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RESEARCH ARTICLE

PHYSICOCHEMICAL STUDY OF DIVERSIFIED INTERACTIONS PREVALENT IN ZYLORIC TABLET AND URIC ACID MIXTURE IN AQUEOUS MEDIUM WITH THE MANIFESTATION OF SOLVATION*- CONSEQUENCE

[1]Ashutosh Dutta, [1]Kanak Roy, [2]Rabindra Dey and *[1]Mahendra Nath Roy

[1]Department of Chemistry, University of North Bengal, Darjeeling-734013, India
[2]Department of Chemistry, Cooch Behar College, CoochBehar-736101, India

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ABSTRACT

The significance of release from gout pain in Biochemic body caused by limitation of precipitation of uric acid by allopurinol has been measured through physicochemical study. Here, we have carried out the density (ρ), viscosity (η) and UV-Vis measurements of allopurinol in w1= 0.00001, 0.00002 and 0.00003 mass fraction of aqueous uric acid binary mixtures at T= 298.15K, 303.15K, 308.15K, 313.15K. These measurements have been performed to ternary mixture (allopurinol+uric acid+water) to develop some important parameters, namely, limiting apparent molar volume (φV0), viscosity B-coefficients from extended Masson equation and Jones-Dole equation respectively. The refractive index (nD) has been calculated on the same ternary mixtures at T=298.15K. Lorentz-Lorenz equation has used to evaluate molar refractive index (RM) and limiting molar index (RM0). Nature of interaction is determined from UV-Visible spectroscopy. These parameters have been interpreted in terms of interactions of solute itself and with solvent.

INTRODUCTION

Gout is the mainly common type of arthritis in men older than age 40 years, and the occurrence of gout is ever-increasing(Kim K, Schumacher HR, Hunsche E, Wertheimer A, Kong S. A. 2003).Gout is a complex inflammatory response to the presence of monosodium urate (MSU) crystals in body joints. MSU crystals are formed when serum urate super saturation concentrations are reached (0.4 mmoles/liter [6.7 mg/dl] at 37°C). Gout typically presents as self-limiting episodes of acute inflammatory arthritis. With increasing time, untreated hyperuricemia and recurrent attacks of gout lead to bone and joint damage due to the deposition of MSU as tophi, and ultimately results disability of men. Gout is also related with improved mortality, mainly that associated to cardiovascular disease (Krishnan E, Baker J.F, Furst D.E, Schumacher H.R. 2006; Choi H, Curhan G. 2007). Hence, the fundamental cause of gout is deposition of uric acid crystals comparatively elevated levels in the blood of Biochemic body. This can also arise for number of reasons, along with diet, genetic predisposition, or under excretion of urate. The curative methods are both way of life changes and medications can reduce uric acid levels (Chen, L. X. Schumacher, H. R, 2008).

Corresponding author:* **Mahendra Nath Roy
Department of Chemistry, University of North Bengal, Darjeeling-734013, India

Allopurinol is a drug used to treat gout which is caused by a build up of sodium urate crystal. Allpurinol is the most commonly used urate lowering therapy. It has the benefits of once-daily dosing as well as effectiveness in patients with renal impairment. Allopurinol is rapidly metabolized to oxypurinol, whichi nhibits xanthine oxidase, thereby preventing the formation of uric acid.The drug is well tolerated by the majority of patients, and serious side effects are rare(Lisa K. S., O'Donnell, J.L., Zhang, M., James,J., Frampton, C., Murray L. B., and Peter T. C., 2011). The chemistry of solutions deals with solutes and solvents and how solutes interact with solvents as they move about in solutions. So that we choose the bio- active compound, allopurinol as a solute and aqueous uric acid as a solvent to study the interaction between them. Studies on the apparent molar volumes and viscosity *B*-coefficients at infinite dilution provide valuable information regarding solute-solute, solute-solvent and solvent-solvent interactions (Lawrence, K. G., Saco, A. 1983). To the best of our knowledge, the studies in the present ternary solution systems have not been reported earlier. Therefore, in present study we have attempt to ascertain nature of interaction of solute itself (allopurinol) and with co-solute (uric acid) in w_1=0.00001, 0.00002 and 0.00003 mass fraction of aqueous uric acid mixture at different temperatures (298.15-313.15)K.

Table 1. Source and purity of the chemicals

Chemical name	Source	mass fraction purity	Purification Method
Allopurinol(Zyloric Tablet)	Sigma-Aldrich	≥0.99	Used as procured
Uric acid	SD Fine-Chem Ltd.	≥0.99	Used as procured

Table 2. Experimental values of density (ρ) and viscosity (η) at different temperatures, refractive index (n_D) at 298.15 K of different mass fraction (w_1) of aq. uric acid mixtures*

Aq. Uric acid Mixture (w_1)	Temperature (K)	$\rho\times10^{-3}$ /kg·m^{-3}	η /mP·s	n_D
0.00001	298.15	0.99691	0.89	1.3311
	303.15	0.99550	0.81	
	308.15	0.99398	0.71	
	313.15	0.99201	0.61	
0.00002	298.15	0.99701	0.89	1.3318
	303.15	0.99559	0.81	
	308.15	0.99396	0.73	
	313.15	0.99231	0.63	
0.00003	298.15	0.99711	0.90	1.3323
	303.15	0.99568	0.82	
	308.15	0.99411	0.74	
	313.15	0.99236	0.65	

*Standard uncertainties u are: $u(\rho)$ =0.00002 kg·m^{-3}, $u(\eta)$ =0.02mP·s, $u\,n_D$) =0.0002, and $u(T)$ =0.01K,

Experimental section

Source and purity of materials: Allopurinol was purchased from Sigma-Aldrich. Uric acid (UA) was purchased from S D Fine-Chem. Ltd. The mass fractions purity of both was ≥0.99. The reagents were always placed in the desiccators over P_2O_5 to keep them in dry atmosphere. These chemicals were used as received without further purification (Scheme 1). The provenance and purity of the chemical used has been depicted in Table 1.

