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# Solubility of ranitidine hydrochloride in solvent mixtures of PEG 200, PEG 400, ethanol and propylene glycol at 25 °C

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ABSTRACT

Experimental solubilities of ranitidine hydrochloride in binary mixtures of ethanol (EtOH)-polyethylene glycol 200 (PEG 200), EtOH-polyethylene glycol 400 (PEG 400), EtOH-1, 2-propanediol (PG), PEG 200-PG and PG-PEG 400 and ternary mixtures of EtOH-PG-PEG 400 at 25 °C are reported. The measured data were fitted to the Jouyban–Acree model and the mean percentage deviations (MPD) of back-calculated solubilities for EtOH-PG, EtOH-PEG 400, EtOH-PEG 200, PG-PEG 200 and PG-PEG 400 were 3.0%, 6.3%, 2.8%, 2.2% and 2.1, respectively, and the overall MPD was 3.3%. The corresponding MPD for solubility in PG-PEG 400-EtOH mixtures was 8.4%. Also, experimental densities of the saturated solutions were measured and then fitted to the Jouyban–Acree equation with the overall MPD of 1.5%.



## 1. Introduction

Ranitidine hydrochloride (Ran.HCl), *N*-[2-[[[-5-[(dimethylamino) methyl]-2-furanyl] methyl] thio] ethyl]-N′-methyl-2-nitro-1, 1-ethenediamine hydrochloride (Fig. 1), is used to treat stomach ulcers, acid reflux, indigestion and Zollinger–Ellison syndrome. Ran.HCl is a class III drug in biopharmaceutics classification system and its bioavailability is restricted by its low permeability [1,2]. It is mainly absorbed from small intestine [1] and has a low protein binding of about 15% [3].

Ethanol (EtOH), propylene glycol (PG) and polyethylene glycols (PEGs) 200 and 400 are among the more frequently used pharmaceutical cosolvents in the preparation of liquid dosage forms. The cosolvents are mainly used for solubilization of poorly soluble drugs and/or to stabilize a number of degradable drugs in aqueous solutions. Besides these applications, these excipients may change the biological activity of drugs which should be considered in their practical applications. EtOH reduces the bioavailability of riboflavin (vitamin $B_2$) and flavin adenine dinucleotide and alters the activities of a number of enzymes [4]. A highly active metabolite of EtOH, i.e. acetaldehyde, affects the bioavailability of drugs [5]. Fiske et al. investigated the effects of EtOH on in vitro dissolution and in vivo pharmacokinetics of oxymorphone extended-release and oxymorphone crush-resistant tablet formulations in which slower dissolution rates were observed for both formulations in the presence of EtOH. However, the required time period for release of 100% were not affected by EtOH. Peak plasma concentrations of the drug were increased by 14 to 80% for both formulations [6].

Solubility of a drug is one of its important physico-chemical properties and needed in a wide range of applications including the choice of the best solvent medium for solubilization/desolubilization of a drug or combination of drugs, for preparation of many commercially available oral or parenteral solutions, soft gelatin capsules, and topical pharmaceutical formulations [7]. There are various methods for alteration of drug solubilities such as solvent mixing which is a more feasible method in solubilization and/or crystallization investigations. In addition to the trial-and-error approach which is commonly employed in practice, an alternative method is to use cosolvency models. There are different mathematical models for solubility prediction of pharmaceuticals in solvent mixtures [8] and among them the Jouyban–Acree model is the most accurate one [9]. The general form of this model for binary mixtures at various temperatures is shown as:

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

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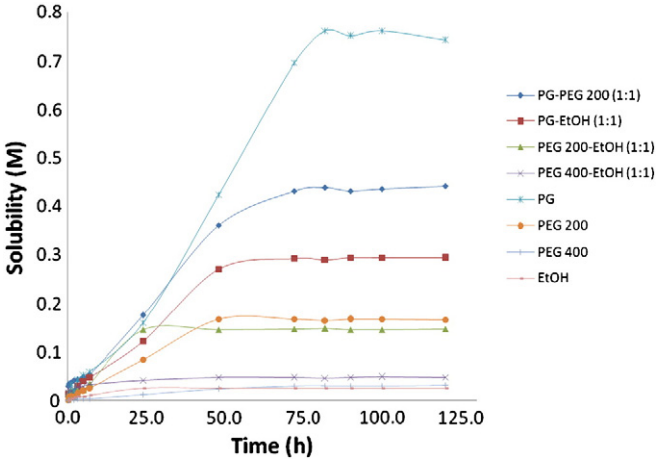


