Scientific research article / https://doi.org/10.15446/rcciquifa.v52n2.110747

Drugs solubility prediction in mono-solvents at various temperatures using a minimum number of experimental data points

Soma Khezri[1,2], Parisa Jafari[3,4], Abolghasem Jouyban[5,6]*

[1]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran.

[2]Biotechnology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

[3]Research Center for Pharmaceutical Nanotechnology, Tabriz University of Medical Sciences, Tabriz, Iran.

[4]Kimia Idea Pardaz Azarbayjan (KIPA) Science Based Company, Tabriz University of Medical Sciences, Tabriz, Iran.

[5]Pharmaceutical Analysis Research Center and Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

[6]Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

*Author to whom correspondence should be addressed: ajouyban@hotmail.com

Received: February 10, 2023
Corrected: May 2, 2023
Accepted: May 7, 2023

Summary

Introduction: Solubility is one of the most basic information in a re-crystallization process and in many cases, there are only a few grams (or even mg or μg) of an expensive pharmaceutical or fine chemical to make a large number of crystallization tests. **Aim:** To develop a computational procedure for prediction of drugs solubility in any mono-solvent and temperature of interest using a minimum number of experimental data points. **Methods:** For achieving this purpose, here, the available solubility data sets were collected from the recently published articles and selected a minimum data point of each dataset to train a simple model based on the well-known van't Hoff equation combined with Abraham, Hansen and Catalan parameters as variables presenting the drug-solvent interactions in the solutions. After obtaining the model parameters, the next solubility data in each dataset was predicted by extrapolation method and the accuracy of model was estimated using the computation the mean percentage deviation of the back-calculated data. **Results:** The model adequately trained using a minimum data point could be used as a practical strategy for predic-

ting the solubility of drugs in mono-solvents at different temperatures with acceptable prediction error and using minimum experimental efforts.

Keywords: Solubility prediction, extrapolation method, mono-solvent systems, van't Hoff equation, Hansen parameters, Catalan parameters.

Resumen

Predicción de solubilidad de fármacos en mono-solventes a varias temperaturas utilizando un número mínimo de puntos de datos experimentales

Introducción: la solubilidad es una de las informaciones más básicas en un proceso de recristalización y, en muchos casos, solo hay unos pocos gramos (o incluso mg o μg) de un producto farmacéutico o químico fino costoso para realizar una gran cantidad de pruebas de cristalización. **Objetivo**: desarrollar un procedimiento computacional para la predicción de la solubilidad de los fármacos en cualquier mono-solvente y la temperatura de interés utilizando un número mínimo de puntos de datos experimentales. **Método**: para lograr este propósito, aquí, los conjuntos de datos de solubilidad disponibles se recopilaron de los artículos publicados recientemente y se seleccionaron puntos de datos mínimos de cada conjunto de datos para entrenar un modelo simple basado en la conocida ecuación de van't Hoff combinada con los parámetros de Abraham, Hansen, Catalán, como variables de presentación de las interacciones fármaco-disolvente en las soluciones. Después de obtener los parámetros del modelo, los siguientes datos de solubilidad en cada conjunto de datos se predijeron mediante el método de extrapolación y la precisión del modelo se estimó mediante el cálculo de la desviación porcentual media de los datos retrocalculados. **Resultados:** el modelo entrenado adecuadamente utilizando puntos de datos mínimos podría utilizarse como una estrategia práctica para predecir la solubilidad de fármacos en mono-solventes a diferentes temperaturas con un error de predicción aceptable y utilizando esfuerzos experimentales mínimos.

Palabras clave: Predicción de solubilidad, método de extrapolación, sistemas mono-solventes, ecuación de van't Hoff, parámetros de Hansen, parámetros de Catalán.

Resumo

Previsão de solubilidade de drogas em monossolventes em várias temperaturas usando um número mínimo de pontos de dados experimentais

Introdução: a solubilidade é uma das informações mais básicas em um processo de recristalização e, em muitos casos, existem apenas alguns gramas (ou mesmo mg ou μg) de um produto farmacêutico ou químico fino caro para fazer um grande número de testes de cristalização. **Objetivo**: desenvolver um procedimento computacional para prever a solubilidade de drogas em quaisquer monossolventes e temperatura de interesse usando um número mínimo de pontos de dados experimentais. **Métodos**: para atingir esse objetivo, aqui, os conjuntos de dados de solubilidade disponíveis foram coletados dos artigos publicados recentemente e selecionados um mínimo de pontos de dados de cada conjunto de dados para treinar um modelo simples baseado na conhecida equação de van't Hoff combinada com os parâmetros de Abraham, Hansen e Catalan como variáveis apresentando as interações fármaco-solvente nas soluções. Depois de obter os parâmetros do modelo, os próximos dados de solubilidade em cada conjunto de dados foram previstos pelo método de extrapolação e a precisão do modelo foi estimada usando o cálculo do desvio percentual médio dos dados calculados de volta. **Resultados**: o modelo adequadamente treinado usando um mínimo de pontos de dados pode ser usado como uma estratégia prática para predizer a solubilidade de drogas em monossolventes em diferentes temperaturas com erro de predição aceitável e usando esforços experimentais mínimos.

Palavras-chave: Previsão de solubilidade, método de extrapolação, sistemas monossolvente, equação de van't Hoff, Parâmetros de Hansen, Parâmetros catalães.

Introduction

In recent times, research upon solubility of a drug/drug-like molecules in the mono-solvents at different temperatures as an important physico-chemical property has become a growing focus in the pharmaceutical fields. The data is required from the early stage of drug synthesis and/or extraction from the natural sources to the large-scale extraction and/or purification stage, wherein the knowledge of solubility is needed to control the desired polymorphic form, supersaturation, yield and particle size [1-5]. Among different mono-solvents, water is a unique solvent in the biologically related processes and aqueous solubility plays a very crucial role in drug discovery and development.

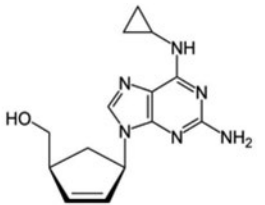
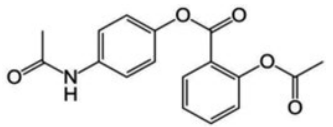
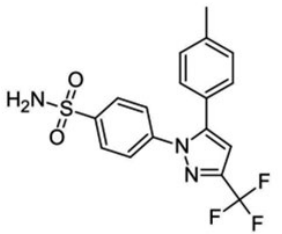
However, 70% [6] or 90% [7] of drug candidates and 40% of the marketed drugs [7] possess low solubility in water and this may cause some problems in their clinical applications and so, the organic solvents are needed for dissolving lipophilic drugs in appropriate dosage forms such as soft gelatin capsules, suppositories, injections and topical preparations. As known, the experimental determination of solubility of a drug/drug-like molecule is still the most reliable method for achieving accurate and valid data and the measurement procedure is a time-consuming process. On the other hand, there are only a few grams/milligrams or even micrograms of an expensive drug/drug-like compound to perform a large number of experiments which is considered as another main limitation of experimental determination. Therefore, any alternative method such as predictive models can be valuable tools for pharmaceutical scientists. Models for the estimation the solubility of drug/drug-like molecules were reviewed by various research groups [8-14].

A high accuracy, simplicity and less required input data of the models are considered as important parameters in their acceptance by the investigators from the viewpoint of pharmaceutical applications. So, the models based on the state equations did not attract more attention in this area. Besides, the purely predictive activity coefficient models such as UNIFAC are needed the bulk properties of the solution to estimate the activity coefficient; hence, they have certain shortcomings because of the complexity of the solute molecules or severe nonideality of the solution [15]. In these cases, semi-empirical or semi-predictive thermodynamic models with a few adjustable parameters can be utilized. The adjustable parameters are trained by a few experimental determinations followed then by extrapolating of their predictive capability over a wide range of operating conditions. Recently, our research group suggested a simple model based on the well-known van't Hoff equation which combined with Abraham, Hansen and Catalan parameters as variables representing the drug-solvent interactions in the solutions to correlate the solubility of drugs in various mono-solvents at working temperatures [16]. The suggested model correlated the solubility of each drug in various mono-solvents at various temperatures with an acceptable accuracy. To continue our systematic investigations for providing computational procedures to predict the solubility of drugs in mono-solvents, the main goal of present study is to collect a minimum number of experimental data points for a drug dissolved in a given mono-solvents at various temperatures for describing a computational procedure to predict the solubility of the drugs in any temperature of interest.

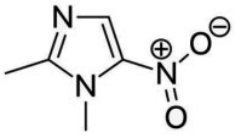
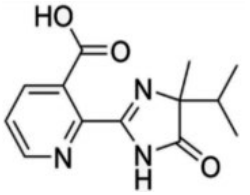
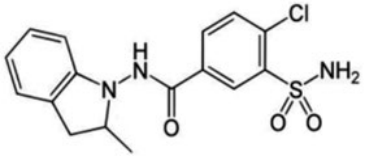
Experimental data and computational section

Details of the collected solubility data of drugs in the mono-solvents at various temperatures from the literature [17-61] are listed in Table 1.

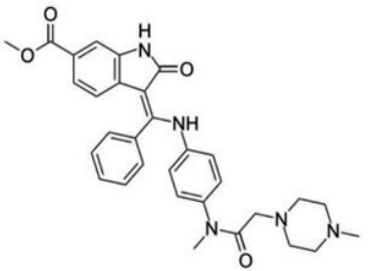
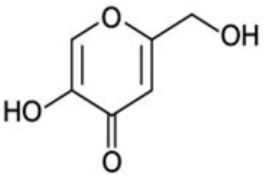
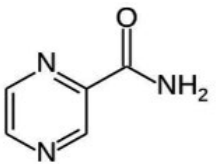
Table 1. A brief summary of the drugs characterization in mono-solvents taken from the literature [17-61], the number of data points in each data set (N) and references.

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Abacavir	286.332	$C_{14}H_{18}N_6O$		0.39	120	[17]
Benorilate	313.309	$C_{17}H_{15}NO_5$		2.48	107	[37]
Celecoxib	381.372	$C_{17}H_{14}F_3N_3O_2S$		4.01	116	[49]

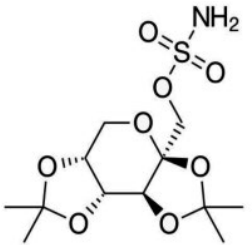
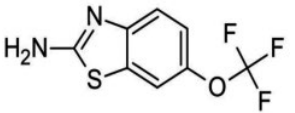
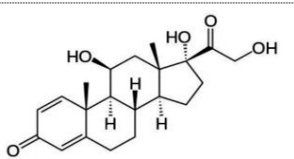
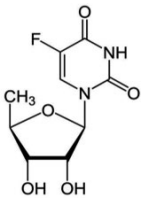
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Dimetridazole	141.130	$C_5H_7N_3O_2$		0.31	107	[50]
Imazapyr	261.280	$C_{13}H_{15}N_3O_3$		0.22	107	[47]
Indapamide	365.835	$C_{16}H_{16}ClN_3O_3S$		2.64	89	[55]

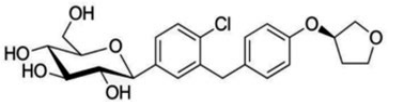
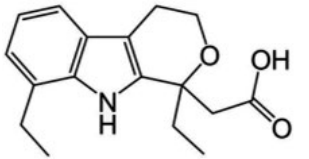
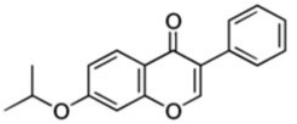
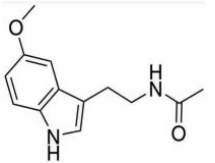
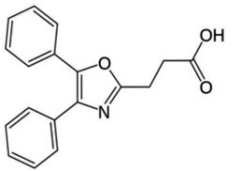
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Nintedanib	539.625	$C_{31}H_{33}N_5O_4$		2.79	94	[39]
Kojic acid	142.109	$C_6H_6O_4$		-0.50	134	[38]
Pyrazinamide	123.113	$C_5H_5N_3O$		-1.20	107	[28]

