the highest, the intermediate and the lowest temperatures and pressures of interest for each entrainer concentration. Both models were trained using the same training data points and these points were selected from previously published data sets; when the model is trained, it is capable of predicting solubility at other temperatures, pressures and entrainer concentrations of interest using the interpolation technique. Although the trained model could be used under the same experimental conditions as in the training process, there is no guarantee that the model can be employed for other conditions. However, the main advantage of the proposed model is its capability to reduce the number of experiments required in designing the supercritical process. This is a valuable tool in practice, since many variations were reported for the solubility of the solutes from various laboratories.[10] Tables 3 and 4 listed the numerical values of the model constants, the number of predicted data points in each set and AARD values, respectively, for Eqs. 2 and 4. The mean values (±S.D.) of AARD for Eqs. 2 and 4 are 14.23±6.13 and 20.85±7.24, respectively, and the difference between the means was statistically significant (s.l.$<$0.0005). A summary of the IARD values for Eqs. 2 and 4 sorted in three error subgroups is shown in Fig. 1. The frequency of IARD being $<$10% is the highest and that of IARD$>$30% is the lowest for Eq. 2. The probability of solubility prediction with an error of less than 30% is 0.95, indicating a good agreement between the model predicted solubilities and the experimental results. The corre-

Table 3. The Model Constants of Eq. 2 Calculated Based on a Minimum Number of Training Data Points, Number of Predicted Data Points in Each Set (*N*) and Average Absolute Relative Deviation (AARD)