Apparatus and procedure: Solubility of the uric acid in water (specific conductance of $1\cdot10^{-6}$ S·cm^{-1}) and the allopurinolin aqueous uric acid had been checked precisely, prior to start of the experimental work and observe that allopurinolsoluble in all proportion of aqueous uric acid solution. The mother solutions of Allopurinol were prepared by mass (Mettler Toledo AG-285 with uncertainty 0.0003g) and then the working solutions (six sets) were prepared by mass dilution. The conversions of molarity into molality (Shoemaker D. P., Garland, C. W., 1967) had been done using experimental density values of respective solutions and adequate precautions were taken to reduce evaporation losses during mixing and throughout the experiment.

The densities (ρ) of the solutions were measured by means of vibrating u-tube Anton Paar digital density meter (DMA 4500M) with a precision of ±0.00005 g.cm^{-3} maintained at ±0.01 K of the desired temperature. It was calibrated by passing deionised, triply distilled water and dry air (Bhattacharjee, A., Roy, M. N., 2010). The viscosities (η) were measured using a Brookfield DV-III Ultra Programmable Rheometer with fitted spindle size-42. The detail description has already been described earlier (Ekka , D., Roy, M. N. 2014). Refractive index (n_D) was measured with the help of a Digital Refractometer Mettler Toledo. The light source was LED, λ=589.3nm. The refractometer was calibrated twice using distilled water and calibration was checked after every few measurements (Roy, M. N., Chakraborti,P., Ekka, D. 2014). The uncertainty of refractive index measurement was ±0.0002 units. UV-Visible study was done by JASCO V-530 Digital Spectrophotometer at 298.15K.

RESULT AND DISCUSSION

The experimental physical parameter of binary mixtures in different mass fractions (w_1=0.00001, 0.00002, 0.00003) of aqueousuric acid (UA)solutions at four different temperatures (298.15K, 303.15K, 308.15K and 313.15K) have been reported in table 2. The experimental measured values of density, viscosity and refractive index of alopurinol (ALP) as a function of concentration (molality), in different mass fractions of aqueousuric acid mixture at different temperatures have been listed in Table 3.

Apparent molar volume: Apparent molar volume (φ_V) and limiting apparent molar volume(φ_V^0) regarded as important tools for understanding of interactions taking place in solute-solvent systems. The apparent molar volume can be measured as the sum of the geometric volume of the central solute molecule and changes in the solvent volume due to its interaction with the solute around the peripheral or co-sphere. Therefore, the apparent molar volumes (φ_V) have been determined from the solutions density values (Ekka D., Roy, M. N., 2013) and are given in Table 4.

$$\varphi_V = M/\rho - 1000\,(\rho - \rho_0)/m\rho\rho_0 \quad \ldots\ldots(1)$$

where, M is the molar mass of the solute, m is the molality of the solution, ρ and $\rho_0$are the densityof the solution and aqueous uric acid mixture respectively. The values of (φ_V) are positive and large for all the systems, signifying strong solute-co-solute interactions. The apparent molar volumes (φ_V) are found to decrease with increasing concentration (molality, m) of ALP in same mass fraction of aqueousuric acid at same temperature. It is also found that apparent molar volumes (φ_V) increase with both increasing temperature as well as mass fraction of aqueous uric acid solution and varied with $\sqrt{m}$ and could be least-squares fitted to the extended Masson equation (Masson, D. O. 1929) from where limiting molar volume, φ_V^0(infinite dilution partial molar volume) have been derived and the values are represented in Table 5.

$$\varphi_V = \varphi_V^0 + S_V^*\sqrt{m} \quad \ldots\ldots(2)$$

Here $\varphi_V^0$is the apparent molar volume at infinite dilution, $S_V^*$is the experimental slope.

Table 3. Experimental values of density (ρ) and viscosity (η) of Allopurinol in different mass fractions of aqueous uric acidmixture (w_1) at three different temperatures

$^a m$ /mol·kg^{-1}	$\rho\times10^{-3}$ /kg·m^{-3}	η /mP·s	$^a m$ /mol·kg^{-1}	$\rho\times10^{-3}$ /kg·m^{-3}	η /mP·s	$^a m$ /mol·kg^{-1}	$\rho\times10^{-3}$ /kg·m^{-3}	η /mP·s
w_1=0.00001				w_1=0.0002			w_1=0.00003	
T = 298.15 K				T = 298.15 K			T = 298.15 K	
0.000100	0.99716	0.90	0.000100	0.99717	0.91	0.000100	0.99721	0.92
0.000252	0.99781	0.91	0.000252	0.99783	0.92	0.000252	0.99791	0.93
0.000404	0.99886	0.92	0.000404	0.99888	0.93	0.000404	0.99892	0.94
0.000556	1.00011	0.92	0.000556	1.00018	0.94	0.000556	1.00019	0.95
0.000709	1.00141	0.93	0.000709	1.00151	0.95	0.000709	1.00152	0.96
0.000863	1.00297	0.94	0.000863	1.00301	0.96	0.000863	1.00308	0.97
T = 303.15 K				T = 303.15 K			T = 303.15 K	
0.0101	0.99571	0.83	0.0101	0.99575	0.83	0.0101	0.99576	0.84
0.0252	0.99640	0.83	0.0252	0.99641	0.84	0.0252	0.99639	0.85
0.0404	0.99745	0.84	0.0404	0.99742	0.85	0.0404	0.99739	0.86
0.0557	0.99869	0.85	0.0557	0.99867	0.86	0.0557	0.99858	0.87
0.0710	1.00001	0.85	0.0710	1.00005	0.87	0.0710	1.00006	0.88
0.0864	1.00151	0.86	0.0864	1.00154	0.87	0.0864	1.00159	0.89
T = 308.15 K				T = 308.15 K			T = 308.15 K	
0.0101	0.99411	0.73	0.0101	0.99411	0.75	0.0101	0.99418	0.76
0.0253	0.99478	0.74	0.0253	0.99479	0.76	0.0253	0.99465	0.77
0.0405	0.99571	0.74	0.0405	0.99577	0.77	0.0405	0.99568	0.78
0.0558	0.99701	0.75	0.0558	0.99701	0.78	0.0558	0.99686	0.79
0.0712	0.99832	0.76	0.0712	0.99836	0.78	0.0712	0.99832	0.79
0.0866	0.99988	0.76	0.0866	0.99987	0.79	0.0866	0.99988	0.80
T = 313.15 K				T = 313.15 K			T = 313.15 K	
0.0101	0.99211	0.63	0.0101	0.99241	0.65	0.0101	0.99241	0.66
0.0253	0.99272	0.64	0.0253	0.99298	0.65	0.0253	0.99298	0.66
0.0406	0.99370	0.64	0.0406	0.99391	0.66	0.0406	0.99388	0.67
0.0559	0.99498	0.65	0.0559	0.99521	0.67	0.0559	0.99502	0.68
0.0713	0.99631	0.66	0.0713	0.99647	0.67	0.0713	0.99641	0.69
0.0867	0.99787	0.66	0.0867	0.99811	0.68	0.0867	0.99802	0.70

