Research Article

ISSN: 2349 – 7106

Asian Journal of Research in Chemistry and Pharmaceutical Sciences

Journal home page: www.ajrcps.com

ION SOLVATION IN BIOLOGICALLY IMPORTANT ANTIBIOTIC OXYTETRACYCLINE WITH AQUEOUS ACETONITRILE MIXED-SOLVENT SYSTEMS

Elsayed T. Helmy[*1], Esam A. Gomaa[2] and Elsayed M. Abou Eleef[3]

[1*]Department of Marine Pollution, Environmental Division, National Institute of Oceanography and Fisheries, Kayet Bey, Elanfoushy, Alexandria, Egypt.

[2]Department of Chemistry, Faculty of Science, Mansoura University, Mansoura, Egypt.

[3]Department of Basic Science, Delta Higher Institute for Engineering and Technology, Dakhlia, Mansoura, Egypt.

ABSTRACT

The aim of this work is to calculate ion-solvent interaction, density of organic-aqueous mixtures of Acetonitrile-water (AN-H_2O), density of saturated solutions of oxytetracycline (OTC), salvation volumes (Van der Waals volume V_W, molar volume V_M and electrostriction volume V_e) and solvated radii (r_o) from solubility experiments. It was found that values of the log activity coefficient ($\gamma_\pm$) of OTC in (AN-H_2O) mixture were decreases by increasing in the content of the organic solvent used. The values of the log ($\gamma_\pm$) found to decrease with the increase in temperature. The densities and the molar volumes of the saturated solutions of OTC decrease by increasing ratio of AN and also increases by increasing in temperature. All the electrostriction volumes calculated for OTC having negative values. The electrostriction volumes increase in negativity on increasing the percentages of the organic solvent. The solvated radii of OTC was increased as the organic solvent content increase and as the temperature increase.

KEYWORDS

Ion-Ion Interactions, Oxytetracycline HCl, Acetonitrile, Solubility and Solvation Volumes.

Author for Correspondence:

Elsayed T. Helmy
Department of Marine Pollution,
Environmental Division,
National Institute of Oceanography and Fisheries,
Kayet Bey, Elanfoushy, Alexandria, Egypt.

Email: stalaat41@yahoo.com

INTRODUCTON

In an ionic solution, the interaction between the ionic solute and solvent is predominantly ion-dipole. The ion-dipole interaction depends on the size of ions and polarity of solvent. The dissolution of ionic salt in a solvent causes a volume contraction due to interaction between ions and solvent molecules. This might affect various properties involving thermo dynamics and acoustics parameters factors. The total electrolyte concentration in solution will affect important properties such as the dissociation or the solubility of different salts. One of the main characteristics of a solution with dissolved ions is the ionic strength. Various models have been used to predict the co solvent/water solubility profiles. These include parabolic and log-linear models. Drug solubility is of vital importance in the pharmaceutical field. Drug solubility and dissolution rate are often the rate limiting factors to drug absorption from the gastrointestinal tract[1,2]. The factors that govern solubility need to be understood before selecting a technique to improving the solubility. There are two major factors that determine the aqueous solubility of a drug. The activity of the drug in aqueous media, and the crystallinity of the compound. The activity/polarity of the drug may be defined using one of the following indices: dielectric constant, solubility parameter, surface tension, interfacial tension and the octanol/water partition coefficient[3]. Evaluated these polarity indexes for the estimation of aqueous solubility. For the purpose of this manuscript the octanol/water partition coefficient will be used as the polarity index of choice. The melting point of a compound is a good indicator of crytsallinity. The more crystalline the compound the higher its melting point. Numerous models have been proposed for the estimation of the aqueous solubility. General solubility equation was applicable by testing it on hundreds of organic non-electrolytes[4-6]. Several methods have been used to increase drug solubility. The choice of method is dependent upon the physicochemical characteristics of the drug as well as its biopharmaceutical and toxicological nature and the route of administration. These methods include pH adjustment, salt formation, micelle formation, complexation and co-solvency. In continuation of our earlier work[7-10] for OTC and other substances that states that they are very important materials for different fields. This work is a further attempt to investigate ion-solvent interaction, density of organic-aqueous mixtures of Acetonitrile-water(AN-H_2O), density of saturated solutions of OTC, salvation volumes (Van der Waals volume V_W, molar volume V_M and electrostriction volume V_e) and solvated radii (r_o) from solubility experiments at temperatures starts from 293.15K to 308.15 K.

