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Solubilization behavior of diclofenac sodium in polyethylene glycol 400/water mixtures: A solubility and thermodynamic study

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Abstract

In this work, the solubility of diclofenac sodium was measured in PEG 400 + water solvent mixtures at temperatures from 298.2 K to 313.2 K using the shake-flask method and UV-Vis spectrophotometry. The experimental data were correlated with several mathematical models (van't Hoff, Jouyban-Acree, Jouyban-Acree-van't Hoff, mixture response surface, and modified Wilson models), with model accuracy assessed by mean relative deviation percentage. Additionally, the solubility data were used to calculate thermodynamic parameters (ΔG° , ΔH° , ΔS° , and $T\Delta S^\circ$) via the van't Hoff and Gibbs equations, providing insights into the energetic aspects of the dissolution process.

Keywords: Diclofenac sodium, Cosolvency, Mathematical correlations, Thermodynamic parameters.

Introduction

Diclofenac sodium, a trivial name of sodium 2-[2-(2,6-dichloroanilino)phenyl]acetate, is a nonsteroidal anti-inflammatory drug (NSAID) that belongs to the phenylacetic acid derivative class. It is widely used for its analgesic, anti-inflammatory, and antipyretic properties [1]. The mechanism of action of diclofenac sodium involves inhibiting cyclooxygenase (COX) enzymes, which subsequently reduces the synthesis of prostaglandins-key mediators of inflammation, pain, and fever. Diclofenac sodium is a drug with high permeability but low aqueous solubility, classified as class II in the biopharmaceutics classification system [2]. These properties affect its bioavailability and absorption levels, particularly after oral administration. Enhancing drug solubility not only improves bioavailability but is also useful for purification, crystallization, separation, and analysis [3]. Various methods have been developed to address the issue of poor solubility including cosolvency, solid dispersion, particle size reduction, crystal engineering, salt formation, utilization of surfactants, complexation, pH adjustment, nanosuspension, chemical modification, and hydrotrophy [4]. Among these methods, cosolvency is a commonly used technique for solubility enhancement and is defined as the combination of two or more miscible solvents in varying proportions and its mechanism is characterized by alterations in molecular conformation as well as intermolecular and intermolecular interactions [5].

Up to now, solubility of diclofenac sodium has been reported in various mono-solvents including acetone, ethyl acetate, dimethyl sulfoxide (DMSO) [6], and aqueous binary mixture of Transcutol-HP [7] and ethanol [8] at different temperatures and also in aqueous binary mixtures of methanol, ethanol, 2-propanol [9] and propylene glycol (PG), polyethylene glycol 400, and glycerin [10]. According to our knowledge, up to now, polyethylene glycol 400 (PEG 400) has not been reported as a cosolvent for solubility enhancement of diclofenac sodium.

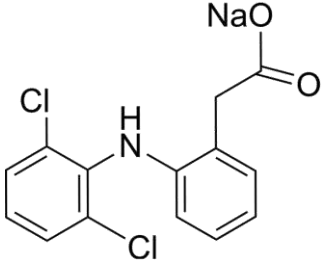
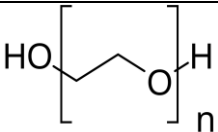
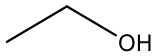
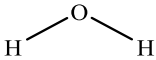
Therefore, herein, the solubility of diclofenac sodium was investigated in binary mixtures of PEG 400 and water at temperatures ranging from 298.2 to 313.2 K, using the shake -flask method following by absorbance determination using a UV-Vis spectrophotometer. The solubility data generated from this research provides valuable insights into the solubilizing potential of PEG 400 + water mixtures, which can inform the optimization of processing and formulation of diclofenac sodium and similar drugs. Additionally, this study included using mathematical models to correlate/predict the measured solubility data. Furthermore, the apparent thermodynamic dissolution properties were also computed using the van't Hoff and Gibbs equations.

Materials and method

Materials

Diclofenac sodium, PEG 400, ethanol, and distilled water were the materials utilized for preparing and diluting the solvent mixtures. [Table 1](#) provided a brief summary of their chemical structures, purities, and sources.

