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Prediction of sulfamerazine and sulfamethazine solubility in some cosolvent mixtures using non-ideal solution models

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Summary

Introduction: Experimental Solubilities of sulfamerazine (SMR) and sulfamethazine (SMT) in some (methanol + water), (ethanol + water) and (1-propanol + water) cosolvent mixtures were collected from the literature at five temperatures from 293.15 to 313.15 K. **Methodology:** The results were analyzed with the van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model, two-parameter Weibull function model. It was determined that the models that best describe the solubility of these sulfonamides in (alcohol + water) mixtures were the van't Hoff and Apelblat models, obtaining correlation indices greater than 0.99 in all cases. **Results:** The results obtained with the Modified Apelblat equation presents a high correlation index for the solubility of SMR and SMT in cosolvent mixtures, followed by the van't Hoff-Yaws model that presents a high fit of the estimated data with respect to the theoretical ones. According to the two-parameter Weibull function model, the solubility of SMR and SMT in the co-solvent mixtures shows important deviations from ideality, which is consistent with the literature. The results are discussed in terms of the solute-solvent interactions that occur in this system.

Keywords: Sulfamerazine, sulfamethazine, solubility, van't Hoff model, Apelblat modified model, Buchowski-Ksiazaczak λh model, van't Hoff-Yaws model, two-parameter Weibull function model.

Resumen

Predicción de la solubilidad de sulfamerazina y sulfametazina en algunas mezclas cosolventes utilizando modelos de solución no ideales

Introducción: las solubilidades experimentales de la sulfamerazina (SMR) y la sulfametazina (SMT) en algunas mezclas cosolvents (metanol + agua), (etanol + agua) y (1-propanol + agua), se revisaron en la literatura a cinco temperaturas de 293,15 a 313,15 K. **Metodología:** los resultados se analizaron con el modelo van't Hoff, Apelblat modificado, Buchowski-Ksiazaczak λh, van't Hoff-Yaws, y el modelo de la función Weibull de dos parámetros. Se determinó que los modelos que mejor describen la solubilidad de estas sulfonamidas en mezclas (alcohol + agua) son los modelos de van't Hoff y Apelblat, obteniendo índices de correlación superiores a 0,99 en todos los casos. **Resultados:** los resultados obtenidos con la ecuación de Apelblat modificada presentan un alto índice de correlación para la solubilidad de SMR y SMT en mezclas de cosolventes, seguido del modelo van't Hoff-Yaws que presenta un alto ajuste de los datos calculados con respecto a los teóricos. Según el modelo de la función de Weibull de dos parámetros, la solubilidad de la SMR y la SMT en las mezclas de cosolventes muestra importantes desviaciones de las ideales, lo que es coherente con la literatura. Los resultados se discuten en términos de las interacciones soluto-solvente que se producen en este sistema.

Palabras clave: Sulfametazina, sulfamerazina, solubilidad, modelo de van't Hoff, modelo de Apelblat modificado, modelo de Buchowski-Ksiazaczak λh, modelo de van't Hoff-Yaws, modelo de Weibull de dos parámetros.

Resumo

Predição da solubilidade de sulfamerazina e sulfametazina em algumas misturas de cosolventes usando modelos de solução não ideais

Introdução: as solubilidades experimentais de sulfamerazina (SMR e sulfametazina (SMT) em algumas misturas de cossolventes (metanol + água), (etanol + água) e (1-propanol + água), foram revisadas na literatura em cinco temperaturas de 293,15 a 313,15 K. **Metodologia:** os resultados foram analisados com o modelo van't Hoff, Apelblat modificado, Buchowski-Ksiazaczak λh, van't Hoff-Yaws e o modelo de

função Weibull de dois parâmetros. Determinou-se que os modelos que melhor descrevem a solubilidade dessas sulfonamidas em misturas (álcool + água) são os modelos van't Hoff e Apelblat, obtendo índices de correlação superiores a 0,99 em todos os casos. **Resultados:** os resultados obtidos com a equação de Apelblat modificada apresentam um alto índice de correlação para a solubilidade de SMR e SMT em misturas de cosolventes, seguido pelo modelo de van't Hoff-Yaws que apresenta um alto ajuste dos dados calculados em relação a teóricos. De acordo com o modelo de função Weibull de dois parâmetros, a solubilidade de SMR e SMT em misturas de cosolventes apresenta desvios significativos dos ideais, o que é consistente com a literatura. Os resultados são discutidos em termos das interações soluto-solvente que ocorrem neste sistema.

Palavras-chave: Sulfametazina, sulfamerazina, solubilidade, modelo van't Hoff, modelo Apelblat modificado, modelo Buchowski-Ksiazaczak λh, modelo van't Hoff-Yaws, modelo Weibull de dois parâmetros.