**Fig 1.** Dissolution rate of Ran.HCl in different solvent systems.

where $C_{m,T}^{Sat}$, $C_{1,T}^{Sat}$ and $C_{2,T}^{Sat}$ are molar solubility of a solute in mixed solvents and mono-solvents 1 and 2 at temperature $T$, respectively, $w_1$ and $w_2$ denote the mass fractions of the solvents 1 and 2, and $J_i$ are the model constants. These constants are related to solvent–solvent and solvent–solute interactions [10] and calculated using a no intercept least square regression of $(\ln C_{m,T}^{Sat} - w_1 \ln C_{1,T}^{Sat} - w_2 \ln C_{2,T}^{Sat})$ against $\frac{w_1 w_2}{T}$, $\frac{w_1 w_2 (w_1 - w_2)}{T}$, and $\frac{w_1 w_2 (w_1 - w_2)^2}{T}$ [11]. Applications of the Jouyban–Acree model could be extended to ternary solvent mixtures as [12,13]:

$$\ln C_{m,T}^{Sat} = w_1 \ln C_{1,T}^{Sat} + w_2 \ln C_{2,T}^{Sat} + w_3 \ln C_{3,T}^{Sat} + \left[\frac{w_1 w_2}{T}\sum_{i=0}^{2} J_i (w_1 - w_2)^i\right] + \left[\frac{w_1 w_3}{T}\sum_{i=0}^{2} J'_i (w_1 - w_3)^i\right] + \left[\frac{w_2 w_3}{T}\sum_{i=0}^{2} J''_i (w_2 - w_3)^i\right] \quad (2)$$

where $C_{3,T}^{Sat}$ and $w_3$ term are the solubility of solute in solvent 3 and mass fraction of solvent 3 in the absence of solute, respectively. The $J_i$ constants of Eq. (2) could be calculated by using the method mentioned previously for binary solvent mixtures and the model does not need any more solubility data in ternary solvent mixtures in its training process. To provide more accurate predictions, ternary interaction terms could be added to the model as [12]:

$$\ln C_{m,T}^{Sat} = w_1 \ln C_{1,T}^{Sat} + w_2 \ln C_{2,T}^{Sat} + w_3 \ln C_{3,T}^{Sat} + \left[\frac{w_1 w_2}{T}\sum_{i=0}^{2} J_i (w_1 - w_2)^i\right] + \left[\frac{w_1 w_3}{T}\sum_{i=0}^{2} J'_i (w_1 - w_3)^i\right] + \left[\frac{w_2 w_3}{T}\sum_{i=0}^{2} J''_i (w_2 - w_3)^i\right] + \left[\frac{w_1 w_2 w_3}{T}\sum_{i=0}^{2} J'''_i (w_1 - w_2 - w_3)^i\right]. \quad (3)$$

The $J'''_i$ terms are calculated employing solubility data in ternary solvent mixtures by regressing

$$\left\{\ln C_{m,T}^{Sat} - w_1 \ln C_{1,T}^{Sat} - w_2 \ln C_{2,T}^{Sat} - w_3 \ln C_{3,T}^{Sat} - \left[\frac{w_1 w_2}{T}\sum_{i=0}^{2} J_i (w_1 - w_2)^i\right] - \left[\frac{w_1 w_3}{T}\sum_{i=0}^{2} J'_i (w_1 - w_3)^i\right] - \left[\frac{w_2 w_3}{T}\sum_{i=0}^{2} J''_i (w_2 - w_3)^i\right]\right\}$$

against $\frac{w_1 w_2 w_3}{T}$, $\frac{w_1 w_2 w_3 (w_1 - w_2 - w_3)}{T}$, and $\frac{w_1 w_2 w_3 (w_1 - w_2 - w_3)^2}{T}$.

The accuracy of fitted and predicted values (solubility/density) was checked by the mean percentage deviation (MPD):

$$MPD = \frac{100}{N}\left(\frac{|Calculated - Experimental|}{Experimental}\right) \quad (4)$$

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

Solubility of Ran.HCl in water has been reported as 1.88 M (or 660 g/L) [14]. Mirmehrabi et al. reported the solubility data of two crystalline forms of Ran.HCl in methanol, 1-propanol and 2-propanol at various temperatures [15]. To the best of our knowledge, no solubility data have been reported in the literature for Ran.HCl in PEGs, PG and EtOH and their mixtures. PEGs have been used in a number of pharmaceutical formulations of Ran.HCl in Germany, the Netherlands and Finland [14]. The solubility data of Ran.HCl in non-aqueous solvents could be used in various applications and this work was aimed to measure the solubility data in the above mentioned solvent systems.