Table 1. Information on the chemical structure, purity and source of the materials used.^a

Material	Molecular formula	Molar mass (g mol ⁻¹)	Molecular structure	Mass fraction purity ^a	Assessment method	Source
Diclofenac sodium	C ₁₄ H ₁₀ Cl ₂ NNaO ₂	318.129		99.7	HPLC-UV ^b	Zahravi pharmaceutical company, Iran
PEG 400	C _{2n} H _{4n+2} O _{n+1}	400		0.992	GC ^c	Merck, Germany
Ethanol	C ₂ H ₅ OH	46.07		>0.935	GC	Jahan Alcohol Teb, Iran
Water	H ₂ O	18.02		Distilled deionized water	Conductivity Measurement	-

^a The purity of the employed chemicals was provided by the suppliers.

^b High-Performance Liquid Chromatography- ultra violet detection

^c Gas Chromatography

Solubility determination

Diclofenac sodium solubility in the binary mixtures of PEG 400 and water was determined under atmospheric pressure at different temperatures (298.2 -313.2 K) using a shake-flask method followed by spectrophotometry detection [11]. For this purpose, excess diclofenac sodium was added to 7 mL microtubes containing different mass ratios of mono- and mixed solvents, totaling 5.0 grams. The tubes were then shaken in an incubator with temperature uncertainty of ± 0.1 K (Nabziran Industrial Group, Tabriz, Iran) for 72 h based on its dissolution rate time. After equilibration, the mixtures were centrifuged to separate the upper solutions and diluted with ethanol/water 30:70 % V/V as required. The UV-Vis absorbance of diluted solutions was measured at 280 nm using a UV-Vis spectrophotometer (UV-1800 model, Shimadzu, Kyoto, Japan). The concentrations of the solutions were interpolated from a previously plotted calibration curve. The experiment was replicated three times and their mean value was reported.

Mathematical correlations

Some mathematical models including the van't Hoff, Jouyban-Acree, Jouyban-Acree-van't Hoff, mixture response surface (MRS), and modified Wilson models were fitted by the generated solubility data. The van't Hoff equation (Eq. 1) relates the dissolution process of a solute in a specific solvent mixture to the temperature [12]. The Jouyban-Acree (Eq. 2) and Jouyban-Acree-van't Hoff (Eq. 3) models [13] offer accurate estimates of solubility by integrating both solvent composition and temperature functions, simultaneously. The MRS model (Eq. 4, [14]) is utilized to relate the drug's solubility in different solvent mixtures at the isothermal condition. Additionally, the modified Wilson model (Eq. 5, [15]), as a non-linear equation, is also employed to correlate solubility data by considering the mixture composition at the isothermal condition.

$$\ln C = A + \frac{B}{T} \quad (1)$$

$$\ln C_m = \beta_1 w'_1 + \beta_2 w'_2 + \beta_3 \left(\frac{1}{w'_1} \right) + \beta_4 \left(\frac{1}{w'_2} \right) + \beta_5 w'_1 \cdot w'_2 \quad (2)$$

$$\ln C_{m,T} = w_1 \ln C_{1,T} + w_2 \ln C_{2,T} + \frac{w_1 \cdot w_2}{T} \sum_{i=0}^2 J_i \cdot (w_1 - w_2)^i \quad (3)$$

$$\ln C_{m,T} = w_1 \left(A_1 + \frac{B_1}{T} \right) + w_2 \left(A_2 + \frac{B_2}{T} \right) + \frac{w_1 \cdot w_2}{T} \sum_{i=0}^2 J_i \cdot (w_1 - w_2)^i \quad (4)$$

$$-\ln C_m = 1 - \frac{w_1 [1 + \ln C_1]}{w_1 + w_2 \lambda_{12}} - \frac{w_2 [1 + \ln C_2]}{w_1 \lambda_{21} + w_2} \quad (5)$$

The solubilities of the drug in mixed solvents and in mono-solvents 1 and 2 are denoted by C_m , C_1 and C_2 , respectively, with the mass fractions of solvent 1 and solvent 2 represented by w_1 and w_2 . $A, B, J_i, A_1, B_1, A_2, B_2, \beta_1 - \beta_5$ and λ_{ij} are the model parameters. Furthermore, the w'_1 and w'_2 are obtained as follows: $w'_1 = 0.96w_1 + 0.02$ and $w'_2 = 0.96w_2 + 0.02$.