*Standard uncertainties u are: u (ρ) =0.00002 kg·m^{-3}, u (η) =0.02mP·s and u (T) =0.01K

[a]molality has been expressed per kilogram of (uric acid + water) solvent mixture

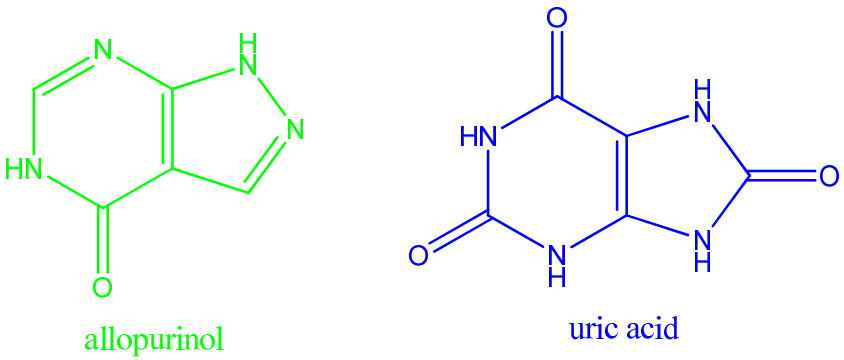
Table 4. Apparent molar volume (φ_V) and $(\eta_r\text{-}1)/\sqrt{m}$ of Allopurinol in different mass fraction (w_1) of aqueous uric acid mixtures at three different temperatures

[a]molality /mol·kg^{-1}	$\varphi_V\times10^6$ /m^{3}mol^{-1}	$(\eta_r\text{-}1)/\sqrt{m}$ /kg$^{1/2}$mol$^{-1/2}$	[a]molality /mol·kg^{-1}	$\varphi_V\times10^6$ /m^{3}mol^{-1}	$(\eta_r\text{-}1)/\sqrt{m}$ /kg$^{1/2}$mol$^{-1/2}$	[a]molality /mol·kg^{-1}	$\varphi_V\times10^6$ /m^{3}mol^{-1}	$(\eta_r\text{-}1)/\sqrt{m}$ /kg$^{1/2}$mol$^{-1/2}$
w_1=0.00001			w_1=0.00002			w_1=0.00003		
T = 298.15 K			T = 298.15 K			T = 298.15 K		
0.0100	194.54	0.13	0.0100	197.23	0.14	0.0100	161.77	0.15
0.0252	180.74	0.15	0.0252	182.78	0.17	0.0252	183.81	0.17
0.0404	167.36	0.18	0.0404	170.11	0.19	0.0404	171.01	0.20
0.0556	157.95	0.19	0.0556	158.91	0.21	0.0556	162.63	0.22
0.0709	152.28	0.21	0.0709	152.88	0.24	0.0709	153.75	0.23
0.0863	145.55	0.23	0.0863	145.61	0.25	0.0863	145.95	0.27
T = 303.15 K			T = 303.15 K			T = 303.15 K		
0.0101	196.88	0.10	0.0101	200.79	0.09	0.0101	205.97	0.08
0.0252	183.41	0.11	0.0252	185.71	0.12	0.0252	188.11	0.13
0.0404	168.66	0.13	0.0404	171.47	0.15	0.0404	173.88	0.17
0.0557	159.46	0.16	0.0557	160.19	0.18	0.0557	164.22	0.19
0.0710	153.12	0.18	0.0710	153.51	0.20	0.0710	155.27	0.21
0.0864	146.55	0.20	0.0864	146.77	0.21	0.0864	147.28	0.24
T = 308.15 K			T = 308.15 K			T = 308.15 K		
0.0101	202.43	0.08	0.0101	205.33	0.07	0.0101	210.45	0.09
0.0253	185.11	0.11	0.0253	187.72	0.11	0.0253	192.31	0.13
0.0405	173.44	0.14	0.0405	173.88	0.14	0.0405	177.46	0.17
0.0558	161.66	0.16	0.0558	161.95	0.17	0.0558	166.44	0.20
0.0712	154.55	0.18	0.0712	154.88	0.19	0.0712	156.27	0.22
0.0866	147.77	0.19	0.0866	147.81	0.21	0.0866	150.10	0.24
T = 313.15 K			T = 313.15 K			T = 313.15 K		
0.0101	207.71	0.08	0.0101	210.37	0.05	0.0101	214.65	0.03
0.0253	190.11	0.12	0.0253	192.34	0.10	0.0253	193.55	0.09
0.0406	176.21	0.14	0.0406	177.27	0.13	0.0406	178.28	0.13
0.0559	164.32	0.18	0.0559	164.95	0.15	0.0559	168.88	0.16
0.0713	155.68	0.19	0.0713	156.85	0.18	0.0713	160.26	0.19
0.0867	148.73	0.22	0.0867	150.74	0.20	0.0867	151.06	0.23