MATERIAL AND METHODS

Reagents and chemicals

Oxytetracycline hydrochloride (OTC) and acetonitrile were purchased from Merck Company with high degree of purity and used without further purification.

Preparation of solutions

The mixed solvents, from deionized water and fairly pure AN. Then, saturated solutions of OTC were prepared by dissolving different amounts in closed test tubes containing different (AN + H_2O) mixtures by value percent of AN = (0 - 100% by volume).

METHODOLOGY

The tubes were placed in a shaking thermostat (Model Gel) for a period of four days till equilibrium reached. The solubility, S (mole/Kg. solvent), of OTC was determined gravimetrically by the solvent evaporating method. All the solubility experiments of were repeated at least three times and the average of results were taken.

RESULTS AND DISCUSSION

For an ionic compound, with the formula AB, we may consider the following equilibrium in its saturated solution at a given constant temperature.

$$AB\ (s) \leftrightarrow A^+_{(aq)} + B^-_{(aq),} \qquad K_{sp\ (th)} = a_+ \cdot a_- \qquad (1)$$

Where $K_{sp\ (th)}$ denotes the thermodynamic solubility product constant and a_+ and a_- refer to activity of A^+ and B^- in the solution, respectively. If the solubility of AB is very low, it may replace the activity of each ion by its concentration, so,

$$K_{sp\ (th)} = S_o^2 \qquad (2)$$

Where s_o represents the molarity of AB in the very dilute solution. The electrostatic interaction becomes very small and the ion association phenomenon may be negligible (the activity coefficient $\gamma_\pm \sim 1$).

The ion association At very low concentration may be negligible (the activity coefficient $\gamma_\pm \sim 1$) because of the electrostatic interaction becomes very small[11-13].

At low concentration, the activity coefficient may be determined by using the Debye- Huckel limiting law:

$$\log \gamma_{\pm} = -Z_{+}Z_{-}A\sqrt{I} \text{ applicable for } I < 10^{-2}\text{ M} \ldots\ldots\ldots (3)$$

Where Z_+ and Z_- are the charges of ions in solutions, $A = 1.823 \times 10^{6}(\varepsilon.T)^{-3/2}$, the ionic strength, I, defined as, $I = \frac{1}{2}\sum_{i} m_i z_i^2$ (z_i is the charge on ion i, and m_i is the molality of ion i) and the ionic strength, I emphasizes the charges of ions because the charge numbers occur as their squares. At relatively high concentration, the electrostatic interaction becomes very large[14-15]. The activity coefficient may be determined using the extend Debye-Huckel law:

$$\log \gamma_{\pm} = -\frac{Z_{+}Z_{-}A\sqrt{I}}{I + Br^{o}\sqrt{I}} \text{ for } I < 10^{-1}\text{ M} \quad \ldots\ldots\ldots (4)$$

Where $B = 50.29 \times 10^{8} (\varepsilon T)^{-1/2}$, and r° is the solvated radius.

At high concentrations, activity coefficients of electrolyte solutions can be determined by using the Davies equation[15] which is an empirical extension of Debye-Huckel theory. The final form of the equation gives the mean molal activity coefficient, $\gamma_\pm$, of an electrolyte which dissociates into ions having charges z_+ and z_- as a function of ionic strength, *I*.

$$\log \gamma_{\pm} = -Z_{+}Z_{-}A\left(\frac{\sqrt{I}}{I+\sqrt{I}} - 0.3I\right) \quad \ldots\ldots (5)$$

The second term, 0.3 *I*, goes to zero as the ionic strength goes to zero, so the equation reduces to the Debye–Huckel equation at low concentration. However, as concentration increases, the second term becomes increasingly important, so the Davies equation can be used for solutions too concentrated to allow the use of the Debye–Huckel equation.

The results of the I and (log ($\gamma_\pm$)) for OTC in (AN-H_2O) mixture are illustrated in Table No.1. The relation between the ($\gamma_\pm$) of OTC and (X_s) of AN in (AN–H_2O) mixed solvents at different temperatures is represented in Figure No.1).

In the calculation, the dielectric constant for water is obtained from[16],

$$D_{H_2O} = 87.74 - (4.0008 \times 10^{-1}t) + (9.398 \times 10^{-4}t^{2}) - (1.41 \times 10^{-6}t^{3}) \ldots (6)$$

Where $t = T - 298.15$ K.