To investigate the accuracy of the prediction values, the mean relative deviation (*MRD* %) (Eq. (6)) was used.

$$MRD\% = \frac{100}{N} \sum \left(\frac{|Calculated Value - Observed Value|}{Observed Value} \right) \quad (6)$$

N is the number of data points.

Thermodynamic aspect

Using the van't Hoff equation, a thermodynamic analysis was performed to give key apparent thermodynamic parameters, including the standard dissolution enthalpy (ΔH°), Gibbs free energy

change (ΔG°), and standard dissolution entropy (ΔS°) for diclofenac sodium dissolution in the PEG 400 + water mixtures [16]. A modified version of van't Hoff equation was used to obtain the ΔH° value for the solvent mixtures, according to the following equation:

$$\frac{\partial \ln C}{\partial \left(\frac{1}{T} - \frac{1}{T_{hm}} \right)_p} = - \frac{\Delta H^\circ}{R} \quad (7)$$

The ΔH° value was computed by plotting $\ln C$ against $\frac{1}{T} - \frac{1}{T_m}$ (Eq. 7). The slope of this plot was then used to obtain ΔH° by this assumption that the change in heat capacity of the solution remains persistent in the temperature range of 298.2 to 313.2 K, leading to ΔH° being considered applicable at the mean harmonic temperature (T_{hm}) of 305.6 K. The ΔG° and ΔH° for this system were obtained from the intercept and slope of the plot from Eq. 7, respectively. Finally, the Gibbs equation was utilized to calculate ΔS° using ΔH° and ΔG° (Eq. 8):

$$\Delta S^\circ = \frac{\Delta H^\circ - \Delta G^\circ}{T_{hm}} \quad (8)$$

The contributions of enthalpy and entropy (ζ_{TS} and ζ_H) as a key parameters in the dissolution process, can be computed by Eqs. 9 and 10:

$$\zeta_{TS} = \frac{|T\Delta S^\circ|}{(|\Delta H^\circ| + |T\Delta S^\circ|)} \quad (9)$$

$$\zeta_H = \frac{|\Delta H^\circ|}{(|\Delta H^\circ| + |T\Delta S^\circ|)} \quad (10).$$

Results and discussion

Solubility profile of diclofenac sodium

Table 2 presented the experimental solubility data of diclofenac sodium in mixed solvent system of PEG 400 + water. The Table included solubility values at various temperatures along with molar solubilities and their corresponding standard deviations. For clarity and better understanding, the solubility profile diagram was also presented in Figure 2. In this mixture, the lowest solubility of diclofenac sodium was observed in pure water at 298.2 K ($x_{m,T} = 6.18 \times 10^{-2}$), with solubility increasing progressively as temperature rose. The highest solubility in this system recorded at a PEG 400 mass fraction of 0.6, ranging from 5.03×10^{-1} at 298.2 K to 6.39×10^{-1} at 313.2 K.

The observed solubility patterns in this system can be related to molecular interactions and solvation effects between diclofenac sodium, the cosolvent (PEG 400), and the solvent (water). These interactions are crucial for diclofenac sodium's solubility and explain the behavior in these cosolvency systems, as noted in reference [17].

The observed solubility profile, was governed by the interplay of drug-solvent interactions, polarity, and hydrogen bonding capacity. Diclofenac sodium possesses both polar (carboxylate, amine) and nonpolar (aromatic rings) functionalities. Pure water, a highly polar protic solvent, strongly solvates polar and ionic species through hydrogen bonding and ion-dipole interactions, but its high cohesive energy density can lead to unfavorable interactions with the nonpolar regions of diclofenac sodium. As PEG 400, a polar aprotic solvent with ether linkages, was introduced, it disrupted the water's hydrogen bonding network. At low PEG 400 fractions, the system remained largely water-dominated, with limited improvement in diclofenac sodium solubility. However, as the PEG 400 fraction increased, PEG 400 began to preferentially solvate the nonpolar portions of diclofenac sodium, while its ether oxygens can also engage in dipole-dipole interactions or weaker hydrogen bonds with the polar groups of the drug. The solubility maximum at approximately 0.6 mass fraction PEG 400 indicated an optimal balance where the mixed solvent system effectively

screened both the polar and nonpolar moieties of diclofenac sodium, minimizing the free energy of solvation. Beyond this point, in PEG 400-rich mixtures, the solvent environment became increasingly dominated by PEG 400, which provided a more consistently favorable solvation sphere for diclofenac sodium compared to pure water, thus sustaining higher solubility.