SN[a]	M_0	M_1	M_2	M_3	M_4	M_5	M_6	N[b]	N[c]	AARD
1	1.8480	6.4350	−14.1690	−2.4880E−05	6.254E−05	0.0169	10.3570	18	78	10.9
2	1.4900	4.6260	−14.1310	−2.6550E−05	6.667E−05	0.0667	10.2570	18	78	11.6
3	3.8110	4.9070	−14.4680	−7.7430E−06	3.259E−05	0.1840	11.0470	18	78	10.0
4	1.2710	3.7720	−13.0920	−2.1380E−05	5.541E−05	0.4040	10.2960	18	78	10.7
5	4.3510	5.6720	−14.3510	−1.2310E−05	3.959E−05	0.2320	11.7180	18	78	12.2
6	3.4080	4.0380	−14.1410	−1.8590E−05	5.145E−05	0.4180	11.8040	18	78	12.9
7	0.5790	4.7740	−9.5970	−1.8000E−05	4.365E−05	0.3000	7.4590	18	78	9.2
8	1.3370	3.8250	−10.0610	−1.4120E−05	3.782E−05	0.1890	7.5220	18	78	8.6
9	4.9340	5.1820	−13.2680	−1.8460E−05	4.916E−05	0.0694	9.9780	18	78	12.0
10	5.7400	4.0850	−13.6750	−1.4240E−05	4.217E−05	−0.0611	10.0200	18	78	11.4
11	1.2460	4.3360	−9.6760	−1.5810E−05	3.902E−05	0.4570	8.2090	18	78	9.9
12	2.1810	3.3070	−10.2210	−1.1220E−05	3.153E−05	0.3690	8.4800	18	78	9.3
13	0.7770	5.8740	−15.8890	−3.4350E−05	8.102E−05	0.1230	11.7720	18	78	13.4
14	0.2990	3.8970	−15.9950	−3.9640E−05	9.076E−05	0.2460	11.9390	18	78	14.2
15	1.3100	5.1770	−11.1920	−1.7880E−05	4.494E−05	−0.1820	6.9250	18	78	10.1
16	1.3450	3.8430	−11.2350	−1.8300E−05	4.579E−05	−0.2160	6.8650	18	78	9.9
17	3.2600	5.5150	−12.2880	−2.7970E−05	6.539E−05	0.5390	10.1310	18	78	12.6
18	3.1150	4.0660	−12.4320	−3.1150E−05	7.089E−05	0.5870	10.2640	18	78	13.2
19	−0.3200	6.2380	−9.6910	−5.6560E−06	1.853E−05	−0.6930	6.0550	18	146	12.7
20	9.5790	2.8380	−15.2550	2.523E−05	−4.4770E−05	−1.8990	8.7990	18	154	17.0
21	6.5000	10.4080	−11.1480	2.749E−05	−5.2430E−05	−2.3080	5.4420	15	84	12.9
22	3.2210	4.1220	−12.3090	−1.5130E−08	6.062E−06	−0.9160	7.9280	18	158	15.1
23	−5.9000	59.3580	−11.9290	0	9.845E−05	0.6250	6.4550	27	26	18.7
24	3.2070	40.0520	−20.7600	0	8.890E−05	−0.1870	9.2740	25	27	15.4
25	17.5510	30.5320	−42.9180	0	1.472E−04	0.3980	19.4470	24	25	23.2
26	−28.2020	99.6510	2.0330	−1.6180E−04	2.730E−04	2.0310	2.3800	22	9	18.3
27	8.3220	56.8630	−15.2530	−5.8440E−06	−1.6030E−05	−3.9080	8.1230	20	17	18.1
28	−7.5770	70.1520	−1.7830		8.567E−06	−1.2010	0.4340	13	20	25.6
29	−25.0990	71.5650	−2.0970	−2.7940E−04	3.756E−04	3.2080	6.4960	15	25	33.7
30	−8.2460	45.5030	−9.3020	−7.9330E−05	1.341E−04	0.9530	7.6670	18	33	22.2
31	−17.0070	66.2120	−5.6200	−1.9410E−04	2.685E−04	2.0860	7.1080	15	27	28.2
32	−4.3430	46.2820	−8.8850	0	3.892E−05	−0.0506	6.1880	13	23	24.4
33	−2.3980	63.2030	−16.2150	9.110E−05	−9.2610E−05	−1.6490	8.5140	17	27	21.0
34	−10.5910	4.9580	−1.8040	−9.5790E−06	1.580E−05	−1.7910	−0.6950	12	30	3.6
35	−7.1050	6.5580	−4.4260	−4.1570E−05	9.109E−05	0.5830	4.1260	18	90	12.4
36	1.0620	9.2230	−8.1150	−7.1120E−06	2.172E−05	−0.5240	5.5950	15	77	6.2
37	6.9210	5.1840	−10.6620	1.571E−05	−2.4850E−05	−1.6610	5.6130	18	102	13.4
38	2.7290	2.4820	−9.4370	−4.8200E−06	1.693E−05	−0.6830	6.1990	18	110	6.5
39	−3.9640	8.6040	−5.7290	−1.1170E−05	3.097E−05	−0.3910	3.9340	18	166	11.8
40	6.1650	2.7470	−12.4970	1.415E−05	−2.0100E−05	−1.1990	8.2350	17	167	10.4
41	8.9830	8.0240	−14.0840	2.632E−05	−4.2660E−05	−1.4390	9.1030	14	98	12.8
42	−5.2270	6.6460	−5.8690	−2.1160E−05	5.116E−05	0.0333	4.6520	19	165	11.7
										14.23±6.13

a) SN is the system number and the details are the same as in Table 1. *b*) *N* is the number of training data points. *c*) *N* is the number of predicted data points.

Table 4. The Model Constants of Eq. 4 Calculated Based on a Minimum Number of Training Data Points, Number of Predicted Data Points in Each Set (*N*) and Average Absolute Relative Deviation (AARD)