Introduction

Sulfamerazine (4-amino-*N*-(4-methylpyrimidin-2-il) benzene-1-sulfonamide) (figure 1) and sulfamethazine (4-amino-*N*-(4,6-dimethylpyrimidin-2-il) benzene-1-sulfonamide) (figure 2) are members of the sulfonamide family [1]. Sulfonamides are derived from *p*-amino-benzene-sulfonamide and are characterized by having a benzene nucleus with an amino group ($-NH_2$) and a sulfonamide group ($-SO_2NH_2$) [2]. These compounds have been used as chemotherapeutic agents for the prevention of bacterial infections in humans [3]. Additionally, they have been recognized as a starting point for the synthesis of new drugs due to the different pharmacological actions that they can carry out, such as: anti-cancer activity, anti-tumor effect, anti-inflammatory effect, among others [4].

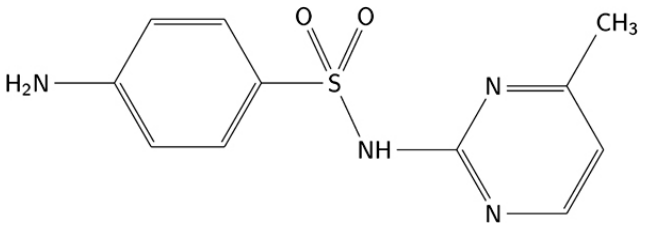

Figure 1. Molecular structure of sulfamerazine.

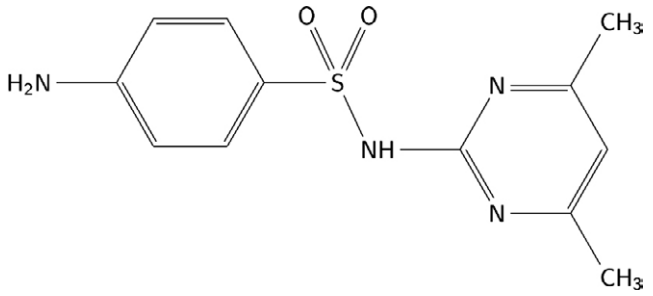

Figure 2. Molecular structure of sulfamethazine.

The solubility data of different compounds, especially the ones with pharmaceutical applications, in neat solvents and their mixtures is a very important parameter influencing the design of the drug, its evaluation, as well as its application and future optimization. It is then understandable that many experiments are carried out in order to quantify this solubility in different solvents. Such efforts are undertaken also in the field of sulfonamides and one can include here the works of Delgado *et al.* [5-9], Cruz *et al.* [10], Kodide *et al.* [11], Martínez *et al.* [12, 13], Romdhani *et al.* [14], and Blanco *et al.* [15-17]. Alongside the experimental measurements, many theoretical solubility models have been developed for accurate prediction of solubility and for better understanding of the interactions occurring in solute-solvent systems [18-22].

At present, the development of mathematical models that allow predicting the solubility of bioactive substances in solvents of industrial/pharmaceutical interest is a line of research of great importance [23-26]. Thus, the development of models allows the development of more efficient industrial processes, which in turn reduce the environmental impact [27-29].

Thus, the objective of this work is to challenge the mathematical models of van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model and two-parameter Weibull function model, from experimental solubility data, Sulfamethazine and Sulfamethazine using Python programming language.

Theoretical

Modified Apelblat Equation

The modified Apelblat equation, which is an empirical model derived from solid-liquid equilibrium [30, 31]:

$$\ln x_3 = A + BT^{-1} + C\ln T \tag{1}$$

x_3 refers to measured mole fraction solubility of drug in selected solvent at absolute temperature T, A and B reflect the variation in the solution activity coefficient, and C represents the influence of temperature on enthalpy of fusion [32].

van't Hoff-Yaws

The Yaws model are semi-empirical model included three-parameters extension that allow correlating the solubility with the temperature as follows [33]:

$$ln\left(x_3\right) = A + \frac{B}{T} + \frac{C}{T^2} \tag{2}$$

where A, B and C are adjustable parameters [34].

Two-parameter Weibull function model

There is little literature that explains the dependence of temperature on the activity coefficient in equilibrium solutions. The activity coefficient in a solution is a function of T and x, but in the direction of increasing temperature, the saturation concentration approaches unity while converging with the ideal case at the limit of Tm, and the following boundary conditions explain the equilibrium activity coefficient [35, 36]:

$$ln(\gamma_3)_{eq} = 0 \tag{3}$$

$$\left(\frac{\partial ln\gamma_3}{\partial(1/T)}\right)_{eq} = 0 \tag{4}$$

$$\left(\frac{\partial^2 ln\gamma_3}{\partial\left(1/T^2\right)}\right)_{eq} = 0 \tag{5}$$

