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Thermodynamic Models for Determination of Solubility of Cellulose Acetate in Various Solvents at Different Temperatures

S Baluja*, Elham Abdullah Mo Alnayab and Asmita Hirapara

Department of Chemistry, Saurashtra University, Rajkot-360005 (Gujarat), India

***Corresponding author:** S Baluja, Department of Chemistry, Saurashtra University, Rajkot-360005, Gujarat, India, E-Mail: shipra_baluja@rediffmail.com

Abstract

The solubility of cellulose acetate in water, methanol, ethanol, 1-propanol, 1-butanol, tetrahydrofuran, ethyl acetate, 1,4-dioxane and N, N-dimethyl formamide was measured by gravimetric method over a temperature range (293.15 to 323.15) K at atmospheric pressure. The solubility is found to increase nonlinearly with temperature in most of the studied solvents. In alcohols and water, solubility is less than other non protic solvents. The solubility data were correlated with temperature by modified Apelblat and Buchowski-Ksiazczak (λh) equations. To understand the dissolution process, some thermodynamic parameters such as dissolution enthalpy, Gibb's free energy, and entropy of mixing have also been calculated by Van't Hoff analysis. The evaluated thermodynamic parameters are interpreted in terms of dominating driving force for dissolution process.

***Keywords**: Cellulose acetate; Solubility; Apelblat equation; Buchowski-Ksiazczak equation; thermodynamic parameters; Van't Hoff analysis.*

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Introduction

In pharmaceutical industry, solubility process is very important because for getting a pure drug, usually the most common method is crystallization. So, for the selection of proper solvent for the crystallization process and in pre formulation studies, solubility data is very important [1]. Further, knowledge of solubility plays an important role in various other pharmaceutical processes such as drug delivery, transport and distribution of drug [2-4].

Cellulose acetate phthalate (CAP) is a microbicide which inactivates sexually transmitted disease pathogens like HIV-1 and is effective in animal models for vaginal infection by HSV-2 and simian immunodeficiency virus. It is known to inhibit infection by the human immunodeficiency virus type 1 and several herpes viruses [5-7]. It has been used for enteric film coating of tablets and capsules [8]. Enteric coatings based on CAP are resistant to acidic gastric fluids, but easily soluble in mildly basic medium of the intestine. So it is used as film coating of tablets, enteric coating of tablets, sustained release, delayed release, pallate coating material [9-14]. It has a well-established safety record for human use [15].

Thus, in continuation with our ongoing research on drug solubility, in the present work, the solubility of cellulose acetate have been determined in various solvents; water, methanol, ethanol, iso-propanol, butanol, tetrahydrofuran, ethyl acetate, 1,4-dioxane and N, N- dimethyl formamide at different temperatures (298.15 K to 328.15 K). The correlation between experimental solubility data and temperature are studied using modified Apelblat and Buchowski-Ksiazczak models. Further,

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using solubility data, some thermodynamic parameters such as enthalpy of dissolution, Gibb's energy and entropy of solutions have been evaluated.

Experimental

Materials

Cellulose Acetate Phthalate was purchased from Otto Chemika Pvt. Ltd. (purity > 99 %). It is also known as cellacefate or cellulose acetate 1,2 - benzene dicarboxylate and CAS number is 9004-38-0. It is a hygroscopic, white to off-white, free-flowing powder, granule, or flake. It is tasteless and odorless, or might have a slight odor of acetic acid. The structure of Cellulose acetate phthalate (CAP) is shown in **FIG. 1**.