SN[a]	*a*	*b*	*c*	*d*	*N*[b]	AARD
1	10.7720	−5817.1690	0	4.2570	78	29.5
2	11.5960	−6127.1850	0	4.1550	78	28.3
3	2.9800	−3217.2610	0	3.5820	78	28.2
4	5.2500	−3976.6640	0	3.5250	78	26.1
5	5.7680	−3799.2430	0	4.2410	78	29.0
6	6.3050	−3986.8120	0	4.3230	78	29.1
7	3.4910	−2851.3040	0	2.4860	78	20.7
8	4.3870	−3157.2210	0	2.4760	78	20.2
9	10.0930	−4586.4010	0	3.7970	78	27.6
10	10.6970	−4797.9360	0	3.8050	78	27.5
11	2.3690	−2356.5050	0	2.5880	78	20.2
12	2.0560	−2262.4680	0	2.6530	78	21.1
13	11.8850	−6711.4810	0	4.8820	78	33.9
14	12.9340	−7072.3560	0	4.9470	78	34.1
15	8.1960	−4694.3370	0	2.3580	78	23.9
16	9.2540	−5047.7720	0	2.4250	78	23.8
17	7.8830	−3757.0910	0	3.5580	78	25.6
18	8.8330	−4073.1690	0	3.6540	78	26.7
19	7.3500	−4574.7090	0.5530	2.7620	92	18.3
20	6.5970	−4583.5970	0.3090	3.1640	100	22.7
21	6.4320	−4023.2380	0.7950	2.0080	30	10.5
22	6.3500	−4466.4420	0.3130	3.1110	104	24.5
23	20.1530	−7158.6190	1.4590	2.0310	20	21.2
24	32.4910	−11692.0000	1.0470	2.2140	22	21.9
25	38.0930	−13391.7800	0.9820	4.0640	19	27.0
26	8.3770	−5644.4230	0.4080	2.8350	5	8.4
27	−1.4580	−2063.3450	0.9200	−2.0810	11	12.5
28	0.5030	0	1.9610	3.1980	9	14.1
29	17.9630	−5691.5540	2.0270	3.5960	14	21.0
30	11.8860	−4732.0850	1.3980	3.6350	22	23.4
31	16.4050	−5372.2730	1.8420	3.9180	16	21.1
32	−1.6670	0	1.5220	3.9470	12	21.4
33	−0.9040	−3634.0530	1.7740	3.8290	16	18.7
34	7.2840	−6241.6840	0.2340	2.8310	23	4.3
35	12.5320	−5336.5570	0.3900	2.9760	40	13.0
36	10.0830	−4401.6830	0.4460	3.1960	27	14.5
37	11.3420	−5086.1680	0.3050	2.7460	52	9.9
38	8.9900	−4546.6120	0.0784	3.1130	60	16.2
39	8.2490	−4540.8240	0.4870	2.4660	108	6.6
40	6.4770	−4140.5770	0.3310	3.1910	109	16.9
41	2.9220	−2613.7890	0.5550	3.4480	40	21.1
42	7.8220	−4484.3630	0.4120	2.7450	107	10.9
						20.85±7.24

a) SN is the system number and the details are the same as in Table 1. *b*) *N* is the number of predicted data points.

sponding probability for Eq. 4 is 0.57, and in 23% of the cases, the solubility could not be predicted.

Conclusions

The proposed model shows a simple and readily available least squares method to calculate the solubility in SC-CO2+entrainer systems with reasonable accuracy. It is more accurate than a similar model from the literature and is also able to predict solubility data under operational conditions with acceptable prediction error. It is suggested that the model can be employed in the pharmaceutical/chemical industry to speed up the process of SCF technology development.

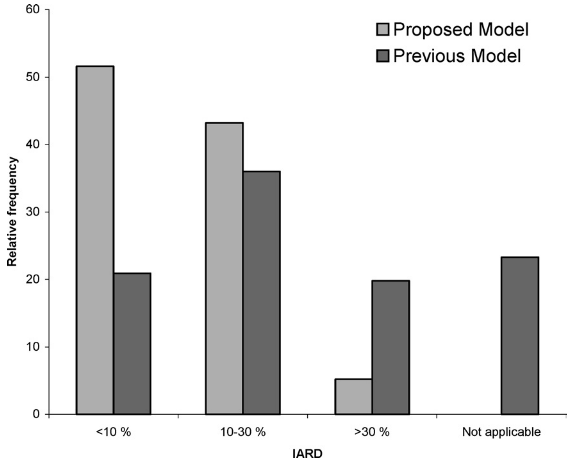

Fig. 1. The Individual Absolute Relative Deviation (IARD) Values for Predictive Eqs. 2 and 4 Trained Using a Minimum Number of Data Points

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