At $T = Tm$

Svärd and Rasmuson [36] identified the necessary boundary conditions for prediction of compound solubilities by extrapolation at higher or lower temperatures to the melting point. They proposed a model that meets these boundary conditions and the mathematical formula used in the probability theory and statistics of the Weibull distri-

bution was adopted. Equation 6 shows the temperature dependence of the activity coefficient of a solution in equilibrium:

$$ln\gamma_3)_{eq} = \frac{A}{T}\left(1 - e^{-\left(\frac{B}{T} - \frac{B}{T_m}\right)^C}\right) \tag{6}$$

where: A and B are adjustable parameters, C is a parameter that has to be above 2 in order to satisfy two boundary conditions in equation 2, Tm refers to the melting point of the substance.

van't Hoff Equation

The van't Hoff equation is also a semi-empirical equation, which reveals the relationship between the mole fraction solubility and the temperature in an ideal solution by taking the solvent effect into account [37].

$$\ln x_3 = A + \frac{B}{T} \tag{7}$$

A and B are parameters, which can be related to thermodynamic parameters such as dissolution enthalpy and dissolution entropy [38].

Buchowski-Ksiazaczak λh model

In 1980, based on the generalized relationship, the Buchowski-Ksiazaczak λh equation was first proposed, which contains two parameters and is widely used to correlate solubility data:

$$\ln\left[1 + \frac{\lambda\left(1 - x_3\right)}{x_3}\right] = \lambda h\left(\frac{1}{T} - \frac{1}{T_m}\right) \tag{8}$$

where λ and h are the two parameters of the λh model, and Tm represents the melting point of drug [18, 39, 40].

Results and discussion

The solubilities of sulfamerazine and sulfamethazine in mixtures of (methanol + water), (ethanol + water) and (1-propanol + water) were taken from Delgado and Martinez [6, 7, 41, 42].

Table 1. The Apelblat modified equation, van't Hoff-Yaws model, two-parameter Weibull function model, van't Hoff and Buchowski-Ksiazaczak λh equations parameters for sulfamerazine in (methanol + water), (ethanol + water) and (1-propanol + water) cosolvent mixtures.

w_1	Modified Apelblat			van't Hoff-Yaws			Weibull		van't Hoff		λh model	
	A	*B*	*C*	*A*	*B*	*C*	*A*	*B*	*A*	*B*	λ	*h*
SMR 1-Propanol												
0.0	11.733	-4332.7	-1.443	1.218	-3395.8	-75706.3	1756.583	4790.2	-3902.5	2.066	0.004	1098107.6
0.1	207.504	-13160.4	-30.477	-12.321	5288.0	-1395432.3	1529.670	5741.3	-3918.6	2.856	0.008	515871.6
0.2	128.602	-9678.2	-18.525	-5.342	1735.6	-878682.6	1255.073	4178.3	-4084.0	4.288	0.023	176729.3
0.3	237.843	-14706.3	-34.627	-12.016	6317.1	-1595026.4	1061.762	1822.0	-4210.6	5.346	0.052	80894.9
0.4	258.769	-15576.6	-37.720	-13.414	7329.3	-1738227.0	948.087	1718.9	-4147.9	5.521	0.070	59160.0
0.5	-8.135	-3382.4	2.002	6.315	-4601.0	92695.2	855.882	1681.0	-3989.7	5.308	0.077	51839.0
0.6	479.454	-25188.8	-70.695	-30.623	17707.3	-3252548.9	780.317	4194.3	-3765.9	4.799	0.071	52700.6
0.7	-181.060	4804.3	27.610	18.108	-11921.1	1266047.4	723.333	4217.9	-3569.6	4.343	0.065	54143.5
0.8	169.983	-10775.3	-24.820	-9.125	4302.4	-1144589.1	715.266	4014.7	-3255.3	3.345	0.044	73386.4
0.9	191.497	-11789.1	-28.036	-10.943	5317.2	-1304296.6	779.124	3969.7	-3301.1	3.286	0.038	86090.1
1.0	110.035	-8330.5	-15.892	-4.912	1485.9	-757562.1	977.737	4157.0	-3532.3	3.393	0.027	128938.1
SMR Methanol												
0.0	11.733	-4332.7	-1.443	1.218	-3395.8	-75706.3	1756.583	4790.2	-3902.5	2.066	0.004	1098107.6
0.1	45.638	-6212.3	-6.251	0.018	-2105.2	-335401.6	1680.233	6083.9	-4373.0	3.847	0.008	516340.7
0.2	-164.225	2701.7	25.412	19.426	-12898.6	1196701.4	1553.577	1543.7	-4991.0	6.370	0.032	158011.0
0.3	-558.912	20641.6	84.194	48.794	-30586.4	3895071.0	1441.694	1474.0	-4890.6	6.438	0.041	118948.9

