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A simple relationship between dielectric constant of mixed solvents with solvent composition and temperature

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Abstract

A simple computational method for calculating dielectric constants of solvent mixtures based on Redlich-Kister extension was proposed. The model was applied to the experimental dielectric constant of binary and ternary solvent mixtures at fixed and/or various temperatures and showed accurate results. Overall average percentage deviation (OAPD) between calculated and experimental dielectric constants was calculated as an accuracy criterion. The OAPDs for correlative and predictive analyses of dielectric constants in binary solvents at a fixed temperature were 0.56 and 1.42%, respectively. The corresponding values for binary solvents at different temperatures were 1.29 and 1.92%, respectively. The OAPDs for correlative and predictive analyses of dielectric constants of a nonaqueous ternary solvent mixture at various temperatures were 1.61 and 3.05%. The accuracy of the proposed models has also been compared with those of previously published models and results showed that the proposed models were superior and capable of providing more accurate results.

Keywords: Dielectric constants; Mixed solvents; Mathematical model; Prediction

1. Introduction

The dielectric constant is a physical property, which is influenced by interatomic and intermolecular attractions. It is a measure of solvent's efficiency for separating the electrolytes into the ions. Solvents with high dielectric constants encourage complete dissociation of the electrolytes whereas in solvents of low dielectric constant, considerable ion pairing occur (Day and Underwood, 1991). The behavior of electrolytes in solutions could be strongly affected by the dielectric constant of the medium and this property could be used as a predictive tool in practice. Dielectric constant can be determined by oscillometry, in which the frequency of a signal is kept constant by electrically changing the capacitance between the two parallel plates. The liquid, of which the dielectric constant is being measured, is placed in a glass container between the two plates during the experiment (Martin et al., 1993).

Mixed solvents have been employed in different fields including pharmaceutical and analytical sciences. The knowledge of dielectric constant of mixed solvents is required to predict the drug's solubility and chemical stability in a water-cosolvent mixture and the analytes behavior in analytical methods like capillary electrophoresis and ion chromatography.

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Drug solubility in mixed solvents (Paruta and Irani, 1966; Prakongpan and Nagai, 1984; Dumanovic et al., 1992), acid dissociation constants of drugs (Newton et al., 1982), chemical stability of pharmaceuticals (Singh and Gupta, 1988; Sanyude et al., 1991) and the concentration of a drug in plasma from mixed solvent vehicles (Pagay et al., 1974) could be explained considering dielectric constant of the solvent system. The effect of dielectric constants on acid conversion of sucrose (Amis and Holmes, 1949), sedimentation rate of concentrated suspensions (Alexander et al., 1992), oxidation–reduction function of a cytochrome c protein (Sivalolundu and Mabrouk, 2000) and photoisomerisation reaction (Ikeda et al., 2002) have also been reported. In addition, electroosmotic flow and electrophoretic mobility of analytes in capillary electrophoresis were explained using dielectric constants as an independent variable (Schwer and Kenndler, 1991; Salimi-Moosavi and Cassidy, 1996). A comprehensive review on the applications of dielectric analysis of pharmaceutical systems has been published by Craig (1995).

The common method to calculate the dielectric constant of mixed solvents is the weighted average of the mixture components by assuming a simple additive function of the concentration of the solvents (Prakongpan and Nagai, 1984; Chien, 1984; Dumanovic et al., 1992). It is obvious that this could be the case for ideal solvent mixtures; however, most pharmaceutical cosolvents exhibit a high degree of intermolecular interactions and their behavior are non-ideal (Amirjahed and Blake, 1975). Therefore, the dielectric constants of such solvent systems would not usually be expected to obey from the additive rule. There are also demands to calculate dielectric constants in mixed solvent systems at various temperatures. The aim of this work is to provide an accurate model to calculate dielectric constant of mixed solvents at fixed and various temperatures and test its applicability on real experimental data. Accuracy of the proposed models is also compared with those of previously published similar models.