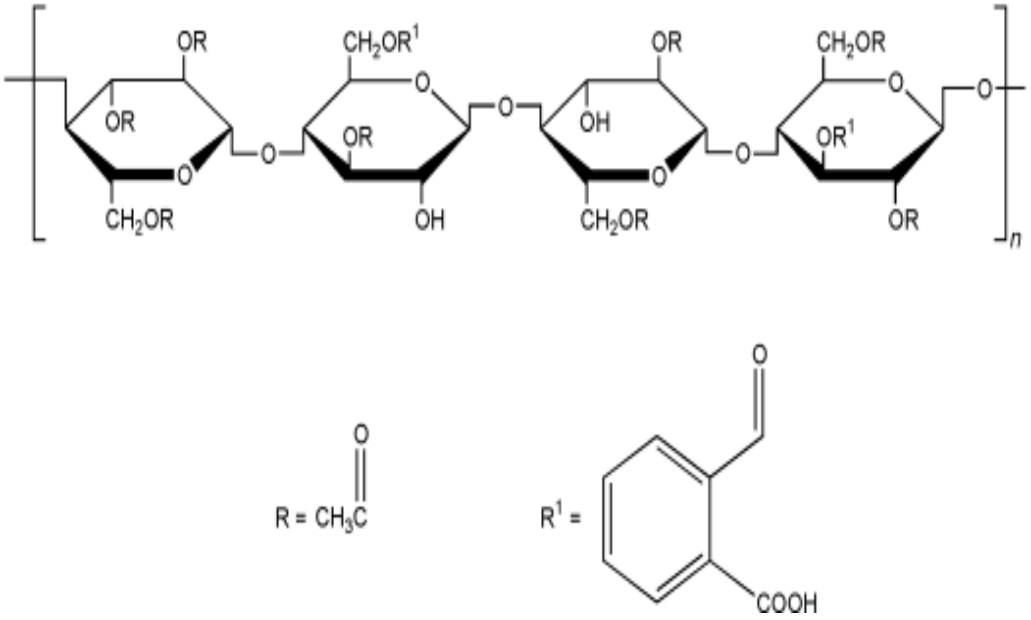


FIG. 1. **Chemical structure of cellulose acetate phthalate.**

The solvents: methanol, ethanol, iso-propanol, and n-butanol, tetrahydrofuran, ethyl acetate,1, 4-dioxane and N, N-dimethyl formamide (DMF) were of HPLC grade reagents and were purified by fractional distillation. The purities of the solvents were confirmed by GC-MS (SHIMADZU-Model No.-QP-2010) and were found be greater than 99.8%. TABLE 1 shows the purity of all the solvents selected for the present study.

TABLE 1. **The source and purity of chemicals used.**

Chemical Name	Source	Purity (%)
Cellulose Acetate Phthalate	Otto.chemi	>99.00
Methanol	Allied chemical corporation	>99.96
Ethanol	Baroda Chemical Industry	>99.94
Iso-Propanol	SpectrochemPvt. Ltd.	>99.98
Butanol	SpectrochemPvt. Ltd	> 99.93
THF	Allied chemical corporation	> 99.10
Ethyl acetate	Allied chemical corporation	> 99.60
1,4-Dioxane	SpectrochemPvt. Ltd	> 99.94
DMF	Allied chemical corporation	> 99.30

The melting point of Cellulose acetate phthalate was determined measured by Differential Scanning Calorimeter (Shimadzu-DSC-60). The observed value of 466.15 K is in agreement with the reported value of 465.15K [15].

Solubility measurement

Gravimetric method was used to determine the solubility of CAP in different solvents at different temperatures. At each temperature and for each solvent, in a known mass of solvent, excess of CAP was added and solution was heated to a constant temperature with continuous stirring for about 5-6 hours. The stirring was stopped and the solution was to approach equilibrium. The upper clear solution was then filtered and a definite volume (2 ml) of this solution was then taken in a weighed vial and the vial with solution was quickly weighed to determine the mass of the sample solution. The solution in the vial was then allowed to evaporate. After complete evaporation, residue is left in the vial and the mass of this residue was recorded. For taking weights, an electronic balance (Mettler Toledo AB204-S, Switzerland) with an uncertainty of ±0.0001 g was used. Each measurement was done thrice and an average value was used to determine the mole fraction solubility. To determine the saturated mole fraction solubility (x_i) of cellulose acetate in each solvent, following equation (1) was used.

$$x_i = \frac{m_2/M_2}{m_1/M_1 + m_2/M_2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

Where M_1 is the molar mass of solvent and M_2 is the molar mass of CAP. $m_1$and $m_2$are the mass of the solvent and CAP respectively. At each temperature, the measurement was conducted three times. By using the average value, mole fraction solubility of CA Pin selected solvents were calculated.