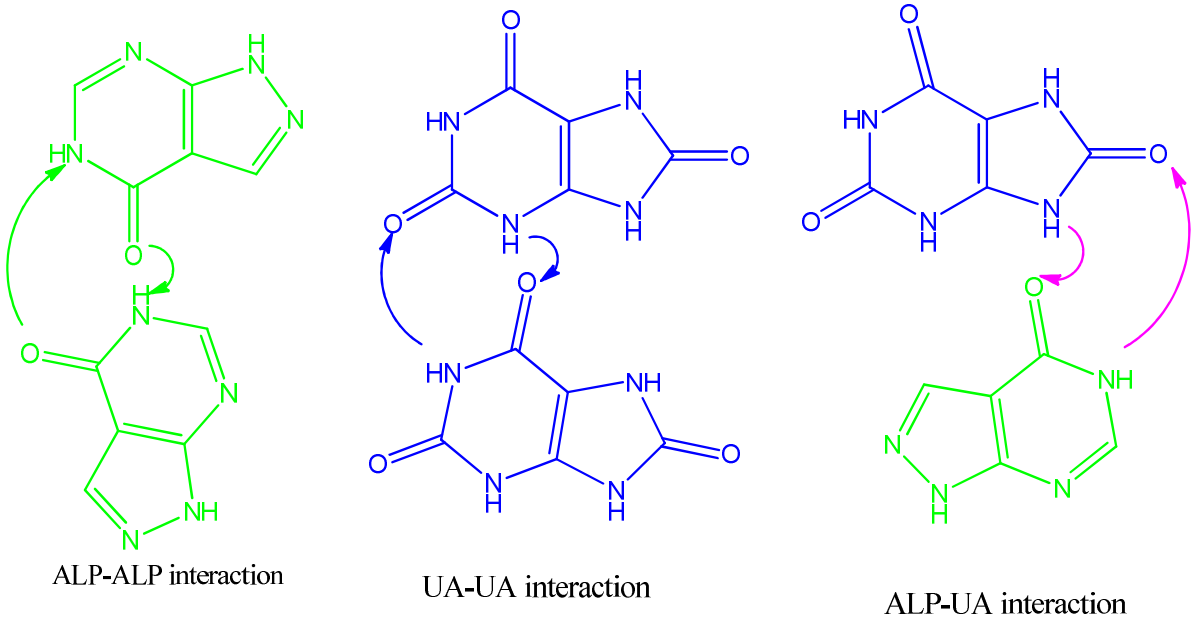
*Standard uncertainties u are: u (T) =0.01K,

[a]molality has been expressed per kilogram of (uric acid + water) solvent mixture

At infinite dilution each solute molecule is surrounded only by the solvent molecules. As a consequence, that $\varphi_V^0$is unaffected byitself interaction of solute molecules (either UA itself or ALP) and it is a measure only of the solute-cosolute (UA -ALP) interaction. From table 5, $\varphi_V^0$are large and positive for all ALP at all the studied temperatures, suggesting the presence of strong solute-cosolute interaction. Comparing φ_V^0 with S_V^* values show that the magnitude of φ_V^0 is greater than



Scheme 1. Molecular structure of allopurinol and uric acid



Scheme 2. Plausible sites of interactions between solute-solute (allopurinol-allopurinol), cosolute-cosolute (uric acid-uric acid) and solute-cosolute molecules (alopurinol-uric acid)

S_V^*, suggesting that solute-cosolute interactions dominates over itself interaction of solute moleculesin all solutions at all studied temperatures. Moreover, S_V^* values are negative at all temperatures indicates force of itself interaction of solute molecules is negligible.

The variation of φ_V^0 with temperature are fitted to a polynomial of the following

$$\varphi_V^0 = a_0 + a_1 T + a_2 T^2 \quad \text{.....(3)}$$

Where$T$ is the temperature in K and a_0, a_1 and a_2 are the empirical coefficients depending on the solute, mass fraction of cosolute UA. Values of coefficients of the above equation for the ALP in aqueous UA mixtures are reported in table 6.
The limiting apparent molar expansibilities, φ_E^0, can be evaluated by the following equation,

$$\varphi_E^0 = (\delta\varphi_V^0/\delta T)_P = a_1 + 2a_2T \quad \text{.....(4)}$$

The limiting apparent molar expansibilities, φ_E^0, change in magnitude with the change of temperature. The values of φ_E^0 for different solutions of studied allopurinol at (T=298.15, 303.15, 308.15 and 313.15)K are reported in Table 7.

All the values of φ_E^0 shown in the Table 7 are positive for ALP in aqueous UA and studied temperature. This fact helps to explain the absence of caging or packing effect for the ALP in solution (Millero ,F. J., 1972).The long-range structure-making and breaking capacity of the solute in mixed system can be determined by examining the sign of $(\delta\varphi_E^0/\delta T)_P$ developed by Hepler(Hepler, L. G., 1969*)*.

$$(\delta\varphi_E^0/\delta T)_P = (\delta^2\varphi_V^0/\delta T^2)_P = 2a_2 \quad \text{.....(5)}$$

The positive sign or small negative of $(\delta\varphi_E^0/\delta T)_P$ signifies the molecule is a structure-maker; otherwise, it is a structure-breaker (Roy, M. N., Dakua ,V. K., Sinha , B., 2007). The perusal of table 6 shows that, $(\delta\varphi_E^0/\delta T)_P$ values of citric acid are all positive under investigation. It shows the more symmetric rearrangement of the interacting molecules (ALP and UA) with the formation of H-bonding, van der waal forces, dipole-dipole interactions etc. The plausible sites of different interactions playing in the ternary solution are shown in scheme 2.This symmetric arrangement is signifies the molecules of ALPand UAis definitely interacting with structure–making tendency in all of the studied solution systems. The table 6 also showing the positively magnitude of $(\delta\varphi_E^0/\delta T)_P$ values in of ALP is depicting this structure–making tendency.