Table 1. *(Continuation.)*

0.4	-392.259	13502.8	59.235	35.103	-22420.9	2722413.1	1277.004	1623.8	-4470.3	5.529	0.038	118728.4
0.5	136.814	-10081.8	-19.586	-4.087	1550.7	-862791.0	1008.556	1783.0	-4134.5	5.273	0.056	73679.2
0.6	-376.555	13276.7	56.848	33.866	-21370.8	2638811.2	873.057	1632.2	-3963.8	5.175	0.070	55990.3
0.7	-545.947	21046.8	82.066	46.577	-28994.6	3813062.5	769.548	1582.9	-3852.6	5.155	0.085	44784.0
0.8	-122.599	2262.6	18.875	13.818	-9330.6	889742.6	676.185	4044.3	-3467.1	4.163	0.066	51720.4
0.9	240.901	-13903.5	-35.368	-14.077	7428.7	-1607687.2	618.454	3816.6	-3188.2	3.441	0.055	57373.5
1.0	-34.039	-1016.3	5.332	4.481	-4279.5	249514.5	575.828	3969.2	-2638.5	1.784	0.029	89196.2
SMR Ethanol												
0.0	11.733	-4332.7	-1.443	1.218	-3395.8	-75706.3	1756.583	4790.2	-3902.5	2.066	0.004	1098107.6
0.1	398.233	-22500.8	-58.524	-23.772	12856.1	-2669109.2	1626.870	3896.7	-4742.6	5.222	0.016	291001.5
0.2	177.760	-12785.5	-25.436	-5.213	2313.7	-1119243.7	1458.665	1493.9	-5048.4	6.887	0.047	106580.9
0.3	-59.975	-1617.7	9.854	11.564	-7864.6	494133.8	1217.839	1529.0	-4594.2	6.156	0.055	82964.2
0.4	137.821	-10195.4	-19.701	-4.304	1746.6	-904578.2	1019.852	1681.7	-4221.9	5.536	0.061	68567.3
0.5	-184.483	4585.1	28.254	19.628	-12712.8	1323340.2	871.392	1659.3	-3978.2	5.223	0.072	55058.6
0.6	119.973	-8932.7	-17.167	-3.667	1349.4	-769384.0	770.688	4134.3	-3723.3	4.690	0.069	53586.1
0.7	-314.192	10805.8	47.448	28.299	-18072.7	2196385.8	714.500	4712.3	-3584.8	4.421	0.069	51807.5
0.8	175.960	-11055.5	-25.694	-9.503	4581.4	-1189175.1	697.835	3941.5	-3279.0	3.479	0.048	67579.1
0.9	202.078	-12286.5	-29.581	-11.294	5626.5	-1355489.4	744.558	3953.0	-3319.5	3.458	0.043	75466.0
1.0	-497.214	19042.1	74.652	40.995	-25998.1	3395639.1	835.163	2998.7	-3623.7	4.155	0.049	73745.7

The experimental solubility data calculations were correlated with Apelblat modified equation (1), Yaws model (2), two-parameter Weibull function model (4), van't Hoff (5), Buchowski-Ksiazaczak λh (6) using *Python 3.6* version using *Pandas* and *NumPy Library*, the parameters of the models were estimated with *SciPy Library* and plots were made with *Plotly Library*.

Table 1 and table 3 show the parameters of the equations of Apelblat modified, van't Hoff-Yaws, two-parameter Weibull function model, van't Hoff, Buchowski-Ksiazaczak λh, for the solubility of SMR and SMT in (methanol + water), (ethanol + water) and (1-propanol + water) cosolvents mixtures.

The figure 3, 4 and 5 show the experimental data *vs.* the estimated data of sulfamerazine in cosolvent mixtures, linear holdings are obtained. Table 2 shows correlation coefficients equal to 0.99, corroborating that these models show good agreement with the experimental solubility data.

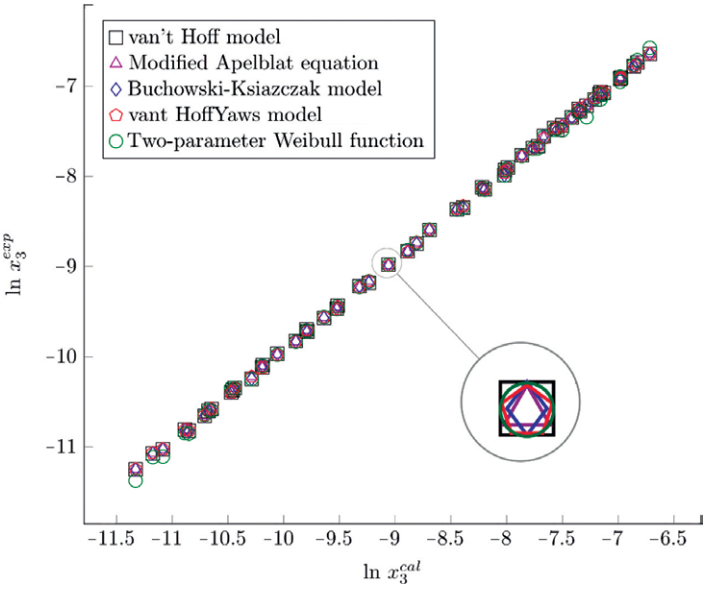

Figure 3. Experimental solubility *vs* estimated solubility by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model and two-parameter Weibull function model of sulfamerazine in (methanol + water) mixtures.