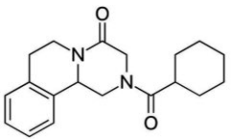
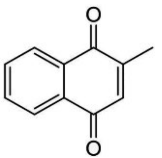
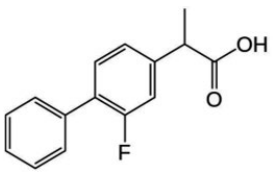
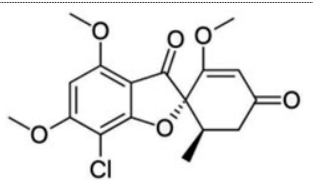
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Topiramate	339.362	$C_{12}H_{21}NO_8S$		0.13	139	[53]
Riluzole	234.198	$C_8H_5F_3N_2OS$		3.40	119	[30]
Prednisolone form II	360.444	$C_{21}H_{28}O_5$		1.27	98	[52]
Doxifluridine	246.192	C9H11FN2O5		-1.20	129	[34]

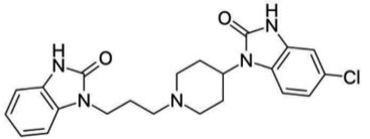
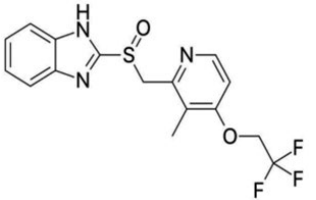
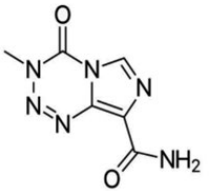
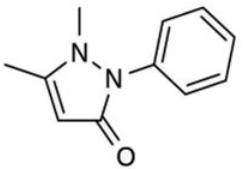
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Empagliflozin	450.910	$C_{23}H_{27}ClO_7$		1.66	80	[61]
Etodolac	287.353	$C_{17}H_{21}NO_3$		3.44	115	[45]
Ipriflavone	280.318	$C_{17}H_{20}N_4O_6$		3.95	116	[36]
Melatonin	232.278	$C_{13}H_{16}N_2O_2$		1.15	119	[46]
Oxaprozin	293.317	$C_{18}H_{15}NO_3$		3.46	126	[35]

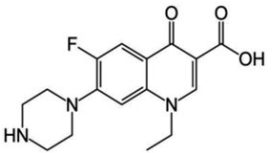
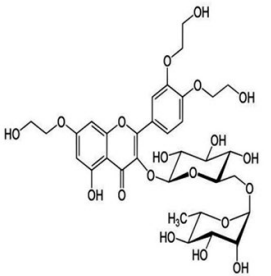
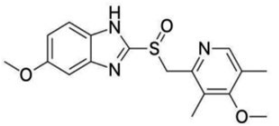
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Praziquantel	312.406	$C_{19}H_{24}N_2O_2$		2.30	109	[33]
Vitamin K3	172.180	$C_{11}H_8O_2$		1.89	78	[43]
Flurbiprofen	244.261	$C_{15}H_{13}FO_2$		3.94	107	[56]
Griseofulvin	352.766	$C_{17}H_{17}ClO_6$		2.17	107	[25]

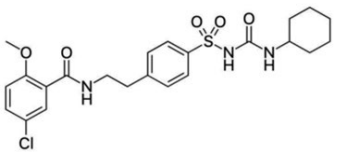
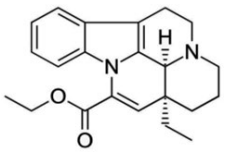
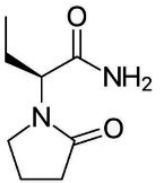
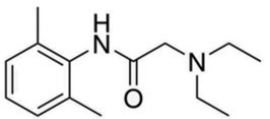
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Domperidone	425.911	$C_{22}H_{24}ClN_5O_2$		2.90	107	[60]
Lansoprazole	369.361	$C_{16}H_{14}F_3N_3O_2S$		3.03	107	[42]
Temozolomide	194.151	$C_6H_6N_6O_2$		-0.28	89	[32]
Antipyrine	188.226	$C_{11}H_{12}N_2O$		1.22	89	[18]

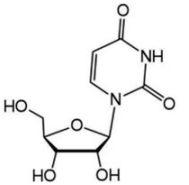
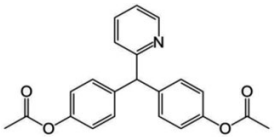
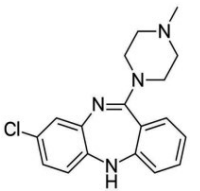
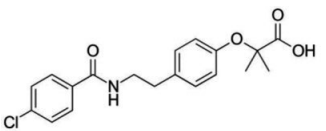
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Norfloxacin	319.331	$C_{16}H_{18}FN_3O_3$		-0.92	87	[27]
Troxerutin	742.675	$C_{33}H_{42}O_{19}$		-2.50	87	[31]
Omeprazole	345.416	$C_{17}H_{19}N_3O_3S$		2.43	95	[29]

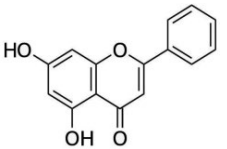
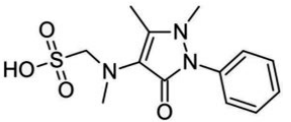
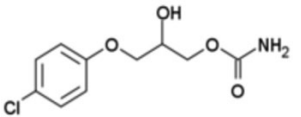
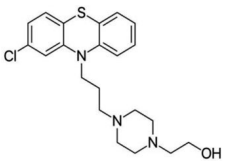
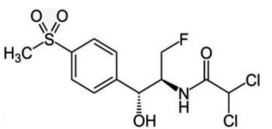
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Glibenclamide	494.004	$C_{23}H_{28}ClN_3O_5S$		3.79	98	[24]
Vinpocetine	350.462	$C_{22}H_{26}N_2O_2$		4.07	80	[54]
Levetiracetam	170.212	$C_8H_{14}N_2O_2$		-0.59	88	[23]
Lidocaine	234.337	$C_{14}H_{22}N_2O$		2.84	71	[44]

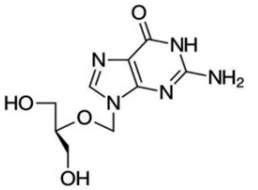
(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Uridine	244.201	$C_9H_{12}N_2O_6$		-2.40	89	[48]
Bisacodyl	361.391	$C_{22}H_{19}NO_4$		3.61	29	[21]
Clozapine	326.823	$C_{18}H_{19}ClN_4$		3.40	104	[40]
Bezafibrate	361.819	$C_{19}H_{20}ClNO_4$		3.99	292	[19]

(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Chrysin	254.238	$C_{15}H_{10}O_4$		3.01	143	[58]
Dipyrone	351.360	$C_{13}H_{16}N_3NaO_4S$		-0.82	88	[41]
Chlorphenesin	202.635	$C_9H_{11}ClO_3$		1.10	89	[20]
Perphenazine	403.969	$C_{21}H_{26}ClN_3OS$		3.69	107	[51]
Florfenicol Form A	358.210	$C_{12}H_{14}Cl_2FNO_4S$		0.67	98	[57]

(*Continued*)

Solute	Molecular weight ($g \cdot mol^{-1}$)	Molecular formula	Structure	Log *P*	N	Ref
Ganciclovir form I	255.231	$C_{99}H_{13}N_5O_4$		-2.20	80	[22]

For many pharmaceutical purposes, especially in re-crystallization investigations, it is essential to measure the solubility of drug/drug-like molecules in a given mono-solvent at different temperatures and to express the data as a solubility-temperature curve. Linear solubility-temperature plots are often considered desirable, due to: (i) they can be interpolated and extrapolated accurately; (ii) they can be treated by the common statistics of linear regression; and (iii) they can provide thermodynamic data for the solution process.

The van't Hoff equation (Eq. (1)) [62] is the simplest solubility-temperature function in the pharmaceutical science/industry which provides a good linear plot in most cases. This equation is expressed as:

$$\log S_{m,T} = A + \frac{B}{T} \tag{1}$$

where A and B denote the model parameters.

For wider temperature ranges which some deviations from linearity are observed, one may add $C \log T$ to the model as Eq. (2).

$$\log S_{m,T} = A + \frac{B}{T} + C \log T \tag{2}$$

in which C is another constant. For obtaining a better picture of the solute (drug/drug-like molecules)–solvent interactions which represents different physico-chemical properties of the solutions involving the solubility of a solute dissolved in a given solvent, it is necessary to introduce suitable parameters into the van't Hoff equation for quantification of these interactions. Hence, various parameters have been considered to quantify these interactions which occurred in the solutions such as Abraham solvation parameters (AP_i) [63], Hansen solubility parameters (HP_i) [64], and Catalan parameters (CP_i) [65]. *APi* can be calculated through the experimental solubility data of different solutes and display a quantitative picture of solute-solvent interactions in the solution where in, HP_i calculated by the help of a group contribution method [64] and have found applications in the polymer science and other fields. Catalan suggested a set of solvatochromic parameters for a generalized treatment of the solvent's effects [8] which includes solvent polarity/polarizability scale (*SPP*), solvent basicity scale (*SB*), and solvent acidity scale (*SA*), with *SPP* parameter recently split into two separate solvent di-polarity (*SdP*) and solvent polarizability (*SP*) scales [65]. In this respect, our research group [66-68] presented that the A and B terms of the van't Hoff equation for different drugs in a given solvent system could be correlated using Abraham solute parameters as:

$$\log S_{m,T} = (\alpha_0 + \alpha_1 E + \alpha_2 S + \alpha_3 A + \alpha_4 B + \alpha_5 V) + \left(\frac{\beta_0 + \beta_1 E + \beta_2 S + \beta_3 A + \beta_4 B + \beta_5 V}{T}\right) \quad (3)$$

In another work, a novel multiple linear regression model according to the van't Hoff equation and using a combination of AP_i, HP_i and CP_i instead of only AP_i suggested for an accurate correlation the solubility of a given drug in different mono-solvents at several temperatures as Eq. (4) [16].

$$\log S_T = \left[\alpha_o + \sum_{i=1}^{5} \alpha_{i,AP} AP_I + \sum_{i=1}^{3} \alpha_{i,HP} HP_i + \sum_{i=1}^{4} \alpha_{i,cp} CP_i\right] + \left[\frac{\beta_o + \sum_{i=1}^{5} \beta_{i\ AP} AP_I + \sum_{i=1}^{3} \beta_{i\ HP} HP_i + \sum_{i=1}^{4} \beta_{i,cp} CP_i}{T}\right] \quad (4)$$

in Eq. (4), α_i and β_i terms correspond to the model parameters determined by a regression analysis. The obtained results were promising and the suggested model could be recommended for practical applications in the chemical/pharmaceutical industries after some further studies. Based on the good accuracy of this simple model in correlation of drugs solubility data in mono-solvents at different temperatures, this model is used in present work to predict the solubility of drug/drug-like molecules in various mono-solvents at working temperatures. For prediction studies, a minimum number of experimental data points were selected as the training set from each data set taken places from the literature [17-61] and utilized to train the model. The rest of data points (prediction set) were predicted with the trained model by extrapolation method. Details of the collected solubility data are listed in Table 1 of supplementary information along with listing the numerical values of AP_i, HP_i and CP_i for the investigated solvents in Table 2. Since, the average percentage deviations (APD) value is a comparable value with relative standard deviation value for repeated experiments and its numerical value is not affected by the solubility unit expression; the APD was employed to check the accuracy of predictions and it computed by Eq. (5):

$$APD = \frac{100}{N} \sum \left(\frac{\left| S_{m,t}^{calculated} - S_{m,t}^{experimental} \right|}{S_{m,t}^{experimental}} \right) \quad (5)$$

here in N relates to the number of data points in each data set.