Results and Discussion

TABLE 2 shows the solubilities (x_i) of CAP in the selected solvents at different temperatures (293.15 to 323.15 K). The variation of solubility with temperature is also shown graphically in **FIG. 2**.

TABLE 2. **The experimental and theoretical mole fraction solubility and relative deviation (RD) of CAP in different solvents.**

Temperature (K)	$x_2^{exp}.10^5$	$x_2^{cal}.10^5$		$RD^2.10^2$	
		$x_2^{cal(a)}$	$x_2^{cal(b)}$	$RD^{(a)}$	$RD^{(b)}$
Water					
298.15	0.8633	0.8814	1.0079	-2.09	-16.74
303.15	1.3311	1.3030	1.2960	2.11	2.63
308.15	1.8176	1.7982	1.6531	1.06	9.05
313.15	2.3301	2.3264	2.0922	0.16	10.21
318.15	2.7537	2.8326	2.6284	-2.86	4.55
323.15	3.2211	3.2578	3.2787	-1.14	-1.78
328.15	3.6014	3.5511	4.0626	1.40	-12.80
Methanol					
298.15	2.8084	2.9009	3.2352	-3.29	-15.19

303.15	4.4022	4.2591	4.2599	3.25	3.23
308.15	6.0817	5.9060	5.5594	2.89	8.58
313.15	7.6900	7.7616	7.1938	-0.93	6.45
318.15	9.7976	9.6983	9.2336	2.01	2.59
323.15	11.4112	11.5564	11.7607	-2.27	-0.57
328.15	13.4707	13.1686	14.8693	2.24	-7.19
Ethanol					
298.15	2.3632	2.3974	2.5254	-1.45	-7.26
303.15	3.2813	3.1921	3.1787	2.72	2.77
308.15	4.0175	4.1167	3.9712	-2.47	0.79
313.15	5.2099	5.1520	4.9261	1.12	5.11
318.15	6.2274	6.2677	6.0694	-0.64	2.20
323.15	7.3411	7.4246	7.4299	-1.13	-1.55
328.15	8.6268	8.5769	9.0394	0.58	-5.13
Iso-propanol					
298.15	3.4671	3.4679	3.4623	-0.02	-0.07
303.15	3.8033	3.8156	3.8094	-0.32	-0.36
308.15	4.1326	4.1853	4.1784	-1.28	-1.31
313.15	4.6399	4.5772	4.5696	1.35	1.32
318.15	4.9723	4.9918	4.9833	-0.39	-0.42
323.15	5.4411	5.4294	5.4199	0.22	0.19
328.15	5.8478	5.8903	5.8798	-0.73	-0.74
Butanol					
298.15	2.3429	2.3915	2.4551	-2.07	-5.13
303.15	2.8899	2.8301	2.8212	2.07	2.06
308.15	3.3251	3.2917	3.2273	1.00	2.6
313.15	3.7722	3.7667	3.6760	0.15	2.24
318.15	4.1441	4.2446	4.17009	-2.42	-0.93
323.15	4.6411	4.7143	4.7121	-1.58	-1.83
328.15	5.2464	5.1651	5.3048	1.55	-1.41
Tetrahydrofuran					
298.15	6.6261	6.7572	7.0744	-1.98	-6.99
303.15	8.8001	8.5219	8.4923	3.16	3.32
308.15	10.3854	10.4554	10.1313	-0.67	2.27
313.15	12.3999	12.4993	12.0187	-0.80	2.90
318.15	14.3110	14.5828	14.1814	-1.89	0.73
323.15	16.822	16.6272	16.6477	1.16	0.87
328.15	18.5385	18.5524	19.4478	-0.08	-5.08
Ethyl acetate					
298.15	5.6304	5.6419	5.8112	-0.20	-3.51
303.15	6.7444	6.8025	6.7834	-0.93	-0.92
308.15	8.1521	8.0466	7.8786	1.29	3.09
313.15	9.3234	9.3488	9.1070	-0.31	2.02
318.15	10.6271	10.6794	10.4792	-0.49	2.13
323.15	11.8835	12.0062	12.0058	-1.06	-1.32
328.15	13.3640	13.2964	13.6979	0.51	-2.76
1,4-dioxane					
298.15	12.5435	12.4217	12.4122	0.97	0.92
303.15	15.1560	15.3580	15.3508	-1.71	-1.81
308.15	18.8403	18.8621	18.8546	-0.12	-0.25
313.15	23.1113	23.0193	23.0067	0.35	0.21
318.15	27.6062	27.9231	27.8980	-1.15	-1.27
323.15	33.9988	33.6766	33.6281	0.95	0.86