The solubility of diclofenac sodium obtained in this study for water (6.18×10^{-2}) at 298.2 K was compared with the literature data which was 6.74×10^{-2} [18] confirming the data proximity and accuracy of the obtained data in this study.

Table 2

Experimental molar solubility ($C_{m,T}$) as the mean of three experiments ($\pm$ standard deviation) determined for diclofenac sodium in studied mixtures at different temperatures under atmospheric pressure.^a

w_1^a	298.2 K	303.2 K	308.2 K	313.2 K
0.00	$6.18 (\pm 0.12) \times 10^{-2}$	$9.05 (\pm 0.09) \times 10^{-2}$	$1.18 (\pm 0.12) \times 10^{-1}$	$1.57 (\pm 0.03) \times 10^{-1}$
0.10	$1.12 (\pm 0.11) \times 10^{-1}$	$1.49 (\pm 0.27) \times 10^{-1}$	$1.69 (\pm 0.18) \times 10^{-1}$	$2.07 (\pm 0.02) \times 10^{-1}$
0.20	$1.16 (\pm 0.01) \times 10^{-1}$	$1.99 (\pm 0.12) \times 10^{-1}$	$2.46 (\pm 0.08) \times 10^{-1}$	$2.82 (\pm 0.03) \times 10^{-1}$
0.30	$2.30 (\pm 0.09) \times 10^{-1}$	$2.66 (\pm 0.15) \times 10^{-1}$	$3.14 (\pm 0.08) \times 10^{-1}$	$3.55 (\pm 0.07) \times 10^{-1}$
0.40	$3.09 (\pm 0.02) \times 10^{-1}$	$3.53 (\pm 0.28) \times 10^{-1}$	$4.12 (\pm 0.15) \times 10^{-1}$	$4.59 (\pm 0.04) \times 10^{-1}$
0.50	$4.07 (\pm 0.04) \times 10^{-1}$	$4.49 (\pm 0.13) \times 10^{-1}$	$5.06 (\pm 0.07) \times 10^{-1}$	$5.61 (\pm 0.10) \times 10^{-1}$
0.60	$5.03 (\pm 0.12) \times 10^{-1}$	$5.40 (\pm 0.21) \times 10^{-1}$	$6.03 (\pm 0.14) \times 10^{-1}$	$6.39 (\pm 0.04) \times 10^{-1}$
0.70	$4.83 (\pm 0.09) \times 10^{-1}$	$5.23 (\pm 0.33) \times 10^{-1}$	$5.68 (\pm 0.07) \times 10^{-1}$	$6.20 (\pm 0.06) \times 10^{-1}$
0.80	$4.35 (\pm 0.11) \times 10^{-1}$	$4.83 (\pm 0.12) \times 10^{-1}$	$5.23 (\pm 0.21) \times 10^{-1}$	$5.75 (\pm 0.06) \times 10^{-1}$
0.90	$4.08 (\pm 0.19) \times 10^{-1}$	$4.45 (\pm 0.17) \times 10^{-1}$	$5.01 (\pm 0.18) \times 10^{-1}$	$5.35 (\pm 0.04) \times 10^{-1}$
1.00	$3.84 (\pm 0.33) \times 10^{-1}$	$4.22 (\pm 0.12) \times 10^{-1}$	$4.66 (\pm 0.06) \times 10^{-1}$	$5.12 (\pm 0.04) \times 10^{-1}$

^a w_1 is the mass fraction of PEG 400 in PEG 400 + water system in the absence of diclofenac sodium.