Eventually, the results of the suggested model were validated through a cross validation analysis using "leave one solvent out" method. In each step, one solvent's dataset has been excluded from the training process, model constants were calculated, and been utilized to predict the drug solubility in the excluded solvent. All mentioned analyses were performed by employing SPSS 16.0 software.

Table 2. List of the investigated solvents, their Catalan parameters [65], the Hansen solubility parameters [69] and the Abraham solvent parameters [Hoy software].

Solvent	Catalan parameters				Hansen solubility parameters			Abraham solvent parameters					
	SA	*SB*	*SP*	*SdP*	δ_d	δ_p	δ_h	**c**	**e**	**s**	**a**	**b**	**v**
1,2-Dichloroethane	0.74	0.03	0.77	0.13	14.65	11.26	8.80	0.183	0.294	-0.134	-2.801	-4.291	4.180
1,4-Dioxane	0.31	0.00	0.74	0.44	19.00	1.80	7.40	0.100	0.350	-0.080	-0.560	-4.830	4.170
2-Methyl-propan-1-ol	0.68	0.31	0.66	0.83	13.38	9.53	14.08	0.130	0.250	-0.980	0.160	-3.880	4.110
(±)-2-Ethyl-1-Hexanol	NA[a]	NA[a]	NA[a]	NA[a]	14.06	7.45	11.01	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]
Acetic acid	0.68	0.69	0.65	0.39	11.52	16.39	27.05	0.175	0.174	-0.454	-1.073	-2.789	3.725
Acetonitrile	0.97	0.04	0.65	0.29	11.59	12.95	16.34	0.410	0.080	0.330	-1.570	4.390	3.360
Benzene	0.27	0.00	0.79	0.12	18.40	0.00	2.00	0.140	0.460	-0.590	-3.100	-4.630	4.490
Butan-1-ol	0.66	0.34	0.67	0.81	16.00	5.70	15.80	0.170	0.400	-1.010	0.060	-3.960	4.040
Butan-2-ol	0.71	0.22	0.66	0.89	13.38	9.53	14.08	0.190	0.350	-1.130	0.020	-3.570	3.970
Butan-2-one	0.87	0.00	0.67	0.52	16.00	9.00	5.10	0.250	0.260	-0.080	-0.770	-4.860	4.150
Butyl acetate	0.54	0.00	0.67	0.53	14.49	7.74	6.53	0.250	0.360	-0.500	-0.870	-4.970	4.280
Pentyl acetate	NA[a]	NA[a]	NA[a]	NA[a]	14.63	7.31	6.25	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]
Chloroform	0.61	0.05	0.78	0.07	17.80	3.10	5.70	0.190	0.110	-0.400	-3.110	-3.510	4.400
Cyclohexane	0.00	0.00	0.68	0.07	16.80	0.00	0.20	0.160	0.780	-1.680	-3.740	-4.930	4.580
Cyclohexanone	0.75	0.00	0.77	0.48	17.80	6.30	5.10	0.040	0.230	0.060	-0.980	-4.840	4.320
Dichloromethane	0.77	0.04	0.76	0.18	18.20	6.30	6.10	0.319	0.102	-0.187	-3.058	-4.090	4.324
DMSO	1.00	0.07	0.83	0.65	18.40	16.40	10.20	-0.190	0.330	0.790	-1.260	-4.540	3.360
Ethane-1,2-diol	0.91	0.72	0.78	0.53	17.00	11.00	26.00	-0.270	0.580	-0.510	0.720	-2.620	2.730

Solvent	Catalan parameters				Hansen solubility parameters			Abraham solvent parameters					
	SA	***SB***	***SP***	***SdP***	δ_d	δ_p	δ_h	**c**	**e**	**s**	**a**	**b**	**v**
Ethanol	0.78	0.40	0.64	0.66	15.80	8.80	19.40	0.220	0.470	-1.040	0.330	-3.600	3.860
Ethyl acetate	0.60	0.00	0.66	0.54	15.80	5.30	7.20	0.328	0.369	-0.446	-0.700	-4.904	4.150
Ethyl format	0.71	0.00	0.65	0.48	15.50	8.40	8.40	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]	NA[a]
Formamide	1.01	0.55	0.81	0.41	10.17	17.29	23.38	-0.171	0.070	0.308	0.589	-3.152	2.432
Heptan-1-ol	0.50	0.30	0.71	0.91	14.08	7.80	12.21	0.035	0.398	-1.063	0.002	-4.343	4.317
Heptane	0.00	0.00	0.64	0.08	14.90	0.00	0.00	0.330	0.670	-2.060	-3.320	-4.730	4.540
Hexan-1-ol	0.55	0.32	0.70	0.88	15.90	5.80	12.50	0.120	0.490	-1.160	0.050	-3.980	4.130
Hexane	0.00	0.00	0.62	0.06	15.30	0.00	0.00	0.360	0.580	-1.720	-3.600	-4.760	4.340
iso-Propyl ether	0.32	0.00	0.63	0.66	13.18	7.97	9.03	0.181	0.285	-0.954	-0.956	-5.077	4.542
Methanol	0.90	0.61	0.61	0.55	15.10	12.30	22.30	0.280	0.330	-0.710	0.240	-3.320	3.550
Methyl acetate	0.64	0.00	0.65	0.53	12.68	11.42	11.79	0.351	0.223	-0.150	-1.035	-4.527	3.972
Methyl tert-butyl ether	0.42	0.00	0.62	0.57	13.01	8.56	9.46	0.341	0.307	-0.817	-0.618	-5.097	4.425
N-Methyl pyrrolidone	0.96	0.02	0.81	0.61	18.00	12.30	7.20	0.150	0.530	0.230	0.840	-4.790	3.670
N,N-Dimethylacetamide	0.99	0.03	0.76	0.65	16.80	11.50	10.20	-0.270	0.080	0.210	0.920	-5.000	4.560
N,N-Dimethylformamide	0.98	0.03	0.76	0.61	17.40	13.70	11.30	-0.310	-0.060	0.340	0.360	-4.870	4.490
Octan-1-ol	0.45	0.30	0.71	0.92	17.00	3.30	11.90	-0.030	0.490	-1.040	-0.020	-4.240	4.220
Octane	0.00	0.00	0.65	0.08	15.50	0.00	0.00	0.223	0.642	-1.647	-3.480	-5.067	4.526
Pentan-1-ol	0.59	0.32	0.69	0.86	13.83	8.82	13.80	0.150	0.540	-1.230	0.140	-3.860	4.080
Propan-1-ol	0.75	0.37	0.66	0.78	16.00	6.80	17.40	0.140	0.410	-1.030	0.250	-3.770	3.990
Propan-2-ol	0.81	0.28	0.63	0.83	12.97	10.35	15.68	0.100	0.340	-1.050	0.410	-3.830	4.030

Solvent	Catalan parameters				Hansen solubility parameters			Abraham solvent parameters					
	SA	***SB***	***SP***	***SdP***	δ_d	δ_p	δ_h	**c**	**e**	**s**	**a**	**b**	**v**
Propan-2-one	0.91	0.00	0.65	0.48	15.50	10.40	7.00	0.313	0.312	-0.121	-0.608	-4.753	3.942
Propane-1,2-diol	0.89	0.48	0.73	0.60	12.43	14.25	26.82	-0.150	0.750	-0.970	0.680	-3.130	3.250
Propanoic acid	0.43	0.61	0.66	0.38	NA	NA	NA	NA	NA	NA	NA	NA	NA
Propyl acetate	0.56	0.00	0.67	0.55	13.73	9.81	9.56	0.362	0.280	-0.390	-0.975	-4.928	4.183
Iso-propyl acetate	NA	NA	NA	NA	13.55	9.88	8.50	NA	NA	NA	NA	NA	NA
Iso-butyl acetate	NA	NA	NA	NA	13.87	9.26	7.93	NA	NA	NA	NA	NA	NA
Tetrahydrofuran	0.63	0.00	0.71	0.59	16.80	5.70	8.00	0.210	0.370	-0.390	-0.240	-4.930	4.450
Toluene	0.28	0.00	0.78	0.13	18.00	1.40	2.00	0.140	0.530	-0.720	-3.010	-4.820	4.550
2-Methoxyethanol	NA	NA	NA	NA	12.93	11.44	17.76	NA	NA	NA	NA	NA	NA
2-Ethoxyethanol	NA	NA	NA	NA	13.26	10.55	16.02	NA	NA	NA	NA	NA	NA
2-Proyethanol	NA	NA	NA	NA	13.49	9.83	14.77	NA	NA	NA	NA	NA	NA
2-Butoxyethanol	NA	NA	NA	NA	13.65	9.24	13.83	NA	NA	NA	NA	NA	NA
Methyl Isobutyl Ketone	NA	NA	NA	NA	15.3	6.10	4.10	NA	NA	NA	NA	NA	NA
3-Methyl-butan-1-ol	NA	NA	NA	NA	13.65	8.87	12.95	0.070	0.360	-1.270	0.090	-3.770	4.270
Water	1.00	1.06	0.68	0.03	15.50	16.00	42.30	-0.990	0.580	2.550	3.810	4.840	-0.870

"[a]NA: Not available."

Results and discussion

The prediction capability of Eq. (4) was investigated by dividing each data set into two subsets, i.e., training data set and prediction data set. In each data set, one point of each mono-solvents with different temperatures was coded as the training data. For example, the solubility of abacavir has been reported in mono-solvents of methanol, ethanol, 1- or 2-propanol, 1- or 2-butanol, 2-methyl-propan-1-ol, 1-pentanol, methyl acetate, ethyl acetate, water and 2-propanone at T = (278.15, 283.15, 288.15, 293.15, 298.15, 303.15, 308.15, 313.15, 318.15 and 323.15) K [17]. In this drug, training data were those reported for methanol at 278.15 K, ethanol at 283.15 K, 1-propanol at 288.15 K, 2-propanol at 293.15 K, 1-butanol at 298.15 K, 2-butanol at 303.15 K, 2-methyl-propan-1-ol at 308.15 K, 1-pentanol at 313.18 K, methyl acetate 318.15 K, ethyl acetate at 323.15 K, water at 278.15 K and 2-propanone at 283.15 K. The rest of data points in each data set were coded as the prediction data set. After that, the coded data points as training data set (degree of freedom = 0) were utilized to compute the model constants and the trained models were used to predict the solubility data of prediction data sets. The model constants of Eq. (4) computed by training data points along with reporting the obtained *APD* values for prediction data sets are given in Table 3. As shown in this Table, most of the parameters were not statistically significant and excluded from the regression model when the data were fitted to Eq. (4) using training data points. The non-significant contribution of the parameters to the model may be ascribed as their inter-correlations and also the low number of experimental solubility data points. The most significant independent variables may provide the most accurate correlative model. The calculated overall *APD* ± SD for all datasets in Table 3 is 71.6% ±105.7 which reached to 46.6% ±54.8 by excluding eight data sets with the relatively high *APD*s marked with bold font in Table 3 (≥ 100%). 46.6% prediction errors can be considered as acceptable errors and the predicted solubility data with this prediction level can provide valuable results for a process designer in the pharmaceutical industry.

Moreover, we utilized "leave one solvent out" method to cross-validate our results of the investigated model. More details of cross-validation of the proposed method are provided in Table 4. As presented in Table 4, the results of overall *APD*s ±SD present an increment in above-mentioned model. Based on the *APD* given in this Table, it is clear that the trained models in most cases have a good reliability for drug solubility prediction in the investigated mono-solvents. The overall *APD* for all investigated drug/solvent data sets (N=434) is 17424% which is relatively large *APD* for cross-validated data. Chrysin in water produced the largest *APD* (3436865.0%) for cross-validation, followed by ganciclovir form I in toluene (884317.1%), chrycin in

hexan-1-ol (785025.8%), ganciclovir form I in propan-2-one (780801.7%) and ethyl acetate (635898.4%), domperidone in acetonitrile (361993.4%) and empagliflozin in ethyl acetate (194200.3%). After excluding these seven very large *APDs*, the overall *APD* is reduced to 1131.3% (N=427). When 8 outlier sets of drugs in correlative study producing > 100% *APD* (in Table 1) for correlations are excluded from calculation of the overall *APD*, value of 9149% is obtained (N=361). These results reveal that further investigations on modeling the solubility data of drugs in mono-solvents at various temperatures are required to provide more accurate correlative/predictive models. Beside these observations, the proposed model is the most comprehensive model to correlate the solubility of a given drug dissolved in various mono-solvents at different temperatures.