328.15	40.2357	40.3922	40.3050	-0.39	-0.43
DMF					
298.15	20607.1	20593.3	205817.5	0.069	0.03
303.15	21249.9	21250.4	212440.1	-0.002	-0.06
308.15	21854.4	21908.4	219050.6	-0.25	-0.32
313.15	22555.5	22567.0	225645.9	-0.05	-0.13
318.15	23246.1	23226.0	232223.1	0.08	0.01
323.15	23882.1	23885.2	238779.6	-0.01	-0.07
328.15	24537.7	24544.5	245313.0	-0.03	-0.06

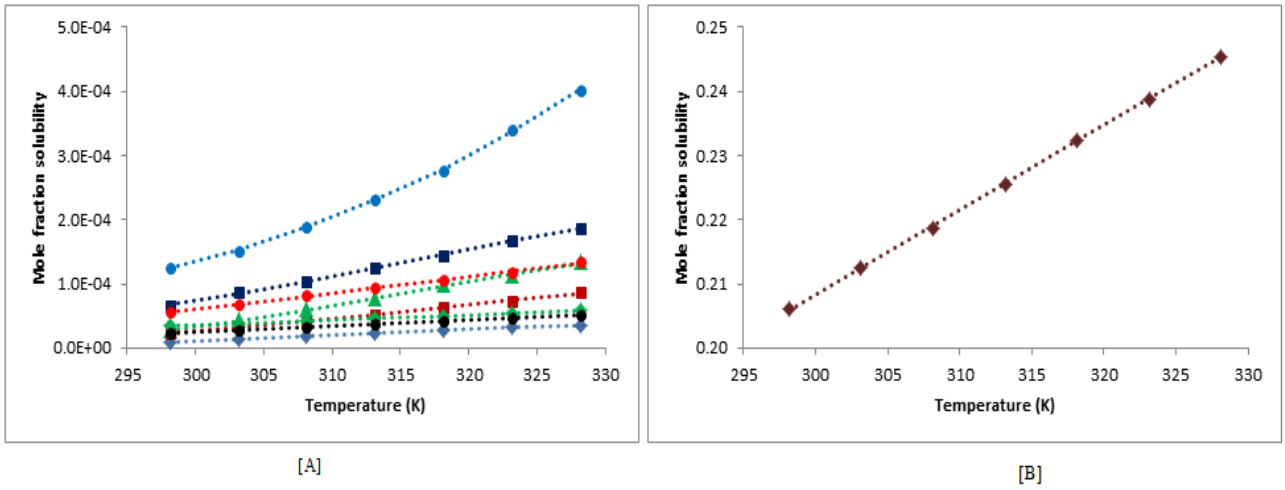


FIG. 2. **The variation of experimental and calculated mole fraction solubility by Apelblat model with temperature for CAP in different solvents.[A] ♦: Water; ▲: Methanol; ■ : Ethanol; ♦: Isopropanol; ●: Butanol; ■ : Tetrahydrofuran; ●: Ethyl acetate; ●: 1,4-dioxane;[B]♦: DMF.**

It is observed that the solubility is minimum in water and maximum in N, N –dimethylformamide. Among alcohols, the order of solubility is: methanol > ethanol > iso-propanol > n-butanol. Whereas in aprotic solvents, order is: DMF > 1,4-dioxane > tetrahydrofuran > ethyl acetate. Further, solubility increases with increase in temperature. Thus, in alcohols, as CH_2 group increases, solubility decreases.