2. Computational methods

A solution model (i.e. the combined nearly ideal binary solvent/Redlich-Kister equation, CNIBS/R-K) presented by Acree (1992) has been used to correlate different physico-chemical properties in mixed solvent systems; including the solubility of polycyclic aromatic hydrocarbons in non-aqueous binary mixtures (Acree, 1995), solubility of drugs in water-cosolvent mixtures (Jouyban-Gh. et al., 1999), electrophoretic mobility of analytes in mixed solvent electrolyte systems (Jouyban-Gh. et al., 2000; Jouyban et al., 2003), the acid dissociation constants (Jouyban et al., 2002a) and the instability rate constants (Jouyban et al., 2002b) in binary solvent systems. The model constants of the CNIBS/R-K represent the solute–solvent and solvent–solvent interactions in the mixtures (Acree, 1992). Therefore, it should be able to calculate any other physico-chemical property in mixed solvents which is a function of solute–solvent and/or solvent–solvent interactions. An adopted form of the equation representing the dielectric constants of binary solvent mixtures at a constant temperature is:

$$\ln \varepsilon_{\mathrm{m}} = \phi_1 \ln \varepsilon_1 + \phi_2 \ln \varepsilon_2 + \phi_1\phi_2 \sum_{i=0}^{2} K_i (\phi_1 - \phi_2)^i \tag{1}$$

where ε_{m}, ε_1 and ε_2 are the dielectric constants of the mixture and solvents 1 and 2, respectively, ϕ_1 and ϕ_2 are the volume (weight or mole) fractions of solvents 1 and 2 in the mixture and K_i represent the model constants calculated using a least square method.

A previous method for calculating dielectric constant of a binary mixture (Prakongpan and Nagai, 1984; Chien, 1984; Dumanovic et al., 1992) is as follows:

$$\varepsilon_{\mathrm{m}} = \phi_1\varepsilon_1 + \phi_2\varepsilon_2 \tag{2}$$

Since $\phi_2 = 1 - \phi_1$, Eq. (2) could be rearranged as:

$$\varepsilon_{\mathrm{m}} = \varepsilon_2 + (\varepsilon_1 - \varepsilon_2)\phi_1 = M_0 + M_1\phi_1 \tag{3}$$

where M_0 and M_1 are the intercept and slope of the equation. Amirjahed and Blake (1974) extended the linear Eq. (3) into a polynomial function of ϕ_1 and represented as:

$$\varepsilon_{\mathrm{m}} = M_0 + M_1\phi_1 + M_2\phi_1^2 + M_3\phi_1^3 + M_4\phi_1^4 \tag{4}$$

where $M_0 - M_4$ are the model constants.

King and Queen (1979) have used a non-linear relationship to calculate the dielectric constants of binary solvent mixtures. Their model is as follows:

$$\ln \varepsilon_{\mathrm{m}} = \frac{\alpha_0 + \alpha_1\phi_1}{\beta_0 + \beta_1\phi_1} \qquad (5)$$

in which α_0, α_1, β_0 and β_1 are the model constants.

To correlate the dielectric constants of binary solvents at various temperatures (T), an extended form of Eq. (1) could be used for calculating the dielectric constant with respect to ϕ_1 and T, and is proposed in this work as:

$$\ln \varepsilon_{\mathrm{m},T} = \phi_1 \ln \varepsilon_{1,T} + \phi_2 \ln \varepsilon_{2,T} + \phi_1\phi_2 \sum_{j=0}^{2} \left[\frac{A_j(\phi_1 - \phi_2)}{T}\right] \qquad (6)$$

where $\varepsilon_{\mathrm{m},T}$, $\varepsilon_{1,T}$ and $\varepsilon_{2,T}$ are the dielectric constants of the mixture and solvents 1 and 2 at temperature T, respectively, and A_j represent the model constants. The proposed model could also be extended to ternary solvents at different temperatures as:

$$\begin{aligned}\ln \varepsilon_{\mathrm{m},T} &= \phi_1 \ln \varepsilon_{1,T} + \phi_2 \ln \varepsilon_{2,T} + \phi_3 \ln \varepsilon_{3,T}\\ &\quad + \phi_1\phi_2 \sum_{j=0}^{2} \left[\frac{A_j(\phi_1 - \phi_2)^j}{T}\right]\\ &\quad + \phi_1\phi_3 \sum_{j=0}^{2} \left[\frac{B_j(\phi_1 - \phi_3)^j}{T}\right]\\ &\quad + \phi_2\phi_3 \sum_{j=0}^{2} \left[\frac{C_j(\phi_2 - \phi_3)^j}{T}\right]\\ &\quad + \phi_1\phi_2\phi_3 \sum_{j=0}^{2} \left[\frac{D_j(\phi_1 - \phi_2 - \phi_3)^j}{T}\right] \qquad (7)\end{aligned}$$

where $\varepsilon_{3,T}$ is the dielectric constant of the solvent 3 at temperature T, ϕ_3 denotes the volume (weight or mole) fraction of the third solvent and A_j, B_j, C_j and D_j are the model constants.