Conclusion

In this study, we gathered available solubility data sets from papers published from 2016 to 2022 (43 data sets, 4654 data points totally) and analyzed them using minimum number of data points; as a matter of practical fact, the van't Hoff model combined with solvent parameters of Abraham, Hansen and Catalan is sufficiently accurate predicting solubility in mono-solvents and could be utilized as a practical strategy for predicting the solubility of drugs in mono-solvents at different temperatures with an acceptable prediction error and using minimum experimental efforts. These sorts of predictions are highly in demand in the pharmaceutical industry.

Acknowledgement

The research protocol was approved and supported by Student Research Committee (grant # 71580), Tabriz University of Medical Sciences Tabriz, Iran.

Disclosure of statement

The authors report there are no competing interests to declare.

Table 3. The model constants and APDs% for the predicted solubility data of drugs in the investigated systems using Eq. (4) trained by selection of one experimental data point at each temperature

drug	α_0	$\alpha_{i,AP}$	$\alpha_{i,HP}$	$\alpha_{i,CP}$	β_0	$\beta_{i,AP}$	$\beta_{i,HP}$	$\beta_{i,BP}$	APD
Abacavir	-19.682	e = -1.257 s = -0.791	δ_d= -0.118	SP = 23.045 SdP = 0.064 SA = 2.893	-	c = 700.618 b = 35.136	δ_h= 0.157	SP = -442.999 SB = 520.990	46.5
Benorilate	11.273	e = 2.232 p = 0.229	-	SP = -13.423 SdP = -4.653	-	v = -1817.650	δ_d = 74301 δ_h = 83.405	SP = 6525.125 SB = 662.603	26.1
Celecoxib	35.410	c = 10.412	δ_d = -0.425	SP = -22.095	-4580.591	e = 286.408	δ_p = -123.828 δ_h = -52.882	SA = 1116.553 SB = -469.441	71.5
Dimetridazole	8.392	c = 3.569 e = -1.628	-	SA = 2.233	-5921.801	b = -339.611 v = -431.611	δ_d = -33.194	SP = 4693.172 SB = -304.933	10.3
Imazapyr	7.381	e = 0.542 a = -0.476	δ_p = 0.027	SP = 1.767 SA = 1.768	-3147.548	b = -13.969 v = -294.228	-	SdP = 194.939 SB = -181.083	16.3
Indapamide	5.488	c = 1.897 b = 0.226	-	SP = -5.507	-8592.495	s = 318.581	δ_d = 293.999 δ_p = 150.828	SA = -1134.282 SB = 2226.803	64.2
Nintedanib	1.136	a = 1.907	δ_d = -0.370 δ_p = -0.627	SdP = 3.494 SA = 4.814	-1195.012	e = -2964.613 v = 943.640	-	SB = -3313.272	61.0
Kojic acid	-24.315	e = -3.826 a = 0.141	-	SP = 41.935	-1387.726	s = -774.090	δ_d = -44.979	SdP = 1115.142 SA = 626.510 SB = -2466.816	29.0
Pyrazinamide	9.099	s = -0.157	δ_d = -0.041	SP = 5.401 SdP = 2.809 SA = -1.578	-5953.921	e = 749.455	-	SB = -320.166	47.5

drug	α_0	$\alpha_{i,AP}$	$\alpha_{i,HP}$	$\alpha_{i,CP}$	β_0	$\beta_{i,AP}$	$\beta_{i,HP}$	$\beta_{i,BP}$	APD
Topiramate	10.769	e = -0.264	-	SP = -4.355	-	c = -369.588 a = -149.214	δ_d = -98.316 δ_p = -71.218	SdP = 742.272 SB = -2382.668	26.2
Riluzole	16.963	-	-	-	-1310.338	-	δ_d = -23.999 δ_p = 0.378	SP = -6228.735 SdP = 203.252 SB = 481.726	**137.0**
Prednisolone form II	-24.804	e = -5.366 a = 3.718 v = -0.587	δ_d = -0.206	SP = 52.770	-2716.537	c = 2439.545	-	SdP = 655.307 SB = -907.527	9.3
Doxifluridine	-18.304	c = 0.379 e = -1.797 v = 2.590	δ_d = -0.061 δ_h = 0.214	SP = 32.535 SdP = 1.733	-	b = -30.521 v = -1437.516	-	SB = -1773.076	**112.4**
Empagliflozin	-20.792	b = 0.039	δ_d = 0.760	SA = 8.391	606.824	e = -4364.285	-	SP = 1280.793 SdP = -1105.205 SB = -867.520	71.6
Etodolac	-0.285	e = -7.073	δ_d = 0.324	SdP = 3.507	-8847.899	c = -1100.808 b = -1264.544	δ_h = 85.132	SB = 677.165	14.9
Ipriflavone	-9.548	b = 0.155 v = 6.144	δ_d = -0.086 δ_h = -0.04	SA = 1.952	-5722.758	c = 1554.534 e = -686.757	δ_p = 24.361	SdP = 485.161 SB = -329.238	28.4
Melatonin	12.177	c = 0.631 e = 0.334 v = -0.306	δ_d = -0.016 δ_h = 0.103	SdP = -0.319	-4909.873	a = 94.009	-	SB = -24.638	10.1
Oxaprozin	14.148	v = -3.841	δ_d = -0.007 δ_h = 0.001	SP = 21.527 SdP = -3.245	-3229.086	e = -1426.305 a = 683.816	-	SA = -1243.951 SB = -648.864	40.8
Praziquantel	-20.593	a = 1.164 v = 2.315	δ_d = 0.999	SP = -5.010	-	-	-	SdP = -1655.537 SB = -627.441	37.1

drug	α_0	$\alpha_{i,AP}$	$\alpha_{i,HP}$	$\alpha_{i,CP}$	β_0	$\beta_{i,AP}$	$\beta_{i,HP}$	$\beta_{i,BP}$	APD
Vitamin K3	-12.993	e = -1.439	δ_d = 0.004 δ_h = 0.086	SP= 11.057 SdP = 1.721	-	c = 142.971 b = -38.620	-	SA = -1663.346 SB = 196.505	69.3
Flurbiprofen	-21.017	c = 10.344 e = 4.743 s = 2.856 v = 2.449	-	SP = 4.230	-	-	δ_d = -35.009 δ_p = 31.697	SB = 2327.147	91.5
Griseofulvin	-22.091	c = -0.940	δ_d = 0.171	SP = -4.099	-	e = -2034.664 b = -109.350	-	SP = 9983.085 SA= - 1083.258 SB = -2008.944	**203.5**
Domperidone	-10.821	c = 9.8634 e = -1.368 a = 2.373	δ_d = 0.427	SdP = -0.448	-9434.558	s = 686.935	δ_p = 81.664	SP = 7288.807 SA = -118.561 SB = 3301.489	60.2
Lansoprazole	-47.240	e = 0.169 b = -0.595	δ_h = 0.145	SP = 54.079 SdP = 9.912 SA = 1.604	-	c = 3444.692	δ_d = -150.051 δ_p = -24.07	SB = 508.685	49.2
Temozolomide	1.193	a = 1.098 b = -0.038	δ_d = 0.529 δ_p = 0.064	SdP = -0.670	-	e = -2031.915 v = -1061.107	-	SA = -832.888 SB = -422.814	38.7
Antipyrine	2.499	e = -2.178 a = 0.388	δ_d = 0.441 δ_p = 0.208	SP = -4.930 SdP = -3.461 SA = -0.212	-2193.084	-	-	SB = 553.639	31.6
Norfloxacin	-8.928	v = 0.361	δ_h = -0.189	-	-	e = -1856.797	δ_d = 95.705 δ_p = 10.118	SA = 2318.342 SB = -754.933	**102.3**
Troxerutin	7.652	e = 1.159 b = -0.484 v = -3.939	-	-	-2325.136	-	δ_d = 81.110 δ_p = 90.663 δ_h = 97.579	SdP = -2050.713 SA = -2161.060 SB = 209.287	75.6

drug	α_0	$\alpha_{i,AP}$	$\alpha_{i,HP}$	$\alpha_{i,CP}$	β_0	$\beta_{i,AP}$	$\beta_{i,HP}$	$\beta_{i,BP}$	APD
Omeprazole	-67.548	e = -11.989	δ_d = 1.043	SP = 49.693 SdP = 1.865	6282.885	s = -1050.104	-	SB = -3600.018	238.9
Glibenclamide	-10.418	-	δ_h = -0.039	SP = 45.884	-	c = -3181.009 e = -71.593	δ_d = 186.324 δ_p = 151.188	SP = -12804.222 SdP = -2485.137 SB = -1798.231	76.2
Vinpocetine	-13.064	s = 1.560	δ_p = -0.120	SP = 35.303	-	c = 301.6 v = 175.502	δ_d = -17.186	SP = -7066.415 SB = -64.579	6.6
Levetiracetam	29.726	b = 0.143	δ_d = 0.262	-	-10490.284	c = -1117.399 s = -416.755*st+ a = 660.627	-	SdP = 1368.999 SA = 859.871 SB = -2763.378	**309.5**
Lidocaine	-13.507	v = -0.178	δ_d = -0.110	SP = 12.386 SdP = 0.305	-	b = -303.230 v = 195.796	-	SB = 266.002	55.4
Uridine	5.739	-	δ_d = -0.113	SdP = 1.990	-4509.827	e = -1703.893	-	SP = 4335.731 SA = -86.787 SB = -1619.55	24.4
Bisacodyl	4.598	c = 0.981 e = -4.780	δ_p = -0.142	SdP = 2.140	-1954.709	b = -68.684 v = -650.054	δ_d = 34.730	SP = 1545.059 SA = -1345.805 SB = -493.487	7.7
Clozapine	-30.677	c = 3.826 s = 17.4 v = 4.14	δ_d = -0.721	SdP = 1.689 SB = 61.178	-	s = -4602.226	δ_d = 252.315	SP = 2384.508 SA = 1056.813 SB = -17741.240	99.3
Bezafibrate	7.998	c = 6.640 e = 0.073 b = -0.947	δ_d = -0.630 δ_h = 0.298	SdP = 9.646 SA = -0.766	-12702.156	a = 79.841	δ_p = -92.178	SP = 11740.893 SB = -485.044	57.5

drug	α_0	$\alpha_{i,AP}$	$\alpha_{i,HP}$	$\alpha_{i,CP}$	β_0	$\beta_{i,AP}$	$\beta_{i,HP}$	$\beta_{i,BP}$	APD
Chrysin	98.346	e = -16.612 a = 3.677	δ_d = 2.395 δ_p = -0.079	SP = -130.339 SdP = -3.94 SA = -15.862	-14223.674	-	-	SB = 1060.898	**361.6**
Dipyrone	-104.819	c = 6.891 e = 3.701	δ_d = -1.565 δ_h = -0.516	SP = 95.95 SdP = -3.013 SA = 16.538	21468.862	-	-	SB = -3147.338	**>100**
Chlorphenesin	-15.611	e = -8.554 v = 4.208	δ_d = 0.604 δ_h = 0.025	SdP = 0.547	340.954	c = 2586.822 b = 857.158	-	SA = -1096.866 SB = -343.222	35.9
Perphenazine	-12.705	-	-	SP = 22.269 SdP = -1.168	-2071.553	-	δ_d = 19.898 δ_h = 3.747	SB = 95.080	43.7
Florfenicol Form A	-15.823	s = -7.736	-	-	-	b = 504.372 v = 589.873	-	SB = -148.699	63.2
Ganciclovir form I	19.445	v = -7.236	δ_p = -0.074	-	-9956.953	e = 1752.323	δ_d = -130.712	SP = 13750.585 SA = 1198.921 SB = 2860.655	44.4
Overall APD									71.6

Table 4. Leave-solvent-out cross validation for the used model.