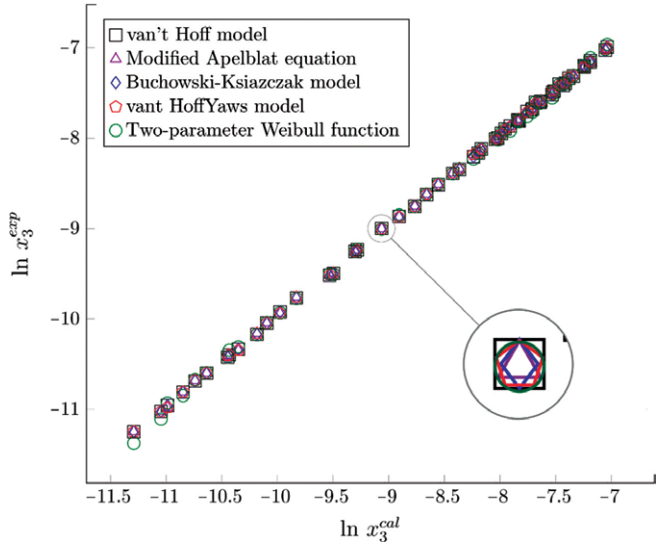

Figure 4. Experimental solubility *vs* estimated solubility by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model and two-parameter Weibull function model of sulfamerazine in (ethanol + water) mixtures.

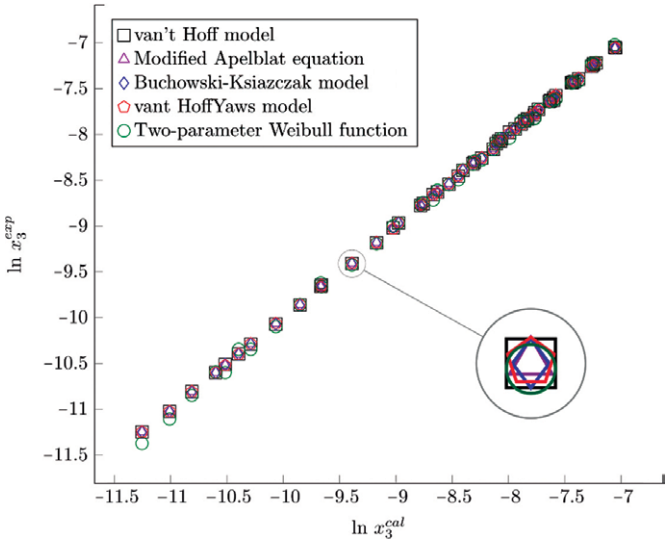

Figure 5. Experimental solubility *vs* estimated solubility by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model and two-parameter Weibull function model of sulfamerazine in (propanol + water) mixtures.

The values of the obtained equation parameters of the solubility studied were estimated by minimizing the value of the mean squared deviation (RMSD), equation 9, and the mean absolute percentage error (MAPE) shown in equation 10, as criteria to assess the quality of the fit and the comparison between the models. The difference between these two parameters is that MAPE express precision as a percentage, it measures the size of the absolute error in percentage. While the RMSD, it is a comparative measure between two sets of data, in this case the experimental and the estimated value.

$$RMSD = \sqrt[2]{\frac{1}{N}\sum_{i=1}^{N}\left(x_i^{est} - x_i^{exp}\right)^2} \tag{9}$$

where: x_i^{est} is the estimated mole fraction value, x_i^{exp} is the experimental mole fraction value and N is the number of experimental points.

$$MAPE = \frac{1}{N}\sum_{i=1}^{N}\left|\frac{\left(x_i^{est} - x_i^{exp}\right)}{x_i^{exp}}\right| * 100 \tag{10}$$

Table 2 shows the statistical measurements of sulfamerazine in cosolvents mixtures, when evaluating the mean absolute percentage error (MAPE) and the mean square deviation (RMSD) it is evidenced that the modified Apelblat and van't Hoff-Yaws model have lowest percentage in the three solvents, 1.1% in methanol and ethanol and 0.6% in propanol, therefore these models are the ones that have the best agreement with the experimental solubility data, in the same way the Buchowski-Ksiazczak model and van't Hoff model have equal MAPE values being a value of 1.5% in methanol, 1.2% in ethanol and 0.8% in 1-propanol. However, these values are very similar for the four models, which shows good agreement with the experimental data of solubility of sulfamerazine. Additionally, Two-parameter Weibull function model shows higher values for absolute percentage error in three solvents, it is the weakest model to correlate the solubility data of the SMR at different temperatures.

Table 2. Statistical measures by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model and two-parameter Weibull function model of sulfamerazine in (methanol + water), (ethanol + water) and (1-propanol + water) mixtures.