Parameters describing and correlating the solvent ability of liquids have been based on a great variety of chemical and physical properties. The ability of organic liquids to donate or accept hydrogen bond is one of these properties which can be determined by Hildebrand solubility parameter. **TABLE 3** shows the dielectric constants, dipole moment and hydrogen bond capacity i.e., total Hildebrand solubility parameter of the studied solvents. The solubility data are correlated with dielectric constants, dipole moment and hydrogen bond capacity and it is observed that the effect of hydrogen bond capacity is pronounced in all the studied solvents. Comparison of hydrogen bond capacity with solubility data indicates that among alcohols, as hydrogen bond capacity decreases, solubility decreases whereas in other solvents, the solubility increases with increase in hydrogen bond capacity.

TABLE 3**. Dipole moments, Dielectric constants and hydrogen bond capacity (δ_H) of studied solvents.**

Solvent	***Dipole moment***	***Dielectric constant***	δ_H
Water	1.82	80.10	47.9
Methanol	1.70	32.70	29.6
Ethanol	1.69	24.55	26.5
Iso-propanol	1.66	17.90	23.5
Butanol	1.66	17.80	23.3
Tetrahydrofuran	1.75	7.58	19.4
Ethyl acetate	1.88	6.02	18.1
1,4-Dioxane	0.45	2.25	20.5
DMF	3.86	36.70	24.8

The solubility data was also correlated with temperature by the modified Apelblat model [17]:

$$\ln x_{ci}^{a} = A + \frac{B}{T} + C\ln T \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \qquad (2)$$

The values of parameters *A*, *B* and *C* were evaluated by non-regression method and are given in Table 4. These parameters are used to evaluate mole fraction solubility values (x_{ci}^{a}) which are also plotted against temperature along with experimental mole fraction solubility (x_i) as shown in **FIG. 2**. It is evident from **FIG. 2** that there is good agreement between the experimental and calculated solubility values.

TABLE 4**. Parameters of modified Apelblat equation for CAP in studied solvents**

Solvent	***A***	***B***	***C***	***RMDS.10^7***	***AAD.10^2***	γ
Water	1417.0507	-70054.29	-209.5144	4.08	-0.1951	0.9993
Methanol	1132.1703	-57124.531	-166.9166	16.35	0.5570	0.9985
Ethanol	574.3419	-30623.729	-84.6444	6.91	-0.1848	0.9993
Iso-Propanol	-4.6056	-1721.971	0.0193	3.62	-0.1681	0.9991
n-Butanol	296.6736	-16364.437	-44.3046	6.459	-0.1869	0.9978
Tetrahydrofuran	506.3720	-26696.263	-74.8450	17.78	-0.1584	0.9988
Ethyl acetate	328.0036	-18017.073	-48.6799	7.48	-0.1989	0.9996
1,4-Dioxane	-1.6998	-3586.5426	0.8309	21.31	-0.1557	0.9997
DMF	-2.2552	-452.2473	0.3846	2298.48	-0.0269	0.9999

The solubility data was also correlated with temperature by using the following Buchowski-Ksiazczak (λh) model [18]:

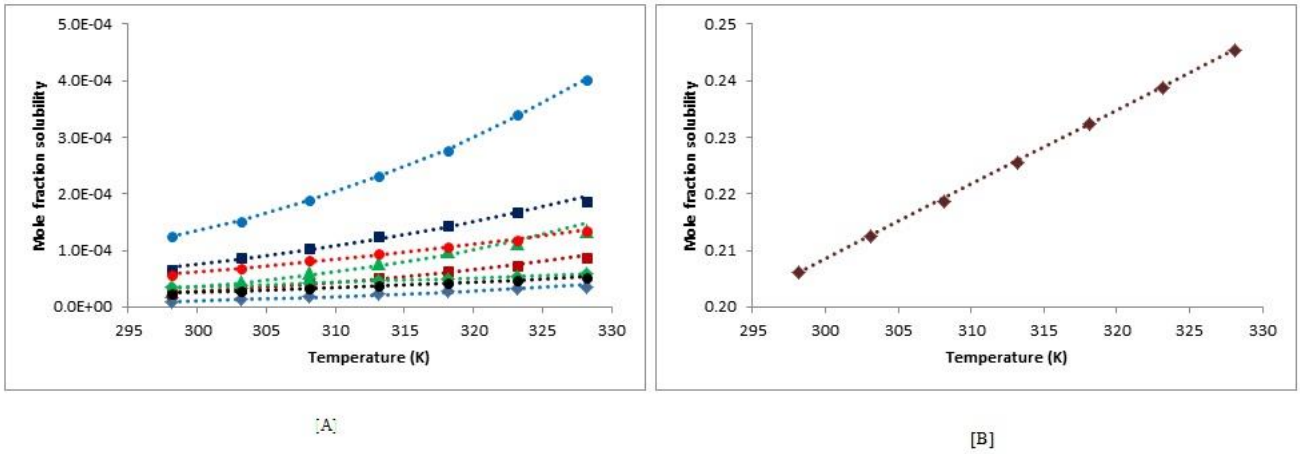
$$\ln\left(1 + \frac{\lambda\left(1 - x_{ci}^{b}\right)}{x_{ci}^{b}}\right) = \lambda h\left[\frac{1}{T} - \frac{1}{T_m}\right] \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \qquad (3)$$