Table 5. Limiting apparent molar volume (φ_V^0), experimental slope (S_V^*), viscosity *A*- and *B*-coefficient of allopurinol in different mass fraction (w_1) of aqueous uric acid mixtures at different temperatures*

Mass fraction (w_1)	T /K	$\varphi_V^0 \times 10^6$ /m^3 mol^{-1}	$S_V^* \times 10^6$ /$m^3 mol^{-3/2} kg^{1/2}$	*B* /kg mol^{-1}	*A* /$kg^{1/2}$ $mol^{-1/2}$
	298.15	224.26	-327.12	0.32	0.06
	303.15	229.47	-345.75	0.50	0.05
0.00001	308.15	235.71	-346.99	0.63	0.02
	310.15	238.82	-347.11	0.73	0.01
	313.15	241.42	-348.19	0.84	-0.02
	298.15	230.78	-338.66	0.46	0.05
	303.15	234.42	-358.44	0.64	0.07
0.00002	308.15	240.26	-366.99	0.75	-0.03
	310.15	243.31	-367.45	0.84	-0.01
	313.15	247.10	-386.22	0.88	-0.05
	298.15	234.75	-354.92	0.58	0.06
	303.15	239.24	-353.38	0.76	0.07
0.00003	308.15	245.11	-362.77	0.88	-0.04
	310.15	248.29	-381.18	0.99	-0.03
	313.15	252.25	-399.74	1.15	-0.08

*Standard uncertainties values of *u* are: *u* (*T*) =0.01K

Table 6. Values of various coefficients of equation-3 for allopurinol in different aqueous uric acid solutions*

Aq. Uric acid Mixture (w_1)	$a_0 \times 10^6$ /m^3 mol^{-1}	$a_1 \times 10^6$ / m^3 $mol^{-1}K^{-1}$	$a_2 \times 10^6$ / m^3 $mol^{-1}K^{-2}$	$(\delta\varphi_E^0/\delta T)_P \times 10^6$ / m^3 mol^{-1} K^{-2}
0.00001	68.13	-0.10	0.002	0.004
0.00002	2721	-17.06	0.03	0.06
0.00003	2219	-14.11	0.02	0.04

Table 7. Limiting apparent molar expansibilities (φ_E^0) for allopurinol in different mass fraction of aqueous uric acid (w_1) at different temperature

Aq. Uric acid Mixture (w_1)	$\varphi_E^0 \times 10^6$/ m^3 mol^{-1} K^{-1}				
T/ K	298.15	303.15	308.15	310.15	313.15
0.00001	1.091	1.112	1.132	1.141	1.152
0.00002	0.529	0.829	1.129	1.277	1.429
0.00003	0.7975	1.047	1.297	1.397	1.497

Viscosity: The observed viscosity data for studied solutions are listed in table 3. The relative viscosity (η_r) has been calculated using extended Jones-Dole equation (Jones ,G. and Dole ,D., 1929) or non electrolytes.

$$(\eta/\eta_0 - 1)/\sqrt{m} = (\eta_r - 1)/\sqrt{m} = A + B \cdot \sqrt{m} \quad \ldots\ldots\ldots\ldots\ldots\ldots(6)$$

Where $\eta_r = \eta/\eta_0$ is the relative viscosity, η and η_0 are the viscosities of ternary solutions (ALP + aqueous UA) and solvent (aqueous mixture of UA) respectively and *m* is the molality of ALP in ternary solutions. Where *A* is known as Falkenhagen coefficient as it is determined by the ionic attraction theory of Falkenhagen-Vernon and *B*is empirical constants known as viscosity*B*- coefficients, which are specifying to the interaction of solute itself and/or with cosolute molecules respectively. The values of *A*- and *B*-coefficients are estimated by least-square polynomial method by plotting $(\eta_r - 1)/\sqrt{m}$ against $\sqrt{m}$ with second order and reported in table 4. It is observed from table 4 the values of the *A*-coefficient are found to decrease with increase in temperature. This fact indicates the presence of very weak solute-solute interaction and also in excellent agreement with those obtained from S_V^* values. The valuable information about the solvation of the solvated solutes and their effects on the structure of the cosolute uric acid in the local vicinity of the solute (ALP) molecules in solutions has been obtained from viscosity *B*-coefficient (Pandey, J. D., Mishra, K., Shukla, A., Mishran, V., Rai, R. D., 1987). It is found from table 4; the values of *B*-coefficient are positive and much higher than *A*-coefficient which signifies solute-cosolute interactionis dominant over solute-solute and cosolute-cosolute interaction. It is also observed that the positive magnitude of viscosity *B*-coefficient increases with increasing temperature and also increases with an increase in mass fraction of aqueous uric acid mixture which suggests that solute-cosolute interaction is strengthened with rise in temperature as well as mass fraction of aqueous uric acid mixture. These results are in good agreement with those obtained from limiting apparent molar volume φ_V^0 values. It is observed from table 4 that the values of the *B*-coefficient of citric acid increases with temperature, i.e., the *dB/dT* values are positive. From table 8, the small positive *dB/dT* values for the allopurinol behave almost as structure-maker. The free energy of activation of viscous flow per mole of solvent, $\Delta\mu_1^{0\neq}$ as proposed by Eyring and co-workers (Glasstone, S., Laidler, K. J., Eyring ,H. 1941) could be calculated from the following equation:

$$\eta_0 = (hN_A/V_1^0)\exp(\Delta\mu_1^{0\neq}/RT) \quad \ldots\ldots\ldots\ldots\ldots\ldots(7)$$