## 2. Experimental

### 2.1. Materials

Ran.HCl (99.96%) was gifted by Daana Pharmaceutical Company (Tabriz, Iran). Ethanol (purity of 99.5% in mass fraction) was purchased from Scharlau (Spain) and PEG 400 (purity of 99.5% in mass fraction), PG (purity of 99.5% in mass fraction), PEG 200 (purity of 99.5% in mass fraction) were purchased from Merck (Germany).

### 2.2. Apparatus and procedures

The binary and ternary mixtures of used solvents were prepared with addition of solvents in appropriate mass fraction with accuracy of 0.1 g. The solubility determination methods are reviewed in a recent publication [16] and the saturation shake-flask method of Higuchi and Connors [17] was used in this work. The time period of reaching equilibrium conditions is determined by profiling the dissolution rate of Ran.HCl in a number of solvent systems. All temperature dependent experimental works were carried out in an incubator equipped with a temperature controlling system that maintained within ±0.2 °C (Nabziran, Tabriz, Iran). Excess amount of Ran.HCl was added to the prepared solvents and after 3 days, the saturated solutions were centrifuged at 13,000 rpm for 15 min (MSE Micro Center MSB010.CX2.5, Sanyo, Japan) and then diluted with water and assayed at 325 nm ($\varepsilon = 11684.97$ to $\varepsilon = 12119.21$ $L.mol^{-1}.cm^{-1}$) using a UV–vis spectrophotometer (Pharmacia Biotech-Ultraspec 2000, England). The concentrations of diluted solutions were determined with an absorbance versus concentration calibration curve. The dynamic range of calibration curve was $2.85 \times 10^{-5}$ to $1.14 \times 10^{-4}$ $mol.L^{-1}$ (Table 1). Each experimental solubility data point represents the average of at least three experimental measurements with the measured $mol \cdot L^{-1}$ solubilities being reproducible to within the mean relative standard deviations (RSDs) of 3.7% (the RSDs vary between 0.2 and 6.9%). Calculated standard deviations varied from $\sigma_{n-1} = 0.0004$ to 0.0394 $mol.L^{-1}$. Densities of saturated solutions and solute free PG + EtOH mixtures were measured using a calibrated 5 mL pycnometer with the mean relative standard deviations of 1.2%.

**Table 1**
Details of the calibration curve of Ran.HCl.

| ε ($L.mol^{-1}.cm^{-1}$) | C ($mol.L^{-1}$) | Correlation coefficient | Calibration curve |
|---|---|---|---|
| 11684.97 to 12119.21 | $2.85 \times 10^{-5}$ to $1.14 \times 10^{-4}$ | 0.999 | (y:Absorbance) $y = 12208C - 0.012$ |

## 3. Results and discussion

To obtain appropriate time required for equilibration of the saturated solutions, the dissolution rates of Ran.HCl in a number of solvent systems were determined. As the results shown in Fig. 1, 72 h is an appropriate time for saturation of the solutions. The solubility data of Ran.HCl in binary and ternary mixtures of PG-EtOH, PEG 400-EtOH, PEG 200-EtOH, PG-PEG 200, PG-PEG 400 and ternary mixture of PEG 400-EtOH-PG at 25 °C are listed in Tables 2 and 3. Results showed that the maximum and minimum solubilities of Ran.HCl among investigated solvent systems were observed in neat PG and EtOH, respectively. This demonstrates that PG is a more effective solvent for increasing the solubility of Ran.HCl and could be employed as solubilizing solvent for conditions in which water is not suitable e.g. soft gel formulations whereas EtOH is a suitable solvent for crystallization purposes. With the addition of PG into PG-EtOH, PG-PEG 200 and PG-PEG 400 mixtures, solubility of Ran.HCl was increased while in PEG 200-EtOH mixture a different pattern was observed; i.e. the solubility was increased with increasing the mass fraction of PEG 200 and reached to the maximum amount at 0.80 mass fraction and decreased with further addition of PEG 200. Also, for PEG 400-EtOH mixture with the addition of EtOH the solubility of Ran.HCl was increased up to 0.30 mass fraction of EtOH. Investigating the thermogram obtained from DSC using the excess solid Ran.HCl collected from ethanolic solutions (with the melting point of ~150 °C) reveals that the form II of the drug existed in the saturated solution.