T and T_m are the experimental and melting temperature of CAP, λ and h are two adjustable parameters which are evaluated using experimental solubility data. The evaluated λ and h values are reported in TABLE 5.

TABLE 5**. Parameters of Bukowski-Ksiazaczak equation for CAP in studied solvents.**

Solvent	***h***	***λ***	***RMDS.10^6***	***AAD.10^2***	***γ***
Water	464812.40	0.0098	2.19	-0.6972	0.9990
Methanol	82923.49	0.0599	6.67	0.6590	0.9749
Ethanol	304375.00	0.0136	2.19	-0.4387	0.9900
Iso-Propanol	3651912.00	0.0005	0.36	-0.1978	0.9980
n-Butanol	71188.07	0.0455	0.82	-0.3365	0.9890
Tetrahydrofuran	30421.51	0.0655	4.48	-0.2796	0.9888
Ethyl acetate	698681.50	0.0040	2.13	-0.3761	0.9935
1,4-Dioxane	92061.93	0.0417	2.0485	-0.2504	0.9990
DMF	1168.977	0.4897	306.42	-0.0861	0.9998

The solubility (x^b_{ci}) is calculated from equation (3) using these evaluated λ and h values. These values are also compared with experimental mole fraction solubility (x_i) by plotting against temperature as shown in **FIG. 3**.



[A] [B]

FIG. 3. **The variation of experimental and calculated mole fraction solubility by Buchwski model withtemperature for CAP in different solvents [A] ♦: Water; ▲: Methanol; ■: Ethanol; ♦: Isopropanol; ●: Butanol; ■: Tetrahydrofuran; ●: Ethyl acetate; ●: 1,4-dioxane;[B]♦: DMF**

Further, the deviation between experimental and calculated solubility values were determined by calculating root-mean-square deviations (RMSD) and average relative deviations (ARD) using following equations:

$$RMSD = \left[\sum_{i=1}^{N} \frac{(x_{ci}^{a/b} - x_i)^2}{N-1}\right]^{\frac{1}{2}} \quad \ldots\ldots\ldots\ldots\ldots \quad (4)$$

$$ARD = \frac{1}{N}\sum_{i}^{N}\frac{(x_i - x_{ci}^{a/b})}{x_i} \quad \ldots\ldots\ldots\ldots\ldots \quad (5)$$

Where *N* is the number of experimental points. These values are listed in TABLES 4 and 5 for Apelblat and Buchowski–Ksiazczak models respectively. Comparison of these values of Apelblat and Buchowski-Ksiazczak (λh) models shows that in the studied systems, although both models fit well, Apelblat model gives better results.

The Buchowski-Ksiazczak parameter λ is related to the average value of associated solute (CAP) molecules. In the present study, it is observed that λ values are very low indicating thereby that there is not obvious association in the dissolution process of CAP in selected solvents.

Further, using experimental solubility data, enthalpies of solution (ΔH^0_{sol}), Gibb's energy of dissolution (ΔG^0_{sol}) and entropy of solutions (ΔS^0_{sol}) have been evaluated.