Where *h*, $N_A$andV_1^0 are the Planck's constant, Avogadro's number and partial molar volume of the solvent respectively. The equation (7) can be rearranged as follows we get

$$\Delta\mu_1^{0\neq} = RT \ln(\eta_0 V_1^0/hN_A) \quad \ldots\ldots\ldots\ldots\ldots\ldots(8)$$

Feakins et al Feakins, D.,. Bates, F. M.,. Waghorne, W. E. Lawrence, K. G. 1993; Feakins, D. , Freemantle, D. J., Lawrence, K. G. 1974) suggested that if equations (6) and (8) are obeyed, then

Table 8. Values of *dB/dT*, A_1 and A_2 coefficients for the allopurinol in different mass fraction of aqueous uric acid (w_1) at studied temperatures*

Aq. Uric acid Mixture (w_1)	*dB/dT*	A_1	A_2
0.00001	0.338	-0.133	0.0002
0.00002	0.503	-0.388	0.0005
0.00003	0.649	-0.527	0.0009

*Standard uncertainties values of *u* are: *u* (*T*) =0.01K

Table 9. Values of V_1^0, $(V_1^0-V_2^0)$, $\Delta\mu_1^{0\neq}$, $\Delta\mu_2^{0\neq}$, $T\Delta S_2^{0\neq}$ and $\Delta H_2^{0\neq}$ for allopurinol in different mass fraction (w_1) of aqueous uric acid mixture at different temperatures*

Mass fraction	*T*/ K	$V_1^0.10^6$ /$m^3.mol^{-1}$	$(V_1^0-V_2^0).10^6$ /$m^3.mol^{-1}$	$\Delta\mu_1^{0\neq}$ /KJ.mol^{-1}	$\Delta\mu_2^{0\neq}$ /KJ.mol^{-1}	$T\Delta S_2^{0\neq}$ / KJ.mol^{-1}	$\Delta H_2^{0\neq}$ /KJ.mol^{-1}
w_1=0.00001	298.15	18.05	-206.21	10.21	83.77	-1519.12	-1440.79
	303.15	18.08	-211.39	10.18	109.95	-1543.73	-1438.89
	308.15	18.11	-217.61	9.98	126.77	-1568.23	-1446.83
	310.15	18.13	-220.69	9.81	143.42	-1578.15	-1440.27
	313.15	18.14	-223.28	9.75	159.47	-1592.91	-1438.62
w_1=0.00002	298.15	18.05	-212.73	10.28	101.21	-467.16	-370.34
	303.15	18.08	-216.34	10.11	126.08	-571.12	-450.26
	308.15	18.11	-222.15	10.01	145.55	-650.27	-511.31
	310.15	18.12	-225.19	9.84	155.32	-698.19	-547.68
	313.15	18.14	-228.96	9.75	166.41	-745.24	-584.05
w_1=0.00003	298.15	18.05	-216.71	10.29	113.11	-654.32	-546.05
	303.15	18.08	-221.16	10.13	145.58	-840.06	-698.72
	308.15	18.11	-227.01	10.01	161.01	-918.55	-763.21
	310.15	18.12	-230.17	9.93	181.76	-1031.86	-855.95
	313.15	18.14	-234.11	9.88	201.05	-1144.66	-948.68

Table 10. Refractive index (n_D), molar refraction (R_M) and limiting molar refraction (R_M^0) allopurinol in different mass fraction of aqueous uric acid solutions at 298.15 K

[a]molality /mol·kg^{-1}	n_D	$R_M\times10^6$ / m^3 mol^{-1}	$R_M^0\times10^6$ / m^3 mol^{-1}
w_1=0.00001			
0.0100	1.3320	43.24	
0.0252	1.3323	43.25	
0.0404	1.3329	43.25	43.27
0.0556	1.3335	43.26	
0.0709	1.3338	43.26	
0.0863	1.3345	43.27	
w_1=0.00002			
0.0100	1.3325	43.29	
0.0252	1.3327	43.30	
0.0404	1.3333	43.31	43.31
0.0556	1.3339	43.31	
0.0709	1.3345	43.32	
0.0863	1.3352	43.32	
w_1=0.00003			
0.0100	1.3333	43.37	
0.0252	1.3337	43.37	
0.0404	1.3345	43.38	43.38
0.0556	1.3351	43.38	
0.0709	1.3355	43.39	
0.0863	1.3367	43.40	

$$B = (V_1^0 - V_2^0) + V_1^0\,[(\Delta\mu_1^{0\neq} - \Delta\mu_2^{0\neq})/RT] \quad \ldots\ldots\ldots\ldots\ldots\ldots(9)$$

Where V_2^0 is the limiting partial molar volume (φ_V^0) of the solute and $\Delta\mu_2^{0\neq}$ is the ionic activation energy per mole of solute at infinite dilution . Rearranging the equation (9) we get

$$\Delta\mu_2^{0\neq} = \Delta\mu_1^{0\neq} + (RT/V_1^0)[B - (V_1^0 - V_2^0)] \quad \ldots\ldots\ldots\ldots\ldots(10)$$

From table 8, it is evident that $\Delta\mu_2^{0\neq}$values are all positive and much larger than $\Delta\mu_1^{0\neq}$, suggesting that interaction between solute (ALP) and solvent (aqueous uric acid mixture) molecules in the ground state is stronger than in the transition state. According to free energy terms the salvation of solute in the transition state is unfavourable.