Drug	Solvent	APD ± SD	Drug	Solvent	APD ± SD
Abacavir	Methanol	62.1 ± 7.6	Dimetridazole	Methanol	81.2 ± 1.4
	Ethanol	66.7 ±10.5		Ethanol	77.0 ± 0.7
	Propan-1-ol	74.6 ± 8.0		Propan-1-ol	74.5 ± 1.1
	Propan-2-ol	55.4 ± 15.6		Propan-2-ol	66.3 ± 5.4
	Butan-1-ol	72.2 ± 8.0		Butan-2-ol	74.6 ± 1.7
	Butan-2-ol	76.8 ± 8.1		Pentan-1-ol	81.2 ± 1.4
	2-Methyl-propan-1-ol	65.4 ± 13.3		Propan-2-one	86.3 ± 0.2
	Pentan-1-ol	80.4 ± 7.1		2-Butanone	83.1 ± 0.5
	Methyl acetate	648.2 ± 102.4		Cyclohexanone	82.0 ± 1.4
	Ethyl acetate	367.1 ± 83.6		Ethyl acetate	86.6 ± 0.3
	Water	40.4 ± 7.8		Propyl acetate	- [a]
	Propan-2-one	349.4 ± 100.9		Isopropyl acetate	-
Benorilate	Methanol	272.3 ± 20.0	Imazapyr	Methanol	80.0 ± 1.7
	Ethanol	282.5 ± 21.9		Ethanol	67.7 ± 4.8
	Propan-1-ol	324.6 ± 86.5		Propan-1-ol	62.5 ± 3.4
	Propan-2-ol	489.2 ± 64.5		Propan-2-ol	53.9 ± 5.8
	Butan-1-ol	294.6 ± 26.2		Butan-1-ol	59.2 ± 4.2
	2-Methyl-propan-1-ol	465.3 ± 46.9		2-Methyl-propan-1-ol	48.0 ± 4.6
	Ethyl formate	-		Butan-2-ol	64.7 ± 3.9
	Ethyl acetate	146.9 ± 13.7		Propan-2-one	40.1 ± 4.8
	Isopropyl acetate	-		2-Butanone	19.1 ± 8.9
	Methyl acetate	352.0 ± 41.2		Ethyl formate	-
	Acetonitrile	46.9 ± 5.2		Methyl acetate	36.3 ± 4.1
	Propan-2-one	30.8 ± 17.5		Ethyl acetate	11.3 ± 6.5

Drug	Solvent	*APD ± SD*	Drug	Solvent	APD ± SD
Celecoxib	Ethyl acetate	93.5 ± 1.8	Melatonin	Methanol	88.7 ± 1.3
	Propyl acetate	-		Ethanol	88.5 ± 0.5
	Isopropyl acetate	-		Propan-1-ol	84.9 ± 1.6
	Isobutyl acetate	-		Butan-1-ol	80.2 ± 1.7
	Acetonitrile	95.9 ± 0.3		2-Methyl-propan-1-ol	73.3 ± 2.9
	Methanol	80.1 ± 3.4		Pentan-1-ol	81.3 ± 0.6
	Ethanol	79.9 ± 3.7		Hexan-1-ol	78.3 ± 1.1
	Propan-1-ol	66.4 ± 3.7		Methyl acetate	28.2 ± 20.8
	Propan-2-ol	67.1 ± 1.1		Ethyl acetate	30.6 ± 9.3
	Butan-1-ol	50.5 ± 4.5		Propyl acetate	-
	2-Methyl-propan-1-ol	16.1 ± 3.8		Butyl acetate	49.2 ± 12.6
	Butan-2-ol	61.7 ± 3.0		Pentyl acetate	-
	Pentan-1-ol	46.9 ± 6.2			
Kojic acid	Methanol	61.8 ± 3.9	Topiramate	2-Methoxyethanol	-
	Ethanol	59.0 ± 4.5		2-Ethoxyethanol	-
	Propan-1-ol	43.6 ± 5.6		2-Propoxyethanol	-
	Ethyl acetate	133.6 ± 11.5		2-Butoxyethanol	-
	2-Methoxyethanol	-		Methanol	94.7 ± 0.9
	2-Ethoxyethanol	-		Ethanol	
	1,4-Dioxane	38.1 ± 3.6		Propan-1-ol	85.8 ± 1.5
	N,N-Dimethylacetamide	85.1 ± 3.7		Propan-2-ol	85.8 ± 1.9
	DMSO	83.6 ± 2.8		Butan-1-ol	78.2 ± 2.3
	Acetic acid	-		2-Methyl-propan-1-ol	66.1 ± 6.2
	NMP	89.6 ± 3.2		Pentan-1-ol	73.5 ± 1.5

Drug	Solvent	APD ± SD	Drug	Solvent	APD ± SD
	N,N-Dimethylformamide	75.5 ± 3.9		3-Methyl-butan-1-ol	-
	Propan-2-one	43.2 ± 6.1		Hexan-1-ol	70.5 ± 2.2
	Water	90.1 ± 3.6		Heptan-1-ol	45.9 ± 4.2
Pyrazinamide	Water	80.4 ± 3.8	Etodolac	Propan-1-ol	95.1 ± 1.3
	Pentan-1-ol	14.1 ± 9.8		Propan-2-ol	94.8 ± 0.9
	3-Methyl-butan-1-ol	-		Butan-1-ol	95.1 ± 1.3
	Cyclohexanone	83.0 ± 11.5		2-Methyl-propan-1-ol	92.8 ± 0.8
	Hexan-1-ol	7.5 ± 3.6		Methyl acetate	84.4 ± 3.2
	Heptan-1-ol	99.9 ± 11.7		Butyl acetate	92.0 ± 1.7
	Octan-1-ol	16.5 ± 4.7		Isobutyl acetate	-
	Ethyl formate	-		Pentyl acetate	-
	Methyl acetate	123.6 ± 26.6		Isopentyl acetate	-
	Propane-1,2-diol	60.9 ± 7.8		Toluene	17.7 ± 9.9
	Propyl acetate	-		Propan-2-one	94.3 ± 1.5
	Butyl acetate	99.9 ± 11.4		Dichloromethane	64.0 ± 1.7
Riluzole	Ethanol	98.4 ± 0.8	Prednisolone form II	Methanol	28.0 ± 16.9
	Propan-1-ol	98.5 ± 0.7		Ethanol	28.8 ± 17.1
	Butan-1-ol	98.5 ± 0.7		Propan-1-ol	25.7 ± 16.2
	Pentan-1-ol	98.7 ± 0.7		Propan-2-ol	30.9 ± 21.3
	Propan-2-one	98.2 ± 0.7		Butan-1-ol	29.8 ± 19.4
	Pentyl acetate	-		Methyl acetate	1055.1 ± 133.4
	Isopropyl acetate	-		Ethyl acetate	477.5 ± 84.5
	N,N-Dimethylacetamide	79.5 ± 2.7		Propyl acetate	-
	2-Methoxyethanol	-		Propan-2-one	193.0 ± 33.4

Drug	Solvent	*APD ± SD*	Drug	Solvent	APD ± SD
	2-Propoxyethanol	-		1,4-Dioxane	15.0 ± 11.6
	Acetonitrile	99.3 ± 0.2		Tetrahydrofuran	45.5 ± 7.2
Doxifluridine	Methanol	21.6 ± 15.5	Flurbiprofen	Propan-1-ol	96.9 ± 0.6
	Ethanol	95.2 ± 29.0		Propan-2-ol	97.3 ± 0.5
	Propan-1-ol	220.6 ± 15.2		Butan-1-ol	96.9 ± 0.6
	Butan-1-ol	312.1 ± 8.5		2-Methyl-propan-1-ol	95.7 ± 0.6
	2-Methyl-propan-1-ol	565.6 ± 84.6		3-Methyl-butan-1-ol	-
	Pentan-1-ol	301.2 ± 16.1		Propyl acetate	-
	Hexan-1-ol	309.0 ± 18.3		Methyl tert-butyl ether	97.5 ± 0.8
	Octan-1-ol	434.5 ± 62.1		iso-Propyl ether	-
	(±)-2-Ethyl-1-Hexanol	-		Acetonitrile	94.3 ± 1.3
	Propan-2-one	63.5 ± 30.6		Octane	62.2 ± 1.9
	N,N-Dimethylformamide	81.9 ± 5.6		Heptane	73.2 ± 3.3
	DMSO	86.8 ± 5.6		Hexane	65.2 ± 1.9
Ipriflavone	Methanol	65.6 ± 14.6	Domperidone	Methanol	19974.3 ± 703.4
	Ethanol	9.6 ± 7.2		Ethanol	12570.3 ± 521.5
	Propan-1-ol	27.9 ± 6.8		Propan-2-ol	12352.5 ± 496.8
	Butan-1-ol	40.2 ± 6.8		Propan-1-ol	9065.7 ± 209.0
	Pentan-1-ol	54.5 ± 3.2		Butan-1-ol	8699.9 ± 227.5
	Methyl acetate	52.6 ± 5.5		Acetonitrile	361993.4 ± 130948.1
	N,N-Dimethylformamide	39.2 ± 8.1		2-Methyl-propan-1-ol	1178.6 ± 245.1
	N,N-Dimethylacetamide	64.9 ± 1.6		N,N-Dimethylformamide	15269.0 ± 5269.3
	Propan-2-one	66.2 ± 4.6		DMSO	5619.1 ± 991.2

Drug	Solvent	APD ± SD	Drug	Solvent	APD ± SD
	Acetonitrile	79.1 ± 5.5		N,N-Dimethylacetamide	1573.0 ± 46.8
	Dichloromethane	92.6 ± 1.3		Ethane-1,2-diol	9583.1 ± 433.8
	Toluene	90.5 ± 0.4		Water	2555.7 ± 808.1
Oxaprozin	Methanol	25.2 ± 3.5	Bezafibrate	Methanol	21.3 ± 8.0
	Ethanol	51.3 ± 4.4		Ethanol	22.0 ± 13.9
	Propan-1-ol	55.2 ± 2.2		Propan-1-ol	26.9 ± 10.0
	Butan-1-ol	54.2 ± 1.7		Propan-2-ol	6.7 ± 4.6
	Pentan-1-ol	61.4 ± 2.9		Butan-1-ol	21.7 ± 7.6
	Methyl Acetate	2.0 ± 1.1		2-Methyl-propan-1-ol	36.6 ± 3.2
	Ethyl Acetate	41.1 ± 3.2		Butan-2-ol	38.7 ± 8.4
	Propyl Acetate	-		Pentan-1-ol	39.5 ± 9.1
	Butyl Acetate	13.7 ± 3.4		3-Methyl-butan-1-ol	-
	Pentyl acetate	-		Ethyl Acetate	356.1 ± 23.2
	N,N-Dimethylformamide	80.8 ± 4.1		Propyl Acetate	-
	N,N-Dimethylacetamide	88.5 ± 3.3		Butyl Acetate	716.0 ± 49.4
	DMSO	83.8 ± 1.7		Methyl Propionate	-
				Butan-2-one	138.5 ± 3.5
				Cyclohexanone	24. 0 ± 11.1
				Acetonitrile	447.0 ± 153.4
Vitamin K3	Dichloromethane	96.0 ± 0.4	Temozolomide	Methanol	1096.3 ± 229.0
	1,2-Dichloroethane	93.4 ± 0.6		Ethanol	2149.5 ± 89.1
	Methyl acetate	87.8 ± 0.4		Propan-1-ol	2423.3 ± 127.5
	Propan-2-one	89.8 ± 0.7		Propan-2-ol	4497.0 ± 688.1
	Acetonitrile	96.0 ± 0.4		Propan-2-one	1198.8 ± 31.8