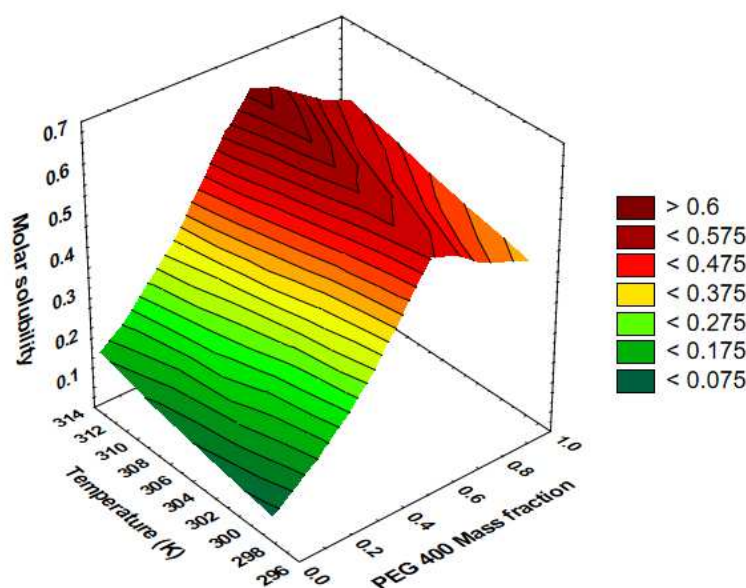


Figure 2 Solubility profile of diclofenac sodium in PEG 400 + water mixtures at different temperatures

Solubility data correlation

The solubility data of diclofenac sodium in the binary solvent mixtures of PEG 400 + water were correlated using several models, namely the van't Hoff, Jouyban-Acree, Jouyban-Acree-van't Hoff, MRS, and modified Wilson models, as summarized in [Tables 3–6](#). All parameters of these models listed in the Tables are dimensionless. The selection of these models was motivated by findings from our previous work, which demonstrated their suitability for solubility correlation. Specifically, the van't Hoff equation was applied due to its reliability in describing the temperature dependence of solubility over relatively narrow temperature ranges. In this study, solubility measurements of diclofenac sodium were conducted at four temperatures, each separated by a five-degree Kelvin interval, allowing accurate fitting to the van't Hoff model. The subsequent model considered was the MRS model, which expresses solubility as a function of solvent composition through a linear relationship. In contrast, the modified Wilson model represents a nonlinear

correlation between solubility and solvent composition. Finally, the Jouyban-Acree and Jouyban-Acree-van't Hoff models incorporate both solvent composition and temperature as variables influencing solubility. These models were selected owing to their capability to correlate and predict all experimental solubility data across different temperatures and solvent compositions within a single equation, providing high predictive accuracy consistent with our previous findings. The accuracy of each model was evaluated using the *MRD*% values.

As shown in [Table 3](#), the van't Hoff model produced overall *MRD*% values of 0.9 for the solubility of diclofenac sodium in PEG 400 + water solvent system. The corresponding model parameters (*A* and *B*) were also reported for both mixtures. The relatively low *MRD*% values indicated that the van't Hoff model effectively predicted the solubility of diclofenac sodium in these solvent mixtures. [Table 4](#) listed the parameters for the Jouyban-Acree and Jouyban-Acree-van't Hoff models, yielding overall *MRD*% values of 6.7 and 6.9 for this system. In [Table 5](#), the MRS model constants at various temperatures, along with the corresponding *MRD*% values, were presented. The back-calculated solubility *MRD*% values were 3.6 for this mixture, confirming the accuracy of the model predictions. Similarly, [Table 6](#) provided the parameters of the modified Wilson model at different temperatures together with their *MRD*% value, which was 14.4%. Overall, the variations in *MRD*% among the models were minimal, suggesting that all employed models deliver reliable solubility predictions for diclofenac sodium in the studied binary mixtures. The selection of the most appropriate model ultimately depended on the system characteristics (e.g., aqueous vs. non-aqueous) and experimental conditions, such as temperature and solvent composition.