The calculated dielectric constants were compared with experimental (observed) values and the mean of the absolute percentage deviation (APD) was used as an accuracy criterion. The APD was calculated using:

$$\mathrm{APD} = \frac{100}{N} \sum \frac{|\mathrm{Calculated} - \mathrm{Observed}|}{\mathrm{Observed}} \qquad (8)$$

where N is the number of data points in each set.

3. Computational results and discussion

Details of experimental dielectric constants for various aqueous and non-aqueous binary solvents were shown in Table 1. The experimental data fitted to Eqs. (1)–(2) and (4)–(5), and the back-calculated dielectric constants have been used to calculate APDs, which were also shown in Table 1. The minimum APDs for Eqs. (1)–(2) and (4)–(5) were 0.05, 0.80, 0.13 and 0.14%, respectively, and the maximum APDs were 3.14, 20.91, 3.17 and 44.95%. The overall APD (OAPD) values were 0.56 (±0.70), 6.39 (±5.49), 0.82 (±0.83) and 5.18 (±11.71), respectively for Eq. (1) with Eqs. (2) and (4)–(5). The OAPD differences between Eqs. (1)–(2) and (5) were statistically significant (paired t-test, $P < 0.004$). This type of calculations could be employed in collecting experimental data for detecting possible outliers for re-determination. When no experimental data for a given binary solvent is available, a researcher may wish to collect a minimum number of experiments and then predict at other solvent compositions. To show the applicability of the models under consideration for such predictions after collecting the minimum number of experimental data, the dielectric constants at $\phi_1 = 0$, 0.3, 0.5, 0.7 and 1 from each binary solvent system at a constant temperature were used to train the models, then the dielectric constants at other solvent compositions were predicted and APDs were computed. Fig. 1 shows OAPD and standard deviations for Eqs. (1)–(2) and (4)–(5) where the differences between OAPD of Eqs. (1), (2) and (5) were compared using paired t-test and the results show that both equations produced significantly high OAPD ($P < 0.006$). However, no significant difference existed between OAPDs of Eqs. (1) and (4) ($P > 0.53$).

To test the applicability of the proposed equation (i.e. Eq. (6)) for calculating dielectric constants in binary solvent mixtures at various temperatures, all data points from each binary solvent at different temperatures were fitted to Eq. (6) and the back-calculated dielectric constants were used to compute APDs, which were presented in Table 2. The correlation coefficients, F values and the model constants for this analysis were listed in Table 3. The higher the correlation coefficients and also F values, mean the more significant correlation exists between dependent variable (i.e. dielectric constant of solvent

Table 1
Details of average percentage deviations (APDs) for different numerical analyses of dielectric constants of binary solvents at a constant temperature