Model	MAPE %	RMSD * 105	R2
Methanol			
Modified Apelblat equation	1.1	0.60	0.99973
Buchowski-Ksiazczak model	1.5	0.73	0.99960
van't Hoff model	1.5	0.73	0.99960
van't Hoff-Yaws model	1.1	0.60	0.99974
Two-parameter Weibull function	2.6	2.29	0.99614
Ethanol			
Modified Apelblat equation	1.1	0.43	0.99973
Buchowski-Ksiazczak model	1.2	0.56	0.99954
van't Hoff model	1.2	0.56	0.99954
van't Hoff-Yaws model	1.1	0.43	0.99973
Two-parameter Weibull function	2.1	1.00	0.99854
1-Propanol			
Modified Apelblat equation	0.6	0.23	0.99990
Buchowski-Ksiazczak model	0.8	0.41	0.99969
van't Hoff model	0.8	0.41	0.99970
van't Hoff-Yaws model	0.6	0.23	0.99990
Two-parameter Weibull function	2.6	0.99	0.99823

The figure 6, 7 and 8 show the experimental data *vs.* the estimated data of sulfamethazine y cosolvent mixtures, linear holdings are obtained. Table 4 shows correlation coefficients equal to 0.99, corroborating that these models show good agreement with the experimental solubility data.

Table 3. The Apelblat modified equation, van't Hoff-Yaws model, two-parameter Weibull function model, van't Hoff and Buchowski-Ksiazaczak λh equations parameters for sulfamethazine in (methanol + water), (ethanol + water) and (1-propanol + water) cosolvent mixtures.

w_1	Modified Apelblat			van't Hoff-Yaws			Weibull		van't Hoff		λh model	
	A	*B*	*C*	*A*	*B*	*C*	*A*	*B*	*A*	*B*	λ	*h*
SMT 1-Propanol												
0.0	-29.735	-2645.3	4.938	5.595	-5459.2	199425.5	1785.7	17758299.2	-4169.4	3.511	0.004	941865.3
0.1	-257.059	7864.0	38.817	22.989	-15676.3	1783934.1	1498.6	17681476.5	-3908.3	3.592	0.008	472168.4
0.2	-431.979	15808.9	65.017	37.238	-23708.1	3001369.3	1188.3	17460186.3	-3909.2	4.604	0.022	172087.1
0.3	-560.615	21798.3	84.177	46.373	-29055.3	3838862.1	1001.8	17165885.0	-3761.4	4.730	0.035	107231.1
0.4	-854.144	35223.9	127.873	68.256	-42230.8	5862557.5	864.2	16769658.0	-3592.3	4.627	0.044	80173.0
0.5	-408.747	15274.8	61.504	35.042	-22059.1	2831894.2	765.4	16391865.3	-3380.4	4.258	0.047	70268.7
0.6	-278.147	9457.58	42.050	25.407	-16153.3	1949227.4	693.7	15991168.5	-3294.3	4.210	0.054	60066.6
0.7	-247.743	8098.78	37.544	23.475	-14883.2	1757892.8	640.2	15651579.0	-3290.8	4.374	0.064	50554.8
0.8	-184.613	5281.2	28.134	18.205	-11683.4	1278195.5	621.5	15486345.3	-3256.2	4.322	0.065	49007.6
0.9	-129.034	2946.9	19.732	13.631	-9207.1	935364.1	666.0	15839057.3	-3046.3	3.492	0.043	68737.1
1.0	-1170.531	50403.7	174.480	88.345	-55451.4	8025134.5	868.3	16811669.7	-2601.9	1.383	0.012	202486.7
SMT Methanol												
0.0	-29.735	-2645.3	4.938	5.595	-5459.2	199425.5	1785.7	17758299.2	-4169.4	3.511	0.004	941865.3
0.1	129.514	-10010.8	-18.601	-4.783	1329.4	-863936.4	1647.8	17730292.1	-4377.9	4.637	0.009	496244.4
0.2	-218.239	5588.4	33.340	22.461	-14730.99	1547498.0	1485.2	17681247.1	-4520.3	5.628	0.017	257011.1