The values of dielectric constants for methanol, ethanol and water at different temperatures (293.15, 298.15, 303.15 and 308.15 K) were taken from previous publications[17-18] and dielectric constants of AN-H_2O mixtures were calculated from the equation (7):

$$\mathcal{E} = X_{s(1)(H_2O)} \cdot \mathcal{E}_{(H_2O)} + X_{s(2)(orgsolvent)} \cdot \mathcal{E}_{(orgsolvent)} \ldots (7)$$

For calculating dielectric constant of water and ethanol at different temperatures other than those reported by Akerl of, we interpolated the data with following equation described by Akerl of[18]:

$$\ln \varepsilon = \ln a - bT \ldots\ldots\ldots (8)$$

Where (ln a) and b are the intercept and coefficient of the regression, respectively. The calculated values of dielectric constant for H_2O and AN at different temperatures were used in a previously trained version of the Jouyban - Acree model for prediction of dielectric constant of the water + ethanol at different temperatures[19]:

$$ln\varepsilon_{M,T} = f_W ln\varepsilon_{W,T} + f_E ln\varepsilon_{E,T} + 246.8\left[\frac{f_W f_E}{T}\right] + 22.1\left[\frac{f_W f_E(f_W - f_E)}{T}\right] - 51.5\left[\frac{f_W f_E(f_W - f_E)^2}{T}\right] \ldots (9)$$

Where $\varepsilon_{M,T}$, $\varepsilon_{W,T}$, and $\varepsilon_{E,T}$ are dielectric constants of the solvent mixture, water, and ethanol at temperature *T* (Kelvin); f_W and f_E are the volume fractions of H_2O and AN, respectively.

The resulted equations for dielectric constant prediction of water and ethanol at different temperatures are as follows, respectively:

$$\ln\varepsilon_{W,T} = 5.769 - 0.00471T \quad R^2 = 0.999 \ \ldots\ldots\ldots (10)$$

$$\ln\varepsilon_{E,T} = 5.034 - 0.00619T \quad R^2 = 0.999 \ldots\ldots\ldots (11)$$

The values of dielectric constant (ε) for (acetonitrile -water) mixtures at different temperature were taken from previous publications Table No.2[18].

The results of the density measurements of the (organic-aqueous) mixtures (AN- H_2O) at different temperatures (293.15, 298.15, 303.15 and 308.15 K) are reported in Table No.3.

The results show that the density of (AN- H_2O) decreases with the increase in the organic solvent content. A non-bulky structure with increasing the composition of alcohol or acetonitrile is suggested.

Table No.4 show the density of the saturated solutions of OTC in (AN-H_2O) mixtures, at different temperatures (293.15, 298.15, 303.15 and 308.15 K). It is obvious that the densities of the saturated solutions of OTC decrease by increasing ratio of AN and also increases by increasing in temperature.

From density and molal solubility measurements of the saturated solutions of OTC in (AN-H_2O) mixtures, the molar volumes (V)[20] are calculated, at different temperatures (293.15, 298.15, 303.15 and 308.15 K) according to equation (12).

$$V = \frac{M}{d} \quad \ldots\ldots\ldots (12)$$

Where M is the molecular weight of OTC, *d* is the density of the solution; the molar volume (V) of pure mixed (AN-H_2O). The molecular weights of the binary solvents are calculated using equation (13).

$$M = X_{S(1)(H_2O)} . M_{(H_2O)} + X_{S(2)(O.S)} . M_{(O.S)} \quad \ldots\ldots (13$$

Where $M_{(H_2O)}$ $M_{(O.S)}$ and are the molecular weights of water and organic solvent, respectively, $X_{S(1)(H_2O)}$ and $X_{S(2)(O.S)}$ are the mole fractions of water and the organic solvents used by weight which are calculated by applying equation (14).

$$X_{S(1)} by wt = \frac{\frac{Vol.\%(1)\ X\ d(1)}{M_1}}{\frac{Vol\%(1)\ X\ d(1)}{M_1} + \frac{Vol.\%(2)\ X\ d(2)}{M_2}} \quad \ldots\ldots (14)$$

Where $d_{(1)}$ and $d_{(2)}$ are the densities of the organic solvent and water, respectively, and M_1 and M_2 are the molecular weights of the organic solvent and water respectively, vol. % (1) and vol. % (2) are the volume percentages of the organic solvent and water, respectively.