Drug	Solvent	*APD ± SD*	Drug	Solvent	APD ± SD
	Butan-1-ol	68.0 ± 3.0		Acetonitrile	124.0 ± 11.4
	Propan-1-ol	65.0 ± 3.5		Ethyl acetate	2594.7 ± 141.0
	Propan-2-ol	64.2 ± 1.0		DMSO	236.3 ± 50.8
	Cyclohexane	94.6 ± 0.6		1,4-Dioxane	189.5 ± 45.5
	Methanol	31.6 ± 8.1		N,N-Dimethylformamide	642.6 ± 18.8
Griseofulvin	Methanol	703.7 ± 63.5	Bisacodyl	Methanol	2632.8 ± 264.4
	Ethanol	601.9 ± 104.4		Ethanol	1991.1 ± 284.0
	Propan-1-ol	562.7 ± 85.7		Propan-1-ol	312.2 ± 300.2
	Butan-1-ol	667.3 ± 107.6		Propan-2-ol	2162.5 ± 300.7
	2-Methyl-propan-1-ol	863.0 ± 96.6		Butan-1-ol	1451.5 ± 236.2
	Methyl acetate	135.0 ± 34.5		1,4-Dioxane	120.0 ± 20.3
	Ethyl acetate	71.3 ± 36.4		N,N-Dimethylformamide	759.6 ± 55.3
	Propyl acetate	-		NMP	455.8 ± 52.4
	Butyl acetate	207.4 ± 65.6		Ethyl Acetate	163.5 ± 24.9
	iso-Propyl acetate	-		Propan-2-one	137.9 ± 19.0
	Iso butyl acetate	-		Acetonitrile	27.8 ± 8.4
	Acetonitrile	69.9 ± 3.9		Toluene	142.1 ± 37.2
Lansoprazole	Methanol	92.3 ± 0.2	Nintedanib	Methanol	542.5 ± 132.0
	Ethanol	86.9 ± 1.4		Ethanol	1066.1 ± 169.8
	Propan-1-ol	81.9 ± 2.8		Propan-1-ol	726.5 ± 66.2
	Propan-2-ol	69.5 ± 3.1		Propan-2-ol	1778.5 ± 149.3
	Butan-1-ol	76.5 ± 1.9		Butan-1-ol	1383.5 ± 186.8
	2-Methyl-propan-1-ol	65.8 ± 3.0		Butan-1-ol	184.5 ± 11.4
	Propan-2-one	53.8 ± 7.4		2-Methyl-propan-1-ol	1731.7 ± 252.9

Drug	Solvent	APD ± SD	Drug	Solvent	APD ± SD
	Acetonitrile	80.3 ± 2.1		N,N-Dimethylformamide	1205.5 ± 50.5
	Methyl acetate	21.9 ± 7.6		N,N-Dimethylacetamide	283.0 ± 33.9
	Ethyl acetate	52.3 ± 2.5		1,4-Dioxane	512.5 ± 16.6
	Propyl acetate	-		Dichlormethane	14.2 ± 3.3
	Butyl acetate	26.6 ± 10.1			
Antipyrine	Methanol	97.8 ± 0.6	Indapamide	Methanol	71.3 ± 1.0
	Ethanol	98.0 ± 0.6		Ethanol	74.3 ± 0.7
	Propan-1-ol	98.1 ± 0.6		Propan-1-ol	66.3 ± 1.3
	Propan-2-ol	97.5 ± 0.6		Propan-2-ol	44.9 ± 13.6
	Butan-1-ol	97.9 ± 0.6		Propan-2-one	79.0 ± 3.1
	2-Methyl-propan-1-ol	97.7 ± 0.6		Acetonitrile	75.9 ± 8.1
	Propan-2-one	91.5 ± 1.0		Ethyl acetate	124.3 ± 113.1
	Methyl acetate	82.3 ± 4.8		2-Butanone	70.7 ± 2.8
	Ethyl acetate	89.8 ± 3.0		Toluene	12595 ± 6780.5
	Water	99.8 ± 0.01		Cyclohexane	4227.1 ± 2031.5
Troxerutin	Methanol	1005.0 ± 29.9	Perphenazine	Propan-1-ol	90.5 ± 2.3
	Ethanol	1017.8 ± 218.8		Butan-1-ol	91.2 ± 1.8
	Propan-1-ol	1343.1 ± 128.6		Methyl acetate	23.4 ± 17.9
	Propan-2-ol	1613.1 ± 71.7		Ethyl acetate	70.1 ± 5.6
	Butan-1-ol	2001.3 ± 201.9		Propyl acetate	-
	2-methyl-1-Propanol	4231.5 ± 753.9		Pentyl acetate	-
	Butan-2-ol	1578.5 ± 89.3		2-Methoxyethanol	-
	Pentan-1-ol	2346.2 ± 753.9		2-Ethoxyethanol	-
	Propan-2-one	13345.9 ±2863.6		N,N-Dimethylformamide	43.1 ± 12.6

Drug	Solvent	*APD ± SD*	Drug	Solvent	APD ± SD
	Acetonitrile	8736.2 ± 2804.7		N,N-Dimethylacetamide	76.1 ± 0.4
	1,4-Dioxane	779.1 ± 37.7		Propan-2-one	43.7 ± 19.2
Glibenclamide	Methanol	1213.9 ± 302.1	Dipyrone	Methanol	82.8 ± 4.2
	Ethanol	984.6 ± 172.6		Ethanol	20.5 ± 13.5
	Propan-1-ol	1126.2 ± 190.3		Propan-1-ol	147.9 ± 22.0
	Propan-2-ol	1429.4 ± 331.1		Propan-2-ol	629.2 ± 31.6
	Butan-1-ol	839.4 ± 166.0		Butan-1-ol	579.9 ± 92.6
	Butan-2-ol	1491.7 ± 367.2		Butan-2-ol	619.4 ± 140.1
	Propan-2-one	623.3 ± 111.3		Propan-2-one	4243.6 ± 1205.2
	Acetonitrile	1030.3 ± 360.3		Ethyl Acetate	3704.5 ± 844.4
	Methyl Isobutyl Ketone	-		Methyl Acetate	9251.0 ± 2753.9
	Methyl Acetate	3857.2 ± 665.4		Water	98.9 ± 0.1
	Ethyl Acetate	2255.8 ± 364.9			
Levetiracetam	Methanol	96.7 ± 0.6	Omeprazole	Water	455.8 ± 159.0
	Ethanol	95.0 ± 1.0		Methanol	25.0 ± 6.1
	Propan-1-ol	89.8 ± 1.4		Ethanol	14.6 ± 9.5
	Propan-2-ol	87.8 ± 0.6		Butan-1-ol	11.7 ± 9.8
	Propan-2-one	73.2 ± 1.7		Acetonitrile	44.8 ± 5.1
	1,4-Dioxane	863.2 ± 76.7		Propan-2-one	109.1 ± 14.6
	Acetonitrile	90.7 ± 0.4		Ethyl acetate	155.7 ± 21.0
	Ethyl Acetate	46.5 ± 4.9		Tetrahydrofuran	47.0 ± 17.7
	Toluene	20.4 ± 15.2			
	Cyclohexane	863.2 ± 79.7			

Drug	Solvent	APD ± SD	Drug	Solvent	APD ± SD
Uridine	Methanol	32.1 ± 20.8	Vinpocetine	Methanol	461.9 ± 16.8
	Ethanol	175.2 ± 50.8		Ethanol	189.7 ± 9.8
	Propan-1-ol	187.2 ± 44.4		Propan-1-ol	77.0 ± 7.7
	Propan-2-ol	123.0 ± 49.2		Propan-2-ol	220.9 ± 36.2
	Butan-1-ol	240.1 ± 78.1		Butan-1-ol	35.6 ± 14.3
	2-Methoxy Ethanol	-		Ethyl Acetate	36.5 ± 2.5
	2-Ethoxy Ethanol	-		Methyl Acetate	93.2 ± 28.5
	2-Propoxy Ethanol	-		Cyclohexane	86.2 ± 1.9
	2-Butoxy Ethanol	-		Butan-2-one	24.0 ± 7.3
	Water	98.6 ± 0.3			
	N,N-Dimethylformamide	80.6 ± 5.8			
	Ethane-1,2-diol	81.6 ± 3.1			
Clozapine	Methanol	49.7 ± 19.5	Clozapine	Chloroform	94.1 ± 2.6
	Ethanol	58.9 ± 16.8		Ethyl formate	-
	Propan-1-ol	72.4 ± 9.8		Methyl acetate	42.7 ± 11.5
	Propan-2-ol	37.2 ± 20.2		Ethyl acetate	71.2 ± 6.5
	Butan-1-ol	72.5 ± 10.1		Propyl acetate	-
	2-Methyl-propan-1-ol	60.8 ± 15.4		Butyl acetate	70.4 ± 7.1
	Butan-2-ol	56.9 ± 18.7		Pentyl acetate	-
	Pentan-1-ol	78.2 ± 9.2		2-Methoxyethanol	-
	3-Methyl-butan-1-ol	-		2-Ethoxyethanol	-
	Propan-2-one	65.1 ± 3.8		2-Propoxyethanol	-
	Butan-2-one	77.0 ± 3.6		NMP	62.2 ± 1.8
	Acetonitrile	46.8 ± 13.2		1,2-Dichloroethane	48.7 ± 2.6

Drug	Solvent	*APD ± SD*	Drug	Solvent	APD ± SD
	N,N-Dimethylformamide	71.1 ± 7.0		Benzene	67.9 ±2.9
	Tetrahydrofuran	88.5 ± 3.8		Toluene	55.2 ± 5.1
	DMSO	51.9 ± 3.3			
Chlorphenesin	Methanol	96.6 ± 0.2	Chrysin	Hexan-1-ol	785025.8 ± 269992.2
	Ethanol	97.0 ± 0.2		Ethyl Acetate	588.6 ± 102.3
	Propan-1-ol	95.6 ± 0.4		Propan-2-one	429.7 ± 54.6
	Butan-1-ol	96.1 ± 0.4		Methanol	1785.7 ± 209.4
	Butan-2-ol	96.8 ± 0.4		Ethanol	591.3 ± 112.2
	2-Methyl-propan-1-ol	94.1 ± 1.3		Propan-1-ol	476.9 ± 67.7
	Methyl Acetate	88.5 ± 4.5		Propan-2-ol	427.8 ± 59.9
	Ethyl Acetate	94.3 ± 2.1		Butan-1-ol	419.6 ± 59.6
	Propyl Acetate	-		N,N-dimethylformamide	88.2 ± 54.1
	Tetrahydrofuran	96.2 ± 0.4		Water	3436865.0 ± 3363647.0
	1,4-Dioxane	96.6 ± 0.9			
	Propan-2-one	95.5 ± 0.9			
Florfenicol Form A	Ethanol	5.5 ± 3.2	Lidocaine	Ethanol	99.1 ± 0.3
	Propan-1-ol	35.3 ± 6.3		Propan-1-ol	99.2 ± 0.4
	Butan-1-ol	172.3 ± 20.3		Propan-2-ol	99.2 ± 0.4
	Propan-2-ol	104.4 ± 12.3		Butan-1-ol	99.2 ± 0.4
	2-Methyl-propan-1-ol	419.6 ± 39.0		2-Methyl-propan-1-ol	99.1 ± 0.4
	3-Methyl-1-butanol	-		Propan-2-one	98.6 ± 0.4
	2-Ethyl-1-hexanol	-		Methyl Acetate	97.6 ± 0.6
	Propanoic acid	-		Ethyl Acetate	98.9 ± 0.4