Table 3. *(Continuation.)*

0.3	13.143	-4973.8	-0.953	6.857	-4756.5	11 167.7	1307.7	17 578 586.5	-4671.4	6.698	0.037	125 117.8
0.4	-95.146	-123.3	15.306	15.624	-9614.9	735 315.2	1114.7	17 373 506.8	-4752.7	7.591	0.077	61 829.6
0.5	48.936	-6669.9	-6.039	5.173	-2891.7	-295 165.9	958.0	17 074 271.4	-4854.8	8.435	0.144	33 604.5
0.6	-2.496	-4376.69	1.715	10.025	-5507.7	92 693.8	821.0	16 700 326.8	-4897.8	9.022	0.237	20 623.5
0.7	20.927	-5412.5	-1.711	8.439	-4288.6	-91 772.1	690.1	16 034 911.0	-4904.9	9.472	0.367	13 321.1
0.8	-396.269	13 628.2	60.371	39.239	-22 954.2	2 770 010.5	574.4	15 174 546.0	-4707.1	9.206	0.428	10 973.7
0.9	-184.256	4382.4	28.648	22.158	-12 826.3	1 291 516.8	508.6	14 502 689.3	-4327.9	8.186	0.343	12 569.9
1.0	150.052	-10 567.0	-21.202	-2.918	2293.7	-974 832.5	472.4	14 064 973.4	-4141.5	7.697	0.311	13 241.8
SMT Ethanol												
0.0	-29.735	-2645.3	4.938	5.595	-5459.2	199 425.5	1785.7	17 758 299.2	-4169.4	3.511	0.004	941 865.3
0.1	-481.298	17 498.9	72.437	41.808	-26 736.9	3 375 732.6	1594.0	17 720 052.8	-4461.0	5.109	0.012	384 351.8
0.2	-758.209	29 664.2	113.991	64.651	-39 744.3	5 281 240.3	1378.3	17 639 351.2	-4929.8	7.307	0.040	124 134.9
0.3	-560.132	20664.7	84.652	50.640	-30 696.7	3 894 112.3	1152.2	17 427 724.1	-5018.1	8.331	0.092	54 604.6
0.4	-542.299	20 002.0	82.016	49.224	-29 619.1	3 751 396.4	974.9	17 117 421.5	-4895.7	8.511	0.142	34 295.0
0.5	-475.383	17 254.9	71.981	43.836	-26 340.7	3 299 394.6	823.9	16 695 097.4	-4590.3	8.010	0.164	27 824.3
0.6	-507.294	18 838.7	76.716	46.371	-27 800.8	3 543 259.1	711.6	16 171 414.4	-4429.0	7.851	0.197	22 390.7
0.7	-381.898	13 433.0	57.933	36.280	-21 829.6	2 682 154.3	644.4	15 707 837.2	-4145.6	7.147	0.176	23 334.4
0.8	-311.337	10 540.2	47.275	29.750	-18 140.2	2 174 284.9	614.6	15 431 447.9	-3813.2	6.161	0.131	28 747.5
0.9	-363.547	13 055.1	54.939	33.211	-20 500.9	2 561 126.8	651.8	15 783 238.3	-3610.9	5.380	0.091	39 176.2
1.0	-422.913	15 818.4	63.684	36.342	-22 680.4	2 908 189.6	738.8	16 255 186.4	-3506.3	4.755	0.060	57 362.9

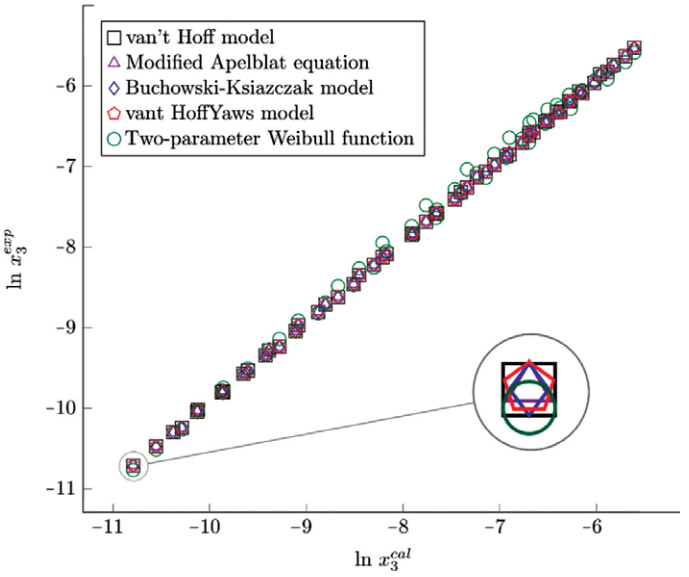

Figure 6. Experimental solubility *vs* estimated solubility by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model, two-parameter Weibull function model of sulfamethazine in (methanol + water) mixtures.

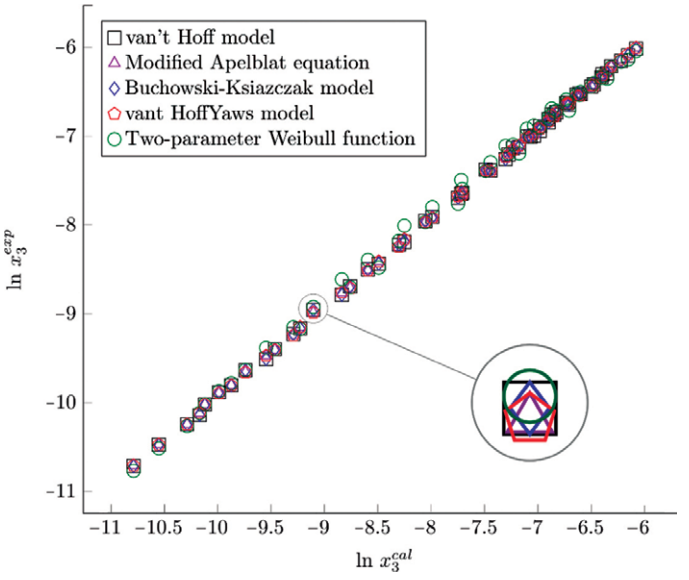

Figure 7. Experimental solubility *vs* estimated solubility by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model, two-parameter Weibull function model of sulfamethazine in (ethanol + water) mixtures.