Number	Solvent system	Reference	Temperature	N[a]	Eq. (1)	Eq. (2)	Eq. (4)	Eq. (5)
1	Water + methanol	Akerlof (1932)	293.15	11	0.15	3.00	0.20	0.22
2		Akerlof (1932)	303.15	11	0.19	2.45	0.27	0.36
3		Akerlof (1932)	313.15	11	0.19	1.95	0.22	0.43
4		Akerlof (1932)	323.15	11	0.20	1.78	0.27	0.48
5		Akerlof (1932)	333.15	11	0.29	1.76	0.35	0.61
6	Water + ethanol	Akerlof (1932)	293.15	11	0.13	1.41	0.13	0.53
7		Akerlof (1932)	313.15	11	0.27	1.57	0.26	0.83
8		Akerlof (1932)	323.15	11	0.24	1.43	0.29	0.83
9		Akerlof (1932)	333.15	11	0.32	1.56	0.35	0.97
10		Akerlof (1932)	353.15	11	0.48[b]	1.73	0.55	1.14
11	Water + 1-propanol	Akerlof (1932)	293.15	11	0.12	5.57	0.27	2.41
12		Akerlof (1932)	313.15	11	0.10	5.76	0.33	2.29
13		Akerlof (1932)	323.15	11	0.12	6.30	0.42	2.38
14		Akerlof (1932)	333.15	11	0.11	6.43	0.38	2.37
15		Akerlof (1932)	353.15	11	0.27	7.51	0.48	2.51
16	Water + 2-propanol	Akerlof (1932)	293.15	11	0.52	5.65	0.75	43.02
17		Akerlof (1932)	313.15	11	0.52	5.90	0.72	44.23
18		Akerlof (1932)	323.15	11	0.53	6.07	0.75	44.19
19		Akerlof (1932)	333.15	11	0.51	6.31	0.70	44.95
20		Akerlof (1932)	353.15	11	0.46	6.39	0.57	2.93
21	Water + *tert*-butanol	Akerlof (1932)	293.15	11	0.26[b]	9.84	0.67	2.43
22		Akerlof (1932)	313.15	11	0.30	12.25	0.80	2.75
23		Akerlof (1932)	323.15	11	0.31	13.95	1.13	2.73
24		Akerlof (1932)	333.15	11	0.48	14.76	1.57	2.36
25		Akerlof (1932)	353.15	11	0.55	18.46	1.24	2.86
26	Water + ethylene glycol	Akerlof (1932)	293.15	11	0.14	4.07	0.36	0.34
27		Akerlof (1932)	313.15	11	0.08	3.33	0.25	0.20
28		Akerlof (1932)	333.15	11	0.05	2.64	0.17	0.14
29		Akerlof (1932)	353.15	11	0.09	1.92	0.14	0.17
30		Akerlof (1932)	373.15	6	0.11	1.33	0.13	0.14
31	Water + glycerol	Akerlof (1932)	293.15	11	0.18	2.22	0.35	0.32
32		Akerlof (1932)	313.15	11	0.20	1.65	0.38	0.36
33		Akerlof (1932)	333.15	11	0.08	1.20	0.25	0.24
34		Akerlof (1932)	353.15	11	0.06	1.14	0.23	0.26
35		Akerlof (1932)	373.15	6	0.06	0.80	0.06	0.23
36	Water + acetone	Akerlof (1932)	293.15	11	0.08	3.48	0.24	0.52
37		Akerlof (1932)	298.15	11	0.14	3.36	0.24	0.49
38		Akerlof (1932)	303.15	11	0.10	3.12	0.24	0.57
39		Akerlof (1932)	313.15	11	0.09	3.22	0.22	0.54
40		Akerlof (1932)	323.15	11	0.10	3.13	0.25	0.58
41	Water + dioxane	Critchfield et al. (1953)	293.15	12	1.27	19.74	0.86	0.19
42		Critchfield et al. (1953)	298.15	12	1.17	20.29	0.72	0.11
43		Critchfield et al. (1953)	303.15	12	1.07	20.59	0.61	0.12
44		Critchfield et al. (1953)	313.15	12	1.00	20.91	0.53	0.13
45	2-Ethoxyethanol + dimethylsulphoxide	Khirade et al. (1999)	293	11	2.84	8.06	2.98	28.06
46		Khirade et al. (1999)	303	11	2.61	7.94	2.64	3.50
47		Khirade et al. (1999)	313	11	3.14	11.17	3.17	3.97
48		Khirade et al. (1999)	323	11	2.02	12.72	2.91	4.00

Table 1 (*Continued*)

Number	Solvent system	Reference	Temperature	N^a	Eq. (1)	Eq. (2)	Eq. (4)	Eq. (5)
49	Ethanol	Khirade et al. (1999)	293	11	0.71	5.38	1.88	1.79
50	+ dimethylsulphoxide	Khirade et al. (1999)	303	11	1.14	4.67	1.99	17.78
51		Khirade et al. (1999)	313	11	0.68	5.50	1.66	1.82
52		Khirade et al. (1999)	323	11	0.35	6.98	2.24	2.37
53	1-Propanol	Khirade et al. (1999)	293	11	1.74	6.60	2.76	3.30
54	+ dimethylsulphoxide	Khirade et al. (1999)	303	11	0.67	4.21	0.74	2.11
55		Khirade et al. (1999)	313	11	1.00	6.68	1.48	2.34
56		Khirade et al. (1999)	323	11	0.71	10.12	1.54	2.48
			OAPD[c] (S.D.)		0.56 (0.70)	6.39 (5.49)	0.82 (0.83)	5.18 (11.71)

[a] N is the number of data points in each set.

[b] Dielectric constant of pure ethanol extrapolated using $\ln\varepsilon = \text{intercept} + \text{slope} \times T$ (Akerlof, 1932).