The enthalpies of solution (ΔH^0_{sol}), was calculated by modified van't Hoff equation [19,20] i.e., from the slope of the plot of l*nx* versus ($1/T - 1/T_{hm}$).

$$\left[\frac{\partial \ln x_i}{\partial\left[\frac{1}{T} - \frac{1}{T_m}\right]}\right]_P = -\frac{\Delta H^0_{sol}}{R} \ldots\ldots\ldots \quad (6)$$

Where *R* is gas constant and *T* is the experimental temperature. Tthe mean harmonic temperature T_{hm} is calculated by the equation:

$$T_{hm} = \frac{n}{\sum_{i=1}^{n}\frac{1}{T}} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (7)$$

where *n* is the number of experimental temperatures. The value of T_{hm} in the present study was calculated to be 312.83 K.

The Gibbs energy change (ΔG^0_{sol}) was evaluated by intercept of the plots using following relation [20]:

$$\Delta G^0_{sol} = -R.T_{hm}.\text{intercept} \quad \ldots\ldots\ldots \quad (8)$$

The entropies of solutions (ΔS^0_{sol}) were calculated by the following equation:

$$\Delta S^0_{sol} = \frac{\left(\Delta H^0_{sol} - \Delta G^0_{sol}\right)}{T_{hm}} \quad \ldots\ldots\ldots\ldots\ldots \quad (9)$$

TABLE 6 summarizes these thermodynamic parameters. It is observed that enthalpy of dissolution (ΔH^0_{sol}) and Gibbs energy of dissolution (ΔG^0_{sol}) are positive for all the solvents. However, entropy of dissolution (ΔS^0_{sol}) is both positive and negative in the studied solvents.

TABLE 6**. Thermodynamic Parameters for dissolutionof CAP in studied solvents.**

Solvent	**ΔHSol. KJ.mol-1**	**ΔGSol. KJ.mol^{-1}**	**ΔSSol. J.mol^{-1}**
Water	37.8028	28.0686	31.1166
Methanol	41.0447	24.8813	51.6683
Ethanol	34.5781	25.8319	27.9583

Isopropanol	14.3666	26.0068	-37.2092
Butanol	20.8870	26.5791	-18.1956
Tetrahydrofuran	27.3982	23.5060	12.4419
Ethyl acetate	23.2537	24.2226	-3.0972
1,4-dioxane	31.9781	21.8218	32.4659
dimethylformamide	4.7598	3.8769	2.8223

The positive dissolution enthalpy indicates that the dissolution of CAP is endothermic process and during dissolution, chemical bond between solvent molecules is broken whereas new bonds are formed between CAP and solvent molecules. The formation of new bond requires energy for which system needs to absorb additional energy in the form of heat.

The positive Gibb's energy of dissolution suggests spontaneous dissolution process. Comparison of ΔG^0_{sol} values with solubility data in different solvents indicates that Gibb's energy is reverse of solubility. It is minimum for methanol where solubility is maximum. In butanol, it is maximum in which solubility is minimum. For aprotic solvents also, ΔG^0_{sol} value is minimum for DMF in which solubility of CAP is found to be maximum.

The positive or negative value of entropy depends on the functional groups present in the solute (CAP) as well as on the solvent. Due to the presence of different groups, there may exist various forces such as electrostatic force, hydrogen bond, hydrophobic interactions etc, which may affect dissolving process. The negative entropy of dissolution is due to more order in the solution [21].

Conclusion

It is concluded that in protic solvents, solubility of CAP is maximum in methanol and minimum in butanol and in different alcohols, order of solubility is: methanol > ethanol > iso-propanol > n-butanol. In the selected non protic solvents, solubility is greater in DMF and minimum in ethyl acetate. The order is: DMF > 1, 4-dioxane > tetrahydrofuran > ethyl acetate. Further, solubility increases with increase in temperature. The positive Gibb's energy and enthalpy of dissolution suggests spontaneous and endothermic dissolution process.