The entropy of activation ($\Delta S_2^{0\neq}$) for the solution has been calculated using relation:

$$\Delta S_2^{0\neq} = -\,d(\Delta\mu_2^{0\neq})/dT \quad \ldots\ldots\ldots\ldots\ldots(11)$$

Here $\Delta S_2^{0\neq}$ has been obtained from the negative slope of the plots of $\Delta\mu_2^{0\neq}$against *T* by using a least-squares treatment. The enthalpy of activation ($\Delta H_2^{0\neq}$) has been obtained from the relation:

$$\Delta H_2^{0\neq} = \Delta\mu_2^{0\neq} + T\Delta S_2^{0\neq} \quad \ldots\ldots\ldots\ldots\ldots(12)$$

The values of $\Delta S_2^{0\neq}$ and $\Delta H_2^{0\neq}$ are also reported in Table 8. It is evident from table 9, that $\Delta\mu_1^{0\neq}$ is practically constant at all the mass fraction of the aqueous uric acid mixture, suggesting that $\Delta\mu_2^{0\neq}$ is mainly dependent on the viscosity coefficients and $(V_1^0 - V_2^0)$ terms.

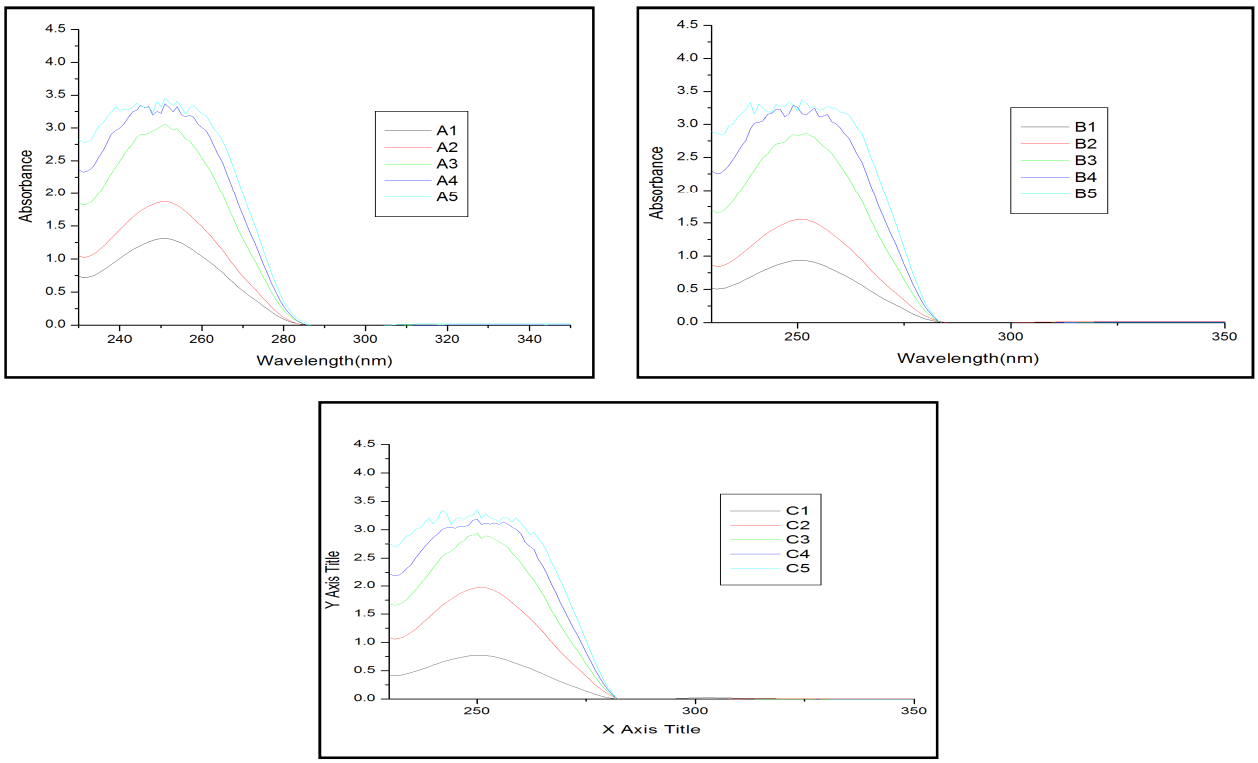


Fig. 1. (a) UV-Visible spectra for allopurinol and uric acid mixture having initial concentration1x10^{-5}; (b) UV-Visible spectra for allopurinol and uric acid mixture having initial concentration1x10^{-5};(c) UV-Visible spectra for allopurinol and uric acid mixture having initial concentration1x10^{-5}

Positive $\Delta\mu_2^{0\neq}$ values at all studied temperature and solvent composition suggests that the process of viscous flow becomes difficult as the temperature and mass fraction of aqueous uric acid mixture increases. Therefore, the formation of transition state becomes lee favourable. Feakins et al proposed that, $\Delta\mu_2^{0\neq} > \Delta\mu_1^{0\neq}$ for solutes having positive *B*-coefficients and indicates a stronger solute –solvent interactions, thereby suggesting that the formation of transition state is accompanied by the rupture and distortion of the intermolecular forces in the solvent structure (Ali, A. , Hyder, S. , Sabir, S. , Chand, D. Nain, A. K., 2006). The negative values of both $\Delta S_2^{0\neq}$ and $\Delta H_2^{0\neq}$ suggest that the formation of transition state is associated with bond-making and an increase in order. Although a detailed mechanism for this is not easily advanced, it may be suggested that the slip-plane is in the disordered state (Friedman, H. L., Krishnan, C. V. 1973). According to Feakins et al. model, as $\Delta\mu_2^{0\neq} > \Delta\mu_1^{0\neq}$, the solute (ALP) behaves as structure makers. This again supports the behaviour of *dB/dT* for the solute in aqueous uric acid mixture. Furthermore, it is attractive to observe that there is linear correlation between viscosity *B*-coefficients of the studied citric acid with the limiting apparent molar volumes (φ_V^0) in different mass fraction of aqueous uric acid solutions. From the above fact it means

$$B = A_1 + A_2\varphi_V^0 \qquad \text{.....(13)}$$

The coefficients A_1 and A_2 are listed in table 8. As both viscosities*B*-coefficient and limiting apparent molar volumes define the solute-solvent interaction in solution. The linear variation of viscosity *B*-coefficient and limiting apparent molar volume (φ_V^0) reflects the positive slope (or A_2). It is evident from this study, that there is a strong interaction between ALP and UA and it becomes stronger with rise in temperature.