In the final step, the predictive performance of the Jouyban-Acree-van't Hoff model for solubility estimation was evaluated. The model was trained using a limited dataset comprising solubility data for the pure solvents at both the lowest and highest temperatures, along with data for solvent

mixtures at mass fractions of 0.3, 0.5, and 0.7 at 298.2 K. The remaining solubility values for other compositions and temperatures were then predicted using the trained model. The resulting *MRD*% values obtained for different temperatures in the studied system were 4.6, 8.2, 12.1 and 19.6 % for 298.2, 303.2, 308.2 and 313.2 K, respectively.

Table 3

The van't Hoff model parameters and the corresponding *MRD*% for diclofenac sodium in studied binary mixtures

w_1	A	B	<i>MRD</i> %
0.00	16.441	-5725.243	2.0
0.10	10.186	-3681.749	2.6
0.20	9.611	-3401.985	1.2
0.30	7.729	-2743.063	0.6
0.40	7.234	-2507.272	0.7
0.50	5.873	-2020.897	0.4
0.60	4.500	-1547.703	0.9
0.70	4.476	-1552.717	0.3
0.80	4.914	-1712.550	0.4
0.90	4.941	-1741.016	0.8
1.00	5.067	-1797.089	0.2
Overall <i>MRD</i>%			0.9

Table 4

Parameters calculated for the Jouyban-Acree, and Jouyban-Acree-van't Hoff model for diclofenac sodium in studied binary mixtures

	Jouyban-Acree		Jouyban-Acree-van't Hoff	
PEG 400 + water	J_0	948.160	A_1	5.067
	J_1	0 ^a	B_1	-1797.089
	J_2	0 ^a	A_2	16.441
			B_2	-5725.243
			J_0	948.324
			J_1	0 ^a
			J_2	0 ^a
<i>MRD</i>%		6.7	6.9	

^a Not statistically significant (p -value >0.05)

Table 5

The MRS model constants at the investigated temperatures and the *MRD*% for diclofenac sodium in studied binary mixtures

Binary system	T (K)	β_1	β_2	β_3	β_4	β_5	$MRD\%$
PEG 400 + water	298.2	-1.063	-2.879	0 ^a	0 ^a	4.182	4.4
	303.2	-0.939	-2.503	0 ^a	0 ^a	3.561	4.2
	308.2	-0.838	-2.263	0 ^a	0 ^a	3.362	3.5
	313.2	-0.883	-2.178	0.005	0.003	3.667	2.1
Overall $MRD\%$							3.6

^a Not statistically significant (p -value >0.05)

Table 6

The modified Wilson model parameters at the investigated temperatures and the $MRD\%$ for diclofenac sodium in studied binary mixtures

T (K)	1-Propanol+ PG		
	λ_{12}	λ_{21}	$MRD\%$
298.2	-0.130	7.918	14.7
303.2	0.145	6.879	14.6
308.2	0.145	6.909	14.6
313.2	0.155	6.452	13.7
Overall $MRD\%$			14.4

Apparent thermodynamic parameters

Thermodynamic parameters governing the dissolution of diclofenac sodium in binary mixtures of PEG 400 + water at 305.6 K were summarized in Table 7. These parameters, encompassing ΔG° , ΔH° , ΔS° , $T\Delta S^\circ$, ζ_H , and ζ_{TS} , collectively indicated a favorable dissolution. The dissolution process was endothermic, as evidenced by positive ΔH° values, signifying heat absorption. Despite positive ΔG° values suggesting non-spontaneity at saturation, the substantial positive ΔS° values revealed a significant entropy-driven contribution, making the overall dissolution favorable. Thus, the dissolution of diclofenac sodium in these binary mixtures was favorably influenced by these thermodynamic factors.

The dissolution of diclofenac sodium was further elucidated by the dimensionless factors ζ_H and ζ_{TS} , detailed in Table 7. These factors represented the relative contributions of enthalpy (ζ_H) and entropy (ζ_{TS}) to the overall dissolution process. An increase in ζ_H signified a greater enthalpic influence, while a rise in ζ_{TS} highlighted the increasing importance of entropy. Based on the enthalpy-entropy compensation analysis presented in Table 7, it can be concluded that both enthalpic and entropic factors were crucial drivers for diclofenac sodium dissolution. However, the diclofenac sodium dissolution in PEG 400 + water system was enthalpy-driven process.