[c] Difference between OAPDs between Eq. (1) with Eqs. (2) and (4)–(5) are statistically significant (paired *t*-test, $P < 0.004$).

mixture) and the independent variables (i.e. solvent composition and temperature). The significance of the listed model constants were checked using *t*-test and were significant at <0.05 level. This analysis was called correlative method and the minimum and maximum APDs were observed for water + glycerol and 2-ethoxyethanol + dimethylsuphoxide mixtures, respectively, and the OAPD was 1.29 (±1.25)%. Similar calculations have been carried out by Harvey and Prausnitz (1987), where the reported APDs for set numbers 2, 3, 4, 6 and 8 in Table 2 were 1.3, 3.9, 4.4, 1.0 and 1.2, respectively. The OAPDs of these sets for Eq. (6) and Harvey–Prausnitz equation were 0.70 (±0.45) and 2.36 (±1.64), respectively, and the difference between OAPDs was statistically significant (paired *t*-test, $P < 0.05$). To evaluate the prediction capability of Eq. (6), the model was trained using dielectric constants at $\phi_1 = 0$, 0.3, 0.5, 0.7 and 1 at the highest and the lowest temperatures (total training points is 10) and the trained models were used to predict the dielectric constants at other solvent compositions and temperatures using dielectric constants of pure solvents at each temperature by interpolation. This analysis was called predictive method and could be employed in practice when the required dielectric constants at interested solvent compositions and/or

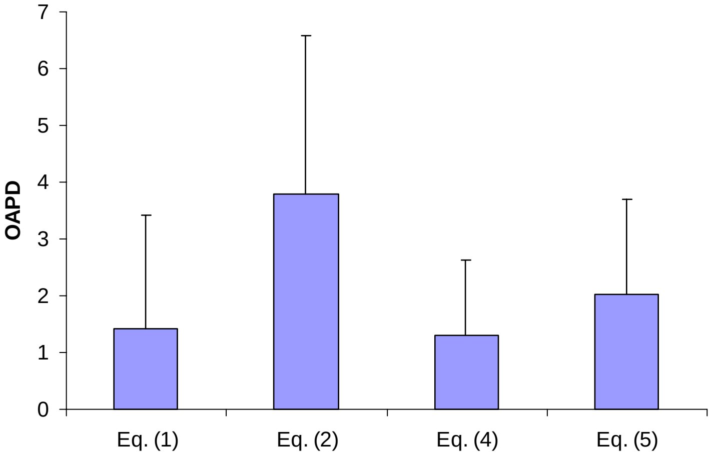

Fig. 1. Overall average percentage deviation (OAPD) for predictive method using five training data points from each set at a constant temperature, Eq. (1) produced more accurate predictions in comparison with Eqs. (2) and (5) (paired *t*-test, $P < 0.006$) and there was no significant difference between Eqs. (1) and (4) (paired *t*-test, $P > 0.55$).

Table 2
Average percentage deviation (APD) and overall APD (OAPD) for correlative and predictive analyses of dielectric constants of binary solvents at different temperatures using Eq. (6)

Number	Solvent system	Correlative		Predictive		Reference
		N[a]	Percentage deviation	N[a]	Percentage deviation	
1	Water + methanol	55	0.33	39	0.52	Akerlof (1932)
2	Water + ethanol	55	0.62	39	1.35	Akerlof (1932)
3	Water + 1-propanol	55	0.66	39	0.89	Akerlof (1932)
4	Water + 2-propanol	55	1.46	39	1.80	Akerlof (1932)
5	Water + *tert*-butanol	55	1.46	39	3.55	Akerlof (1932)
6	Water + ethylene glycol	50	0.27	34	0.36	Akerlof (1932)
7	Water + glycerol	50	0.19	34	0.37	Akerlof (1932)
8	Water + acetone	55	0.49	39	0.58	Akerlof (1932)
9	Water + dioxane	48	1.13	34	1.66	Critchfield et al. (1953)
10	2-Ethoxyethanol + dimethylsulphoxide	44	4.26	30	5.84	Khirade et al. (1999)
11	Ethanol + dimethylsulphoxide	44	1.45	30	1.68	Khirade et al. (1999)
12	1-Propanol + dimethylsulphoxide	44	3.21	30	4.50	Khirade et al. (1999)
		OAPD (S.D.)	1.29 (1.25)		1.92 (1.78)	

[a] N is the number of correlated and predicted data points in each set.

temperatures are not available. When no experimental data for a solvent system of interest is available, a researcher could use this method for determining a minimum number of dielectric constants and then predicting the other data points using simple calculations. As shown in Table 2, the minimum and maximum APDs were 0.36 and 5.84%, respectively, and the OAPD was 1.92 (±1.78)%. A relatively high correlative and predictive APDs were observed for set numbers 10 and 12 in Table 2 and a possible reason for this could be one or two outliers in the experimental data points.