As molecules of UA are engaged with the ALP molecules, the accumulation among the uric acid molecules becomes less effective. Therefore, the process of crystallization and deposition of uric acid gets hampered in presence of ALP. As we know that the gout is the disease occurred due to the crystallization of MSU in the joint of human body. Therefore the interaction of ALP with uric acid in aqueous solution at human body temperature (37^{o}C or 310.15K) is important. We have obtained the derived parameters like, limiting apparent molar volume (φ_V^0), viscosity *B*-coefficient by interpolation and presented in table 5. The positive and significant magnitude of φ_V^0 and *B*-coefficient from table 5 clearly indicates that the limiting apparent molar volume (φ_V^0), viscosity *B*-coefficient is increases with increasing mass fraction of ALP, which indicates the positive effect of hampering in crystallization and deposition of uric acid in joint of the human body, as a result presence of ALP relief the painful effect of gout. The effect also evidence from the values of free energy of activation *(*$\Delta\mu_1^{0\neq}$ and ($\Delta\mu_2^{0\#}$*), entropy (*$\Delta S_2^{0\neq}$) and enthalpy ($\Delta H_2^{0\neq}$) (table 9).The positive values and increasing order of free energy of activation and negative magnitude and decreasing degree of *entropy (*$\Delta S_2^{0\neq}$) and enthalpy ($\Delta H_2^{0\neq}$) also suggesting the positive effect for pain relief of gout in presence of ALP.

Refractive Index

The measurement of refractive index is also a suitable method for investigating the molecular interaction existing in solution. The molar refraction (R_M) can be evaluated from the Lorentz-Lorenz relation (Minkin, V. , Osipov, O., Zhdanov, Y. 1970). The refractive index of a substance is defined as the ratio c_o/c, where c and c_o is the velocity of light in the medium and in vacuum respectively. Stated more simply that the refractive index of a compound describes its ability to refract

light as it passes from one medium to another and thus, the higher the refractive index of a compound, the more the light is refracted (Born, M., Wolf, E. 1999). As stated by Deetlefs et al. (Deetlefs, M. , Seddon, K., Shara, M. 2006) the refractive index of a substance is higher when its molecules are more tightly packed or in general when the compound is denser. Hence, a perusal of table 10 we found that the refractive index and the molar refraction are higher for the studied allopurinol in all the mass fraction of aqueous uric acid, indicating to the fact that the molecules are more tightly packed in the solution.

The Limiting molar refraction (R_M^0) estimated from the following equation (14)and presented in Table 10.

$$R_M = R_M^0 + R_S \sqrt{m} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (14)$$

Accordingly, we found that the higher values of refractive index and R_M^0 which representing the fact that the molecules of allopurinol are more tightly packed and greater solute-solvent interaction with uric acid molecules than solute solvent interaction. This is also in good agreement with the results obtained from apparent molar volume and viscosity *B*-coefficients discussed above. All the above derived parameters suggest that there is strong interaction between ALP (solute) and uric acid (solvent) and these increases with rise in temperature. The solute-solvent interaction is much greater than the solute-solute and solvent-solvent interactions.

UV-Visible study: The absorption spectra of alopurinol and uric acid mixtures at 298.15 K are depicted in Figure 1. Absorbance vs. wavelength spectra clearly shows that there is a increasing trend of absorbance and shifting of λ_{max} with increasing alopurinol concentration in the mixture of alopurinol and uric acid solutions. The absorbance value is greater for the mixture of higher mass fraction i.e., $3x10^{-5}$(m) uric acid solution than the other two mass fractions [($2x10^{-5}$(m) and $1x10^{-5}$(m)]of uric acid, which supports that the solute–solvent interaction is greater with increasing concentration of both uric acid and alopurinol. Thus this UV-Visible spectra study supports the fact that has been discussed earlier in the section of density, viscosity and refractive index study (Roy, M. C., Roy, M. N. 2017).

Structural and biological importance: Uric acid (2,6,8 trioxypurine-$C_5H_4N_4O_3$) is an organic compound that is endogenously produced by animals as a purine metabolite. It is formed by the liver and mainly excreted by the kidneys (65-75%) and intestines (25- 35%). UA is the end product of purine metabolism in humans due to the loss of uricase activity, which led to humans having higher UA levels than other mammals. Due to its double bonds, uric acid has excellent antioxidant capacity, and it can be responsible for 2/3 of total plasma antioxidant capacity. It shows low solubility in water (as well as in plasma), and it would theoretically reach plasma saturation in the concentration of 6.4 mg/dL, which may not occur because solubility increase is provided by its binding to proteins, namely albumin, which is its main transporter. Protein-bound uric acid shows plasma solubility that is 70% higher than in its free state. Allopurinol(APL) is a drug used to treat gout which is caused by a build up of sodium urate crystal. APL is the most commonly used urate lowering therapy. It has the benefits of once-daily dosing as well as effectiveness in patients with renal impairment(Pogue, R., Atkinson, G. 1988; Marcus, Y., Hefter, G. , and Pang, T. S. 1994).

Conclusion

In summary, that there is a strong interaction between uric acid and allopurinol and it becomes stronger with increase in temperature. As molecules of uric acid are interacted with the allopurinol molecules, the accumulation of uric acid molecules becomes less efficient in biochemic body. Therefore, the process of crystallization and deposition of uric acid gets troubled in presence of allopurinol. The above fact suggests that the relief of painful effect of gout can be achieved by consumption of zyloric acid tablets.

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