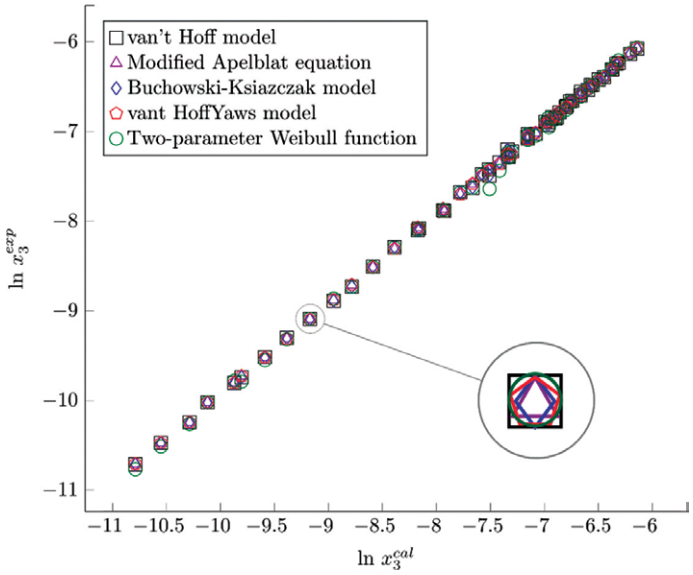

Figure 8. Experimental solubility *vs.* estimated solubility by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model, two-parameter Weibull function model of sulfamethazine in (1-propanol + water) mixtures.

Table 4 shows the statistical measurements of sulfamethazine in cosolvent mixtures, when evaluating the mean absolute percentage error (MAPE), the same behavior as for sulfamerazine is evidenced. The models that show the best relationship are the modified Apelblat model and the van't Hoff-Yaws model. There is a good correlation between the experimental results and those obtained theoretically in this study with these models. Subsequently, a good correlation is found with the data of the Buchowski-Ksiazczak model and van't Hoff model and finally for the Two-parameter Weibull function model the mean absolute percentage error has higher values in the case of the three solvents. For SMR and SMT, it is evident that for most models, the lowest MAPE values are found for the propanol.

Table 2 and table 4 show that in all cases the same behavior mentioned above was obtained for MAPE when the mean square deviation (RMSD) is analyzed, the following behavior is found: **RMSD:** Apelblat modified model = van't Hoff-Yaws model < Buchowski-Ksiazaczak λh = van't Hoff model < Two-parameter Weibull function model.

This statistical measure corroborates that the models that have the best fit with the experimental measures are Apelblat modified model and van't Hoff-Yaws model in all co-solvent mixtures.

Table 4. Statistical measures by van't Hoff, Apelblat modified, Buchowski-Ksiazaczak λh, van't Hoff-Yaws model, two-parameter Weibull function model of sulfamethazine in (methanol + water), (ethanol + water) and (1-propanol + water) mixtures.

Model	MAPE %	RMSD * 105	R2
Methanol			
Modified Apelblat equation	1.2	2.06	0.99 960
Buchowski-Ksiazczak model	1.3	2.28	0.99 951
van't Hoff model	1.3	2.28	0.99 951
van't Hoff-Yaws model	1.2	2.07	0.99 960
Two-parameter Weibull function	5.3	8.20	0.99 368
Ethanol			
Modified Apelblat equation	1.3	1.41	0.99 957
Buchowski-Ksiazczak model	1.9	1.96	0.99 917
van't Hoff model	2.0	1.98	0.99 915
van't Hoff-Yaws model	1.3	1.41	0.99 957
Two-parameter Weibull function	4.3	3.73	0.99 698
1-Propanol			
Modified Apelblat equation	1.0	1.21	0.99 962
Buchowski-Ksiazczak model	1.6	1.81	0.99 915
van't Hoff model	1.7	1.85	0.99 912
van't Hoff-Yaws model	1.0	1.21	0.99 962
Two-parameter Weibull function	4.0	4.24	0.99 537

Conclusions

The use of the Python programming language has proven to be very useful to determine the parameters of the different models developed in this research. The theoretical results, obtained through each of the mathematical models used, present small deviations with respect to the experimental data, also indicating the relevance of the mathematical models to calculate the solubility data of sulfamerazine and sulfamethazine in co-solvent mixtures.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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