REFERENCES

1. Babu NJ, Nangia A, Solubility advantage of amorphous drugs and pharmaceutical cocrystals, Cryst Growth Des, 2011; 11:2662-2679.
2. Fathi-Azarjbayjani A, Mabhoot A, Martinez F. et al. Modelling, solubility and thermodynamic aspects of sodium phenytoin in propylene glycol-water mixtures, J Mol Liqds, 2016;21:68-73.
3. Zingone G, Rubessa F. Preformulation study of the inclusion complex warfarin-β-cyclodextrin, Int J Pharma, 2005;291:3-10.
4. Shah M, Shah V, Ghosh A, et al. Molecular inclusion complexes of β-cyclodextrin derivatives enhance aqueous solubility and cellular internalization of pacilitaxel: Preformulation and Invitro assessments, J Pharm Pharmacol, 2015;2:8-24.
5. Chaurasia G. A review on pharmaceutical preformulation studies in formulation and development of new drug molecules, Int J Pharma Sci Res, 2016;7:2313-2320.

6. Neurath R, Strick N, Li YY, et al. Cellulose acetate phthalate, a common pharmaceutical excipient, inactivates HIV-1 and blocks the correceptor binding site on the virus envelope glycoprotein gp 120. BMC Infect Diseases, 2001;1: 17-28.

7. Huang C, Soenen SJ, Gulck E, et al. Electrospun cellulose acetate phthalate fibers for semen induced anti-HIV vaginal drug delivery, Biomaterials, 2012;33:962-969.

8. Neurath AR, Strick N, Jiang S, et al. Anti-HIV-1 activity of cellulose acetate phthalate: Synergy with soluble CD4 and induction of "dead-end" gp41 six-helix bundles. BMC Infectious Diseases, 2002;2:18

9. Merkle HP, Speiser P. Preparation and in vitro evaluation of cellulose acetate phthalate coacervate microcapsules. J Pharma Sci, 1973;62:1444-1448.

10. Beyger JW, Nairn JG. Some factors affecting the microencapsulation of pharmaceuticals with cellulose acetate phthalate. J PharmSci, 1986;75:573-578.

11. Hua D, Liu Z, Wang F, et al. pH responsive polyurethane (core) and cellulose acetate phthalate (shell) electrospun fibers for intravaginal drug delivery, Carbohydrate Polym, 2016;151:1240-1244.

12. Rramaswamy RK, Mani G, Udumansha U, et al. Preparation, characterization, and in vitro diffusion study of nonwoven electrospun nanofiber of curcumin-loaded cellulose acetate phthalate polymer, Saudi Pharma J, 2017;25: 921-926.

13. Hussain A, Mumtaz AM, Arshad MS, et al. Effect of cellulose acetate phthalate and polyethylene glycol on physical properties and release of theophylline from microcapsules, Braz J Pharm Sci, 2016;52:27-34.

14. Neurath AR, Li YY, Mandeville R, et al. In vitro activity of a cellulose acetate phthalate topical cream against organisms associated with bacterial vaginosis. J Antimicrob Chemo, 2000;45:713-714.

15. Gideon LT, Ericksen B, Hlavaty JJ, et al. Development of a gel permeation chromatographic assay to achieve mass balance in cellulose acetate phthalate stability studies. J Pharma Biomed Ana, 2009;49:240-246.

16. Rowe RC, Sheskey PJ, Owen SC. Handbook of Pharmaceutical Excipients, Fifth Ed, UK.

17. Apelblat A, Manzurola E. Solubilities of L-glutamic acid, 3-nitrobenzoic acid, p-toluic acid, calcium L-lactate, calcium gluconate, mangnesium DL-aspartate and mangnesium L-lactate in water. J Chem Thermodyn, 34:1127-1136.

18. Buchowski H, Ksiazczak A, Pietrzyk S. Solvent activity along a saturation line and solubility of hydrogen bonding solids. J Phys Chem,1980;84:975-979.

19. Delgado DR, Martinez F. Solubility and some thermodynamics of sulfamerazine and sulfamerazine in some ethanol-water mixtures. Fluid Phase Equilb, 2013; 360: 8-96.

20. Krug RR, Hunter WG, Grieger RA. Enthalpy-entropy compensation 2. Separation of the chemical from the statistical effects. J Phys Chem, 1976;80:2341-2351.

21. El-Bindary AA, El-Sonbati AZ, El-Mosalamy EH, et al. Potentiometric and thermodynamic studies of azosulfonamide drugs X. Chem Pap, 2003;57:255-258.