The solubility data of Ran.HCl in five binary and ternary solvent mixtures were fitted to the Jouyban–Acree model, i.e. Eqs. (1) and (2), and then the binary and ternary interactions ($J$ terms) were computed. Then, the back-calculated solubility data employing the calculated $J$ terms was used to compute the MPD values listed in Table 4. Using the $J$ values, it is possible to predict the solubility of Ran.HCl in all composition ranges of the solvent mixtures at various temperatures employing the solubility in the mono-solvents at the corresponding temperatures as were shown for other drugs in earlier works [18,19]. The expected prediction errors vary between 2.1 and 6.3% for solubility of Ran.HCl in binary solvent mixtures and 8.4% for the solubilities in PG-PEG 400-EtOH mixtures. By excluding the

**Table 2**
Experimental molar and mole fraction solubilities and the experimental density of Ran.HCl in binary solvent mixtures at 25 °C.

| Mass fraction of solvent 1 | PG (1)-EtOH (2) | | Density ($g \cdot cm^{-3}$) | |
|---|---|---|---|---|
| | Exp. (molar) | Exp. (mole fraction) | Saturated solvents | Solute free olvents [a] |
| 0.00 | 0.0253 | 0.00150 | 0.7820 | 0.7816 |
| 0.10 | 0.0416 | 0.00257 | 0.8060 | 0.7936 |
| 0.20 | 0.0687 | 0.00446 | 0.8220 | 0.8098 |
| 0.30 | 0.1076 | 0.00729 | 0.8440 | 0.8326 |
| 0.40 | 0.1462 | 0.01026 | 0.8700 | 0.8642 |
| 0.50 | 0.2314 | 0.01697 | 0.9000 | 0.8904 |
| 0.60 | 0.3173 | 0.02429 | 0.9280 | 0.9179 |
| 0.70 | 0.4073 | 0.03220 | 0.9640 | 0.9520 |
| 0.80 | 0.4640 | 0.03782 | 0.9900 | 0.9806 |
| 0.90 | 0.5557 | 0.04703 | 1.0180 | 1.0096 |
| 1.00 | 0.7561 | 0.06847 | 1.0480 | 1.0273 |
| | PEG 400 (1)-EtOH (2) | | | |
| 0.00 | 0.0253 | 0.00150 | 0.7820 | |
| 0.10 | 0.0313 | 0.00314 | 0.8200 | |
| 0.20 | 0.0381 | 0.00530 | 0.8480 | |
| 0.30 | 0.0427 | 0.00749 | 0.8760 | |
| 0.40 | 0.0441 | 0.00918 | 0.9080 | |
| 0.50 | 0.04373 | 0.01042 | 0.9420 | |
| 0.60 | 0.04747 | 0.01268 | 0.9720 | |
| 0.70 | 0.06549 | 0.01908 | 1.0120 | |
| 0.80 | 0.04362 | 0.01366 | 1.0520 | |
| 0.90 | 0.03591 | 0.01194 | 1.0960 | |
| 1.00 | 0.02902 | 0.01021 | 1.1360 | |
| | PEG 200 (1)-EtOH (2) | | | |
| 0.00 | 0.0253 | 0.00150 | 0.7820 | |
| 0.10 | 0.0412 | 0.00320 | 0.8028 | |
| 0.20 | 0.0618 | 0.00569 | 0.8508 | |
| 0.30 | 0.0778 | 0.00806 | 0.9100 | |
| 0.40 | 0.09401 | 0.01103 | 0.9400 | |
| 0.50 | 0.1179 | 0.01525 | 0.9780 | |
| 0.60 | 0.1344 | 0.01839 | 1.0400 | |
| 0.70 | 0.1669 | 0.02467 | 1.0736 | |
| 0.80 | 0.2176 | 0.03439 | 1.1100 | |
| 0.90 | 0.2034 | 0.03456 | 1.1200 | |
| 1.00 | 0.1600 | 0.02841 | 1.1500 | |
| | PG (1)-PEG 200 (2) | | | |
| 0.00 | 0.1600 | 0.02841 | 1.1500 | |
| 0.10 | 0.2653 | 0.04554 | 1.1363 | |
| 0.20 | 0.3058 | 0.05002 | 1.1250 | |
| 0.30 | 0.3711 | 0.05782 | 1.1150 | |
| 0.40 | 0.4115 | 0.06084 | 1.1100 | |
| 0.50 | 0.4574 | 0.06361 | 1.1000 | |
| 0.60 | 0.5332 | 0.06980 | 1.0800 | |
| 0.70 | 0.5929 | 0.07230 | 1.0680 | |
| 0.80 | 0.6383 | 0.07166 | 1.0580 | |
| 0.90 | 0.7256 | 0.07452 | 1.0520 | |
| 1.00 | 0.7561 | 0.06847 | 1.0480 | |
| | PG (1)-PEG 400 (2) | | | |
| 0.00 | 0.7561 | 0.06847 | 1.0480 | |
| 0.10 | 0.6641 | 0.08091 | 1.0513 | |
| 0.20 | 0.5592 | 0.08341 | 1.0619 | |
| 0.30 | 0.4705 | 0.08269 | 1.0695 | |
| 0.40 | 0.4177 | 0.08385 | 1.0850 | |
| 0.50 | 0.3612 | 0.08165 | 1.0937 | |
| 0.60 | 0.3111 | 0.07821 | 1.1006 | |
| 0.70 | 0.2129 | 0.05888 | 1.1051 | |
| 0.80 | 0.1410 | 0.04246 | 1.1150 | |
| 0.90 | 0.06968 | 0.02283 | 1.1210 | |
| 1.00 | 0.02902 | 0.01021 | 1.1360 | |