Drug	Solvent	APD ± SD	Drug	Solvent	APD ± SD
Lidocaine	Ethanol	99.1 ± 0.3	Norfloxacin	Ethanol	121.0 ± 56.6
	Propan-1-ol	99.2 ± 0.4		Butan-1-ol	136.6 ± 86.1
	Propan-2-ol	99.2 ± 0.4		Propan-2-ol	693.1 ± 120.5
	Butan-1-ol	99.2 ± 0.4		Propan-2-one	356.4 ± 52.3
	2-Methyl-propan-1-ol	99.1 ± 0.4		Acetonitrile	219.7 ± 58.6
	Propan-2-one	98.6 ± 0.4		Ethyl acetate	711.3 ± 280.3
	Methyl Acetate	97.6 ± 0.6		Hexane	76.7 ± 6.1
	Ethyl Acetate	98.9 ± 0.4		N,N-dimethylformamide	512.7 ± 243.9
Ganciclovir form I	Methanol	3895.9 ± 1345.4	Empagliflozin	Ethanol	34964.8 ± 4021.4
	Ethanol	2427.2 ± 1074.4		N,N-dimethylformamide	2172.9 ± 514.8
	Propan-1-ol	1263.7 ± 657.0		Ethyl acetate	194200.3 ± 50989.4
	Propan-2-ol	3145.6 ± 1306.4		Formamide	-
	Butan-1-ol	1133.2 ± 573.0		Butan-1-ol	39543.4 ± 12732.3
	Acetonitrile	8716.7 ± 2079.3		Propan-1-ol	49252.4 ± 8775.9
	Propan-2-one	780801.7 ± 13197.2		Acetonitrile	65810.0 ± 25993.3
	Ethyl acetate	635898.4 ± 131976.2		Ethane-1,2-diol	8250.7 ± 514.8
	Toluene	884317.1 ± 169475.9		Methanol	8824.9 ± 361.2
Praziquantel	Propyl acetate	-	Praziquantel	2-Propoxyethanol	-
	Butyl acetate	55.8 ± 4.6		2-Butoxyethanol	-
	Ethanol	83.2 ± 1.2		N,N-Dimethylacetamide	47.2 ± 3.0
	Propan-1-ol	84.0 ± 1.9		N,N-Dimethylformamide	24.8 ± 6.9
	Butan-1-ol	84.5 ± 1.4		Ethane-1,2-diol	10.3 ± 3.0
	2-Ethoxyethanol	-			

a The s values were not reported due to there are no report the parameters of Catalan, Hansen or Abraham for solvent.

References

1. A. Jouyban, *Handbook of Solubility Data for Pharmaceuticals*, CRC Press, Boca Raton (FL), 2010. DOI: https://doi.org/10.1201/9781439804889.

2. F. Martinez, A. Jouyban, W.E. Acree Jr, Pharmaceutical's solubility is still nowadays widely studied everywhere, *Pharm. Sci.*, **23**, 1-2 (2017). DOI: https://doi.org/10.15171/PS.2017.01.

3. R. Sanghvi, R. Narazaki, S.G. Machatha, S.H. Yalkowsky, Solubility improvement of drugs using N-methyl pyrolidone, *AAPS PharmSciTech*, **9**, 366-376 (2008). DOI: https://doi.org/10.1208/s12249-008-9050-z.

4. S.H. Yalkowsky, *Solubility and solubilization in aqueous media*, American Chemical Society and Oxford University Press, New York (NY), 1999. DOI: https://doi.org/10.1021/ja0047424.

5. W. Li, A. Farajtabar, R. Xing, Y. Zhu, H. Zhao, Equilibrium solubility determination, solvent effect and preferential solvation of amoxicillin in aqueous co-solvent mixtures of N, N-dimethylformamide, isopropanol, N-methyl pyrrolidone and ethylene glycol, *J. Chem. Thermodyn.*, **142**, 106010 (2020). DOI: https://doi.org/10.1016/j.jct.2019.106010.

6. T. Loftsson, M.E. Brewster, Pharmaceutical applications of cyclodextrins: Basic science and product development, *J. Pharm. Pharmacol.*, **62**, 1607-1621 (2010), DOI: https://doi.org/10.1111/j.2042-7158.2010.01030.x.

7. T. Takagi, C. Ramachandran, M. Bermejo, S. Yamashita, L.X. Yu, G.L. Amidon, A provisional biopharmaceutical classification of the top 200 oral drug products in the United States, Great Britain, Spain, and Japan, Mol. Pharm., 3, 631-643 (2006). DOI: https://doi.org/10.1021/mp0600182.

8. A. Jouyban, M. Fakhree, A. Shayanfar, Solubility prediction methods for drug/drug like molecules, *Recent Pat. Chem. Eng.*, 1, 220-231 (2008).

9. A. Konczol, G. Dargo, Brief overview of solubility methods: Recent trends in equilibrium solubility measurement and predictive models, *Drug Discov. Today*, **27**, 3-17 (2018). DOI: https://doi.org/10.1016/j.ddtec.2018.06.001.

10. C.A. Lipinski, F. Lombardo, B.W. Dominy, P.J. Feeny, Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings, *Adv. Drug Del. Rev.*, **46**, 3-26 (2001). DOI: https://doi.org/10.1016/S0169-409X(96)00423-1.

11. J. Alsenz, M. Kansy, High throughput solubility measurement in drug discovery and development, *Adv. Drug Del. Rev.*, **59**, 546-567 (2007). DOI: https://doi.org/10.1016/j.addr.2007.05.007.

12. S. Kalepu, V. Nekkanti, Insoluble drug delivery strategies: Review of recent advances and business prospects, *Acta Pharm. Sin. B*, **5**, 442-453 (2015). DOI: https://doi.org/10.1016/j.apsb.2015.07.003.

13. S.S. Ren, B.D. Anderson, What determines drugs solubility in lipid vehicles: Is it predictable?, *Adv. Drug Del. Rev.*, **60**, 638-656 (2008). DOI: https://doi.org/10.1016/j.addr.2007.10.015.

14. W.L. Jorgensen, E.M. Duffy, Prediction of drug solubility from structure, *Adv. Drug Del. Rev.*, **54**, 355-366 (2002). DOI: https://doi.org/10.1016/S0169-409X(02)00008-X.

15. M. Mirmehrabi, S. Rohani, L. Perry, Thermodynamic modeling of activity coefficient and prediction of solubility: Part 1. Predictive models, *J. Pharm. Sci.*, **95**, 790-797 (2005). DOI: https://doi.org/10.1002/jps.20576.

16. A. Jouyban, E. Rahimpour, Z. Karimzadeh, A new correlative model to simulate the solubility of drugs in mono-solvent systems at various temperatures, *J. Mol. Liq.*, **343**, 117587 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.117587.

17. X. Ji CL, J. Li, B. Hou, L. Zhou, Ch. Xie, J. Gong, W. Chen, J. Zhao, Measurement and comprehensive analysis of the solubility of abacavir in twelve pure solvents, *J. Mol. Liq.*, **338**, 116603 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.116603.

18. Zh. Wang, J. Dong, Zh. Li, L. Ding, B. Wang, Measurement and correlation of the solubility of antipyrine in ten pure and water + ethanol mixed solvents at temperatures from (288.15 to 328.15) K, *J. Mol. Liq.*, **268**, 256-265 (2018). DOI: https://doi.org/10.1016/j.molliq.2018.07.061.

19. M. Liu, S. Wang, C. Qu, Z. Zhang, Y. Qu, Solubility determination and thermodynamic properties of bezafibrate in pure and binary mixed solvents, *J. Chem. Eng. Data*, **65**, 2156-2169 (2020). DOI: https://doi.org/10.1021/acs.jced.0c00025.

20. W. Hong, S. Jia, Z. Li, W. Li, Z. Gao, Solubility determination and thermodynamic correlation of chlorphenesin in 12 pure solvents from 288.15 to 328.15 K, *J. Chem. Eng. Data*, **66**, 822-831 (2021). DOI: https://doi.org/10.1021/acs.jced.0c00900.

21. Y. Wu, C. Wu, S. Yan, B. Hu, Solubility of bisacodyl in pure solvent at various temperatures: data correlation and thermodynamic property analysis, *J. Chem. Eng. Data*, **65**, 43-48 (2020). DOI: https://doi.org/10.1021/acs.jced.9b00728.

22. Y. Wu, J. Wu, J. Wang, J. Gao, Effect of solvent properties and composition on the solubility of ganciclovir form I, *J. Chem. Eng. Data*, **64**, 1501-1507 (2019). DOI: https://doi.org/10.1021/acs.jced.8b01080.

23. S. Li, Y. Liu, F. Yin, X. Ye, Solubility measurement and thermodynamic properties of levetiracetam in pure and mixed solvents, *J. Chem. Eng. Data*, **63**, 4669-4681 (2018). DOI: https://doi.org/10.1021/acs.jced.8b00720.

24. Y. Zhao, H. Yang, Z. Shang, T. Gong, X. Zhang, S. Wu, Solubility determination and correlation of glibenclamide in 11 monosolvents and (acetone + acetonitrile) binary solvents from 283.15 K to 323.15 K, *J. Chem. Eng. Data*, **64**, 189-201 (2019). DOI: https://doi.org/10.1021/acs.jced.8b00717.

25. G. Hu, H. Li, X. Wang, Y. Zhang, Measurement and correlation of griseofulvin solubility in different solvents at temperatures from (281.95 to 357.60) K, *J. Chem. Eng. Data*, **55**, 3969-3971 (2010). DOI: https://doi.org/10.1021/je100030j.

26. S. Wang, N. Chen, Y. Qu, Solubility of florfenicol in different solvents at temperatures from (278 to 318) K, *J. Chem. Eng. Data*, **56**, 638-641 (2011). DOI: https://doi.org/10.1021/je1008284.

27. C. L. Zhang, B. Y. Li, Y. Wang, Solubilities of norfloxacin in ethanol, 1-propanol, acetone, and chloroform from 294.15 to 318.15 K, *Can. J. Chem. Eng.*, **88**, 63-66 (2010). DOI: https://doi.org/10.1002/cjce.20247.

28. K. Zhang, H. Shen, S. Xu, H. Zhang, M. Zhu, P. Shi, *et al.*, Thermodynamic study of solubility for pyrazinamide in ten solvents from T = (283.15 to 323.15) K, *J. Chem. Thermodyn.*, **112**, 204-212 (2017). DOI: https://doi.org/10.1016/j.jct.2017.04.014.

29. Y. Hu, G. Wu, P. Gu, W. Yang, C. Wang, Z. Ding, *et al.*, Thermodynamic models for determination of the solubility of omeprazole in pure and mixture organic solvents from T = (278.15 to 333.15) K, *J. Chem. Thermodyn.*, **94**, 177-185 (2016). DOI: https://doi.org/10.1016/j.jct.2015.11.005.

30. H. Niu, Z. Cao, X. Yang, J. Sha, Y. Li, T. Li, *et al.*, The solubility data, Hansen solubility parameter and dissolution thermodynamic properties of riluzole in twelve organic solvents, *J. Chem. Thermodyn.*, **162**, 106569 (2021). DOI: https://doi.org/10.1016/j.jct.2021.106569.

31. Y. Wang, Y. Liu, S. Xu, Y. Liu, P. Yang, S. Du, *et al.*, Determination and modelling of troxerutin solubility in eleven mono-solvents and (1,4-dioxane+2-propanol) binary solvents at temperatures from 288.15 K to 323.15 K, *J. Chem. Thermodyn.*, **104**, 138-149 (2017). DOI: https://doi.org/10.1016/j.jct.2016.09.015.

32. Y. Wu, J. Gao, S. Yan, C. Wu, B. Hu, The dissolution behavior and apparent thermodynamic analysis of temozolomide in pure and mixed solvents, *J. Chem. Thermodyn.*, **132**, 54-61 (2019). DOI: https://doi.org/10.1016/j.jct.2018.11.026.

33. R. Li, X. Chen, G. He, C. Wu, Z. Gan, Z. He, *et al.*, The dissolution behaviour and thermodynamic properties calculation of praziquantel in pure and mixed organic solvents, *J. Chem. Thermodyn.*, **144**, 106062 (2020). DOI: https://doi.org/10.1016/j.jct.2020.106239.