Experimental dielectric constants of ternary solvent mixtures of water + ethanol + glycerine and water + ethanol + propylene glycol at 25 °C (Sorby et al., 1963) have been fitted to the extended form of the proposed equation (i.e. Eq. (7)), then the trained equations were used to back-calculate dielectric constants and APDs obtained were 6.90 and 7.46%, respectively. Experimental dielectric

Table 3
The correlation coefficient (R), F values and the model constants (±S.E.) for Eq. (6)

Number[a]	R	F value[b]	A_0	A_1	A_2
1	0.999	8836	181.0 (1.5)	33.3 (3.0)	−16.9 (6.8)
2	0.998	3696	246.8 (3.0)	22.1 (6.1)	−51.5 (14.0)
3	0.996	2254	221.1 (3.3)	−115.6 (6.6)	−137.5 (15.2)
4	0.990	845	305.7 (7.2)	−95.8 (14.5)	−244.9 (33.2)
5	0.996	7509	488.8 (5.6)	–[c]	–[c]
6	0.999	9385	153.6 (1.1)	57.3 (3.0)	–[c]
7	0.999	7301	112.7 (1.0)	29.4 (2.0)	−29.2 (4.5)
8	0.999	18908	360.1 (2.1)	118.8 (4.1)	22.7 (9.5)
9	0.999	40230	11863.2 (4.9)	760.2 (9.8)	472.7 (21.7)
10	0.963	550	387.9 (16.5)	–[c]	–[c]
11	0.953	423	178.9 (8.7)	–[c]	–[c]
12	0.966	194	249.7 (15.1)	100.8 (30.4)	157.9 (70.0)

[a] The set numbers is the same as in Table 2.

[b] The significance level of F values were <0.0005.

[c] The significance level of these model constants were >0.05 and taken out from the calculations.

constants of 1,2-dichloroethane + 2-methoxyethanol + 1,2-dimethoxyethane at temperatures of −10 to 80 °C taken from a reference (Corradini et al., 1996) have been fitted to Eq. (7) and the resulted equation was:

$$\begin{aligned}\ln \varepsilon_{m,T} = {} & \phi_1 \ln \varepsilon_{1,T} + \phi_2 \ln \varepsilon_{2,T} + \phi_3 \ln \varepsilon_{3,T} \\ & - \frac{189.3\phi_1\phi_2}{T} + \frac{1728.1\phi_1\phi_2(\phi_1-\phi_2)}{T} \\ & - \frac{1519.8\phi_1\phi_2(\phi_1-\phi_2)^2}{T} \\ & + \frac{2074.5\phi_1\phi_3(\phi_1-\phi_3)}{T} \\ & - \frac{2571.8\phi_1\phi_3(\phi_1-\phi_3)^2}{T} - \frac{1075.6\phi_2\phi_3}{T} \\ & - \frac{311.4\phi_2\phi_3(\phi_2-\phi_3)}{T} \\ & + \frac{5552.7\phi_2\phi_3(\phi_2-\phi_3)^2}{T} + \frac{799.3\phi_1\phi_2\phi_3}{T} \\ & - \frac{8220.2\phi_1\phi_2\phi_3(\phi_1-\phi_2-\phi_3)}{T} \\ & + \frac{6447.0\phi_1\phi_2\phi_3(\phi_1-\phi_2-\phi_3)^2}{T} \qquad (9)\end{aligned}$$

Eq. (9) produced accurate results for correlative analysis where APD was 1.61% ($N = 285$). To test the prediction capability of Eq. (7) using a minimum number of experimental data points, 20 experimental data points were employed to train the model and then the predicted dielectric constants were used to calculate APD which was 3.05% ($N = 265$).

As a general conclusion, the proposed model and its extended forms produced more accurate dielectric constants for mixed solvents at a constant and/or various temperatures in comparison with previously published models. The proposed models could be employed for calculation of dielectric constants and by providing accurate dielectric constants the phenomena affected by dielectric constants (e.g. solubility and chemical stability) could be explained more accurately.

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