[a] The rest of solute free density data were taken from Refs. [23,24].

**Table 3**
Experimental molar and mole fraction solubilities and the density of Ran.HCl in PG-EtOH-PEG 400 mixtures at 25 °C.

| Mass fraction | | | Solubility | | Density ($g \cdot cm^{-3}$) |
|---|---|---|---|---|---|
| PEG 400 | PG | EtOH | Exp. (molar) | Exp. (mole fraction) | |
| 0.33 | 0.34 | 0.33 | 0.1963 | 0.03712 | 0.9500 |
| 0.20 | 0.40 | 0.40 | 0.2395 | 0.03539 | 0.9250 |
| 0.40 | 0.20 | 0.40 | 0.1300 | 0.02671 | 0.9625 |
| 0.10 | 0.50 | 0.40 | 0.2876 | 0.03164 | 0.9500 |
| 0.50 | 0.10 | 0.40 | 0.0978 | 0.02325 | 0.9625 |
| 0.40 | 0.40 | 0.20 | 0.2713 | 0.05368 | 1.0500 |
| 0.40 | 0.50 | 0.10 | 0.3766 | 0.07581 | 1.0625 |
| 0.40 | 0.10 | 0.50 | 0.0844 | 0.01674 | 0.9750 |
| 0.10 | 0.40 | 0.50 | 0.2009 | 0.02150 | 0.9250 |
| 0.50 | 0.40 | 0.10 | 0.3175 | 0.07152 | 1.0800 |
| 0.30 | 0.30 | 0.40 | 0.1792 | 0.03120 | 0.9600 |
| 0.40 | 0.30 | 0.30 | 0.2110 | 0.04345 | 0.9875 |
| 0.30 | 0.40 | 0.30 | 0.2626 | 0.04656 | 0.9755 |
| 0.10 | 0.10 | 0.80 | 0.0649 | 0.00659 | 0.8500 |
| 0.80 | 0.10 | 0.10 | 0.0934 | 0.02824 | 1.1000 |
| 0.10 | 0.80 | 0.10 | 0.5385 | 0.06189 | 1.0500 |

**Table 4**
The constants of the Jouyban–Acree model and back-calculated MPD for solubility of Ran.HCl in binary and ternary solvent mixtures.

| Constants | PG-EtOH | PEG 400-EtOH | PEG 200-EtOH | PG-PEG 200 | PG-PEG 400 | PG-PEG 400-EtOH |
|---|---|---|---|---|---|---|
| $J_0$ | 601.680 | 734.985 | 696.398 | 334.927 | 1071.830 | −1589.404 |
| $J_1$ | −120.907 | NS[b] | 155.976 | −321.882 | −884.804 | −3178.466 |
| $J_2$ | −361.750 | NS[b] | 954.571 | 507.512 | 263.361 | NS[b] |
| $N$ | 11 | 11 | 11 | 11 | 11 | 16 |
| MPD | 3.0 | 6.3 | 2.8 | 2.2 | 2.1 | 8.4 |

[b] Not significant ($p > 0.05$).