Table 7

Apparent thermodynamic parameters of diclofenac sodium dissolution in the investigated binary mixtures at $T_{hm} = 305.6$ K.

w_1	ΔG° (kJ.mol ⁻¹)	ΔH° (kJ.mol ⁻¹)	ΔS° (J.K ⁻¹ .mol ⁻¹)	$T\Delta S^\circ$ (kJ.mol ⁻¹)	ζ_H	ζ_{TS}
0.00	5.83	47.61	137.89	42.14	0.530	0.470
0.10	4.73	30.75	85.87	26.24	0.540	0.460
0.20	3.87	28.34	80.76	24.68	0.534	0.466
0.30	3.17	22.85	64.97	19.85	0.535	0.465
0.40	2.46	20.74	60.33	18.44	0.529	0.471
0.50	1.88	16.76	49.10	15.01	0.528	0.472
0.60	1.43	12.87	37.75	11.54	0.527	0.473
0.70	1.54	12.83	37.27	11.39	0.530	0.470
0.80	1.76	14.25	41.23	12.60	0.531	0.469
0.90	1.92	14.452	41.36	12.64	0.533	0.467
1.00	2.07	14.876	42.278	12.92	0.535	0.465

Enthalpy–entropy compensation analysis

Figure 3 illustrated the enthalpy-entropy compensation plots (ΔH° vs. ΔG°) for diclofenac sodium dissolution in PEG 400 + water mixtures at 305.6 K, offering key insights into the interplay of ΔS° and ΔH° . In the system, positive slopes (despite with quantitative difference) across all investigated mass fractions indicate that enthalpy primarily drives solubility enhancement. The observed

enthalpy-entropy compensation phenomenon demonstrated a linear correlation where increases in ΔH° were counterbalanced by corresponding increases in ΔS° , indicating their interrelated and balancing roles in this binary solvent mixture.

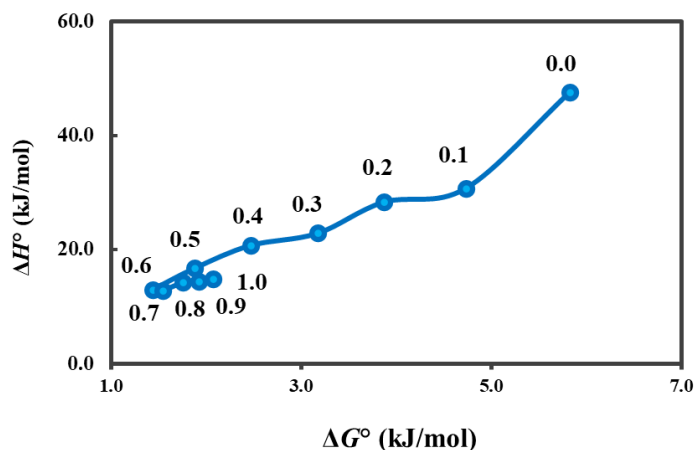


Figure 3. Enthalpy-entropy compensation plot for the solubility of diclofenac sodium in PEG 400 + water mixtures at 305.6 K. The solid points correspond to the mass fraction of PEG 400 in the binary solvent mixtures (before the diclofenac sodium addition).

Conclusion

The solubility and thermodynamics of diclofenac sodium were investigated in binary mixture of PEG 400 + water at temperatures ranging from 298.2 K to 313.2 K. Enhanced diclofenac sodium solubility was observed in these mixtures, with solubility rising with increasing PEG 400 mass fraction up to $w_1=0.6$ and temperature. Mathematical modeling using van't Hoff, Jouyban-Acree, Jouyban-Acree-van't Hoff, MRS, and modified Wilson models proved effective, accurately predicting solubility with an overall *MRD*% below 15%. These validated models can facilitate the estimation of diclofenac sodium solubility and thermodynamic parameters in alternative solvent

environments. Thermodynamically, the dissolution of diclofenac sodium in these mixed solvents was found to be an endothermic process that was entropically favored.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Data supporting this study are included within the article

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Alireza Haririan: Investigation, **Hossein Aligholipour :** Investigation, **Elaheh Rahimpour:** Conceptualization, Writing the first draft. **Abolghasem Jouyban;** Supervision, Writing—review & editing.

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