34. J. Sha, T. Ma, R. Zhao, P. Zhang, R. Sun, G. Jiang, *et al.*, The dissolution behaviour and apparent thermodynamic analysis of doxifluridine in twelve pure solvents at various temperatures, *J. Chem. Thermodyn.*, **144**, 106073 (2020). DOI: https://doi.org/10.1016/j.jct.2020.106062.

35. Z. Cao, R. Zhang, X. Hu, J. Sha, G. Jiang, Y. Li, *et al.*, Thermodynamic modelling, Hansen solubility parameter and solvent effect of oxaprozin in thirteen pure solvents at different temperatures, *J. Chem. Thermodyn.*, **151**, 106239 (2020). DOI: https://doi.org/10.1016/j.jct.2020.106073.

36. Z. Huang, Y. Zun, Y. Gong, X. Hu, J. Sha, Y. Li, *et al.*, Solid-liquid equilibrium solubility, thermodynamic properties, solvent effect of Ipriflavone in twelve pure solvents at various temperatures, *J. Chem. Thermodyn.*, **150**, 106231 (2020). DOI: https://doi.org/10.1016/j.jct.2020.106231.

37. W. Hu, Z. Shang, N. Wei, B. Hou, J. Gong, Y. Wang, Solubility of benorilate in twelve monosolvents: Determination, correlation and COSMO-RS analysis, *J. Chem. Thermodyn.*, **152**, 106272 (2021). DOI: https://doi.org/10.1016/j.jct.2020.106272.

38. R. Sun, H. He, Y. Wan, L. Li, J. Sha, G. Jiang, *et al.*, Kojic acid in fourteen mono-solvents: Solubility data, Hansen solubility parameter and thermodynamic properties, *J. Chem. Thermodyn.*, **152**, 106280 (2021). DOI: https://doi.org/10.1016/j.jct.2020.106280.

39. J. Ma, H. Li, Z. Cao, J. Sha, R. Sun, H. He, *et al.*, Solid-liquid phase equilibrium of Nintedanib in ten pure solvents: Determination, thermodynamic analysis, model correlation and molecular simulation, *J. Chem. Thermodyn.*, **163**, 106595 (2021). DOI: https://doi.org/10.1016/j.jct.2021.106595.

40. S. Yu, Y. Cheng, S. Du, Y. Wang, F. Xu, W. Xing, Thermodynamic analysis of the solubility of clozapine in organic solvents, *J. Chem. Thermodyn.*, **158**, 106451 (2021). DOI: https://doi.org/10.1016/j.jct.2021.106451.

41. L. Ding, B. Wang, F. Wang, J. Dong, G. Zhou, H. Li, Measurement and correlation of the solubility of dipyrone in ten mono and water + ethanol mixed solvents at temperatures from (293.15 to 332.85) K, J. Mol. Liq., 241, 742-750 (2017). DOI: https://doi.org/10.1016/j.molliq.2017.06.072.

42. S. Zong, J. Wang, Y. Xiao, H. Wu, Y. Zhou, Y. Guo, *et al.*, Solubility and dissolution thermodynamic properties of lansoprazole in pure solvents, *J. Mol. Liq.*, **241**, 399-406 (2017). DOI: https://doi.org/10.1016/j.molliq.2017.06.037.

43. Y. Yu, F. Li, S. Long, L. Xu, G. Liu, Solubility, thermodynamic properties, HSP, and molecular interactions of vitamin K3 in pure solvents, *J. Mol. Liq.*, **317**, 113945 (2020). DOI: https://doi.org/10.1016/j.molliq.2020.113945.

44. G. Zhou, B. Wang, L. Ding, J. Dong, F. Wang, C. Feng, Measurement and correlation of the solubility of Lidocaine in eight pure and mixed solvents at temperatures from (292.15 to 332.15) K, *J. Mol. Liq.*, **242**, 168-174 (2017). DOI: https://doi.org/10.1016/j.molliq.2017.06.110.

45. X. Hu, Y. Gong, Z. Cao, Z. Huang, J. Sha, Y. Li, *et al.*, Solubility, Hansen solubility parameter and thermodynamic properties of etodolac in twelve organic pure solvents at different temperatures, *J. Mol. Liq.*, **316**, 113779 (2020). DOI: https://doi.org/10.1016/j.molliq.2020.113779.

46. R. Sun, Y. Wang, H. He, Y. Wan, L. Li, J. Sha, *et al.*, Solubility measurement, solubility behavior analysis and thermodynamic modelling of melatonin in twelve pure solvents from 278.15 K to 323.15 K, *J. Mol. Liq.*, **319**, 114139 (2020). DOI: https://doi.org/10.1016/j.molliq.2020.114139.

47. S. Guo, Z. Li, S. Du, C. Zhao, M. Wang, X. Su, *et al.*, Thermodynamic analysis and molecular dynamic simulation of solid-liquid phase equilibrium of imazapyr in twelve pure organic solvents, *J. Mol. Liq.*, **330**, 115631 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.115631.

48. R. Sun, Y. Wen, H. He, L. Yuan, Y. Wan, J. Sha, *et al.*, Uridine in twelve pure solvents: Equilibrium solubility, thermodynamic analysis and molecular simulation, *J. Mol. Liq.*, **330**, 115663 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.115663.

49. X. Su, C. Yu, P. Zhao, M. Wang, C. Zhao, M. Chen, *et al.*, Solid-liquid equilibrium and thermodynamic analysis of elastically bendable crystal celecoxib in thirteen pure solvents based on experiments and molecular simulation, *J. Mol. Liq.*, **338**, 116706 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.116706.

50. C. Zhao, J. Lin, Y. Gao, S. Guo, R. Liu, S. Wu, Solid-liquid equilibrium behavior, thermodynamic analysis and molecular simulation of dimetridazole in twelve organic solvents, *J. Mol. Liq.*, **336**, 116252 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.116252.

51. Y. Chong, Q. Liu, Z. Wang, L. Zhu, F. Guo, Y. Li, *et al.*, Solubility, MD simulation, thermodynamic properties and solvent effect of perphenazine (Form I) in eleven neat organic solvents ranged from 278.15 K to 318.15 K, *J. Mol. Liq.*, **348**, 118184 (2022). DOI: https://doi.org/10.1016/j.molliq.2021.118184.

52. L. Jia, J. Yang, P. Cui, D. Wu, S. Wang, B. Hou, *et al.*, Uncovering solubility behavior of Prednisolone form II in eleven pure solvents by thermodynamic analysis and molecular simulation, *J. Mol. Liq.*, **342**, 117376 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.117376.

53. L. Yuan, Z. Cao, R. Sun, H. He, Y. Ren, H. Niu, *et al.*, Experimental measurement, thermodynamic analysis and molecular simulation of topiramate solubility in fourteen mono-solvents at various temperatures, *J. Mol. Liq.*, **342**, 116992 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.116992.

54. Z. Yu Yw, M. Zhu, L. Zhou, Measurement and correlation of solubility and thermodynamic properties of vinpocetine in nine pure solvents and (ethanol + water) binary solvent, *J. Chem. Eng. Data*, **64**, 150-160 (2019). DOI: https://doi.org/10.1021/acs.jced.8b00663.

55. Y. Cong CD, M. Wang, Zh. Jiang, K. Xing, Y. Bian, M. Wang, Investigation on the Hansen solubility parameter, solvent effect and thermodynamic analysis of indapamide dissolution and molecular dynamic simulation, *J. Mol. Liq.*, **334**, 116489 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.116489.

56. B. Tian YF, X. Li, J. Yang, Zh. Ding, X. Huang, Q. Yin, Ch. Xie, H. Hao, Solution thermodynamic properties of flurbiprofen in twelve solvents from 283.15 to 323.15 K, *J. Mol. Liq.*, **296**, 111744 (2019). DOI: https://doi.org/10.1016/j.molliq.2019.111744.

57. P. Zhang CZ, R. Zhao, Y. Wan, Zh. Yang, R. He, Q. Chen, T. Li, B. Ren, Measurement and correlation of the solubility of florfenicol form A in several pure and binary solvents, *J. Chem. Eng. Data*, **63**, 2046-2055 (2018). DOI: https://doi.org/10.1021/acs.jced.8b00043.

58. X. Dong Y. Cao, N. Wang, P. Wang, M. Li, Systematic study on solubility of chrysin in different organic solvents: the synergistic effect of multiple intermolecular interactions on the dissolution process, J. Mol. Liq., 325, 115180 (2021). DOI: https://doi.org/10.1016/j.molliq.2020.115180.

59. J. Ma, X. Huang, N. Wang, X. Li, Y. Bao, T. Wang, *et al.*, Solubility and thermodynamic mixing and dissolution properties of empagliflozin in pure and binary solvent systems, J. Mol. Liq., 309, 113004 (2020). DOI: https://doi.org/10.1016/j.molliq.2020.113004.

60. M.J.C. Zheng, G. Chen, A. Farajitabar, H. Zhao, Solubility modelling and solvent effect for domperidone in twelve green solvents, *J. Mol. Liq.*, **261**, 50-56 (2018). DOI: https://doi.org/10.1016/j.molliq.2018.03.121.

61. J. Ma, X. Huang, N. Wang, X. Li, Y. Bao, T. Wang, *et al.*, Solubility and thermodynamic mixing and dissolution properties of empaglifozine inpure and

binary solvent systems, *J. Mol. Liq.*, **309**, 113004 (2020). DOI: https://doi.org/10.1016/j.molliq.2020.113004.

62. J.H. van't Hoff, L'équilibre chimique dans les systèmes gazeux on dissous à l'état dilué, *Archives Neerlandaises des Sciences Exactes et Naturelles*, **20**, 239-302 (1886). DOI: https://doi.org/10.1002/recl.18850041207.

63. D.M. Stovall, C. Givens, S. Keown, K.R. Hoover, R. Barnes, C. Harris, *et al.*, Solubility of crystalline nonelectrolyte solutes in organic solvents: Mathematical correlation of 4-chloro-3-nitrobenzoic acid and 2-chloro-5-nitrobenzoic acid solubilities with the Abraham solvation parameter model, *Phys. Chem. Liq.*, **43**, 351-360 (2005). DOI: https://doi.org/10.1080/00319100500111293.

64. C.M. Hansen, *Hansen solubility parameters: A user's handbook*, CRC Press, Boca Raton (FL), 2007.

65. J. Catalan, Toward a generalized treatment of the solvent effect based on four empirical scales: dipolarity (SdP, a new scale), polarizability (SP), acidity (SA), and basicity (SB) of the medium, *J. Phys. Chem. B*, **113**, 5951-5960 (2009). DOI: https://doi.org/10.1021/jp8095727.

66. A. Hatefi, A. Jouyban, E. Mohammadian, W.E. Acree, Jr., E. Rahimpour, Prediction of paracetamol solubility in cosolvency systems at different temperatures, *J. Mol. Liq.*, **273**, 282-289 (2019). DOI: https://doi.org/10.1016/j.molliq.2018.10.031.

67. E. Rahimpour, E. Mohammadian, W.E. Acree, Jr., A. Jouyban, Computational tools for solubility prediction of celecoxib in the binary solvent systems, *J. Mol. Liq.*, **299**, 112129 (2020). DOI: https://doi.org/10.1016/j.molliq.2019.112129.

68. E. Rahimpour, W.E. Acree, Jr., A. Jouyban, Prediction of sulfonamides' solubilities in the mixed solvents using solvation parameters, *J. Mol. Liq.*, **339**, 116269 (2021). DOI: https://doi.org/10.1016/j.molliq.2021.116269.

69. http://www.ufz.de/lserd.

How to cite this article

S. Khezri, P. Jafari, A. Jouyban, Drugs solubility prediction in mono-solvents at various temperatures using a minimum number of experimental data points, Rev. Colomb. Cienc. Quim. Farm., **52**(2), 908-954(2023). https://doi.org/10.15446/rcciquifa.v52n2.110747