**Table 5**
The constants of the Jouyban–Acree model and back-calculated MPD for density of Ran.HCl in binary solvent mixtures.

| Constants | PG-EtOH | PEG 400-EtOH | PEG 200-EtOH | PG-PEG 200 | PG-PEG 400 |
|---|---|---|---|---|---|
| $J_0$ | NS[b] | −19.692 | −28.703 | 12.780 | 7.380 |
| $J_1$ | NS[b] | 62.749 | 73.861 | NS[b] | 9.934 |
| $J_2$ | NS[b] | −66.166 | NS[b] | NS[b] | 8.875 |
| $N$ | 11 | 11 | 11 | 11 | 11 |
| MPD | 0.4 | 1.7 | 3.6 | 1.1 | 0.6 |

[b] Not significant ($p > 0.05$).

effects of ternary solvent interaction terms from prediction process of Ran.HCl solubility in the ternary solvent mixtures, the MPD value increases to 11.0%. By accepting this prediction error it is possible to predict the solubility of Ran.HCl in PG-PEG200-EtOH mixtures without any further experimental measurement. This approach has also been confirmed in earlier reports [12,13]. One might include the constant T value (at 25 °C) in the model constants (i.e. $J$ terms) which is true for isothermal condition. However, we recommend to use the model as Eq. (1), (2) or (3), since using these versions of the model it is possible to train the model at one temperature and predict the solubility in mixed solvents at other temperature employing the corresponding data in the mono-solvents at temperature of interest [18,19].

As shown in a previous work [20], the Jouyban–Acree model could be used to model the density of solvent mixtures. The model for correlating density of binary solvents (or saturated solutions of a drug in binary solvents) at various temperatures is:

$$\ln \rho_{m,T}^{Sat} = w_1 \ln \rho_{1,T}^{Sat} + w_2 \ln \rho_{2,T}^{Sat} + \frac{w_1 w_2}{T} \sum_{i=0}^{2} A_i (w_1 - w_2)^i \quad (5)$$

where $\rho_{m,T}^{Sat}$, $\rho_{1,T}^{Sat}$ and $\rho_{2,T}^{Sat}$ are the densities of saturated solution in mixture and solvents 1 and 2 at temperature 25 °C, respectively, and $A_i$ is the model constants. The numerical values of $A_i$ terms could be calculated employing solute free density of solvent mixtures and the density of drug saturated solutions could be predicted by employing experimental densities of the saturated solutions in the mono-solvents [21,22]. Table 5 listed the numerical values of $A_i$ terms for the investigated binary solvent systems. By employing the model constants listed in Table 5 and the density of the saturated solutions of Ran.HCl in the mono-solvents at $T$, i.e. $\rho_{1,T}^{Sat}$ and $\rho_{2,T}^{Sat}$, the density of saturated solutions in binary mixtures could be predicted. The MPD values for this analysis are also listed in Table 5, in which the overall MPD of the density data was 1.5%. By including the sub-binary interaction terms, it is also possible to predict the density of saturated solutions of Ran.HCl in PG-PEG 400-EtOH mixtures using:

$$\begin{aligned} \ln \rho_{m,T}^{Sat} = {} & w_1 \ln \rho_{1,T}^{Sat} + w_2 \ln \rho_{2,T}^{Sat} + w_3 \ln \rho_{3,T}^{Sat} \\ & + \left[ 7.380 \frac{w_1 w_2}{T} + 9.934 \frac{w_1 w_2}{T} (w_1 - w_2) + 8.875 \frac{w_1 w_2}{T} (w_1 - w_2)^i \right] \\ & + \left[ -19.692 \frac{w_2 w_3}{T} + 62.749 \frac{w_2 w_3}{T} (w_2 - w_3) - 66.166 \frac{w_2 w_3}{T} (w_2 - w_3)^i \right] \end{aligned} \quad (6)$$

where $\rho_{3,T}^{Sat}$ is the density of saturated solution of Ran.HCl in solvent 3 at temperature $T$. The density of the saturated solutions in ternary solvent mixtures was predicted with the MPD of 1.8%.

## 4. Conclusions

As a main purpose, the solubility and density data of Ran.HCl in neat solvents, binary and ternary mixtures of EtOH, PEG 400, PEG 200 and PG were reported which extends the database of solubility of pharmaceuticals in organic and mixed solvents [9]. Solubility data were fitted to the Jouyban–Acree model and constants of the model were computed. The results showed that the overall MPD value obtained by back-calculated solubility of binary and ternary mixtures was 4.1%. Also, the same computations were done for the densities of saturated solutions of binary and ternary solvent mixtures with the overall MPDs of 1.5% and 1.8%, respectively.

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