The packing density (i.e., the relation between the Van der Waals volumes and the partial molar volumes) of relatively large molecules (more than 40) is found to be constant. Therefore, it is possible to calculate the Van der Waals volumes (V_w) of OTC in (AN-H_2O) salt mixtures in at different temperatures (293.15, 298.15, 303.15 and 308.15 K) by applying equation (15).

$$\text{Packing density (P)} = \frac{V_w}{V} = 0.661 \pm 0.017 \quad \ldots\ldots\ldots (15)$$

Where V_w and V are the Van der Waals and partial molar volumes, respectively.

The electrostriction volume (V_e)[20-21] which is the volume of the solute compressed by the solvent is calculated by using equation (16).

$$V_e = V_w - V \quad \ldots\ldots\ldots (16)$$

The values of *V, V_w* and *V_e* of OTC in (AN- H_2O) mixtures; at different temperatures (293.15, 298.15, 303.15 and 308.15 K) are listed in Tables No.5-6.

In comparing the data of solvation of the substance used, it is was observed that the values of the molar volume of AN mixtures with H_2O are increased by increasing the organic solvents content in the mixtures due to the increase in the volume of organic solvent compared to water.

All the electrostriction volumes calculated for OTC in (AN- H_2O) mixtures having negative values. The electrostriction volumes increase in negativity on increasing the percentages of the organic solvent, indicating the more work (energy) is done by the solvent on the solvation sheaths of the salts.

The solvated radii of the organic-aqueous mixtures; (AN-H_2O) at different temperatures (293.15, 298.15, 303.15 and 308.15 K were calculated using equation (17) by considering the spherical form of the solvated molecules[20].

$$V = \frac{1}{6}\pi N \sigma^3 \quad \ldots\ldots\ldots (17)$$

Where *V* is the molar volume calculated from the densities as described before and σ is the solvated diameter. The solvated radii of OTC were calculated by adding the crystal radius of the salt to the radii of solvent in OTC in (AN- H_2O) mixtures at different temperatures (293.15, 298.15, 303.15 and 308.15 K).

The calculated values of the solvated radii of OTC in (AN- H_2O) mixtures at different temperatures (293.15, 298.15, 303.15 and 308.15 K) as well as the solutions of OTC in (AN- H_2O) mixtures are listed in Tables No.5-6.

It is obvious that the solvated radii of OTC in (AN-H_2O) mixtures are increased as the organic solvent content increase and as the temperature increase.

This may be due to the excess solvation processes, and the higher solvated radii of the organic solvent used than those of water and also to the increasing in the electronic clouds around the solvated molecules as a result of the increase in their vibration and rotation motions with increasing the temperature.

Table No.1: (I) and (log $\gamma_\pm$) for OTC in (AN–H_2O) mixed solvents at different temperatures

S.No	AN vol. %	X_s	I				log $\gamma_\pm$			
			293.15 K	298.15 K	303.15 K	308.15 K	293.15 K	298.15 K	303.15 K	308.15 K
1	0	0	0.3887	0.4057	0.4352	0.4527	293.15 K	298.15 K	303.15 K	308.15 K
2	20	0.0788	0.165	0.1747	0.1836	0.2027	0.7327	0.7298	0.7271	0.7239
3	40	0.1857	0.1471	0.1641	0.173	0.1841	0.7427	0.7376	0.7321	0.7241
4	60	0.3391	0.1368	0.142	0.1598	0.1757	0.7299	0.7196	0.7135	0.7066
5	80	0.577	0.1357	0.1412	0.1484	0.1536	0.7007	0.6931	0.6836	0.6727
6	100	1	0.0285	0.0337	0.0363	0.0416	0.6314	0.6244	0.6249	0.6094

Table No.2: (ε) of (AN-H_2O) mixed solvents at different temperatures

S.No	Vol.% of AN	ε (AN-H_2O) mixtures			
		293.15 K	298.15 K	303.15 K	308.15 K
1	0	80.1	78.3	76.31	74.3
2	10	78.59	76.82	74.87	72.89
3	20	76.8	75.07	73.16	71.23
4	30	74.66	72.97	71.12	69.24
5	40	72.04	70.42	68.62	66.8
6	50	68.78	67.22	65.5	63.76
7	60	64.6	63.13	61.51	59.86
8	70	59.05	57.69	56.19	54.67
9	80	51.3	50.1	48.77	47.42
10	90	39.77	38.78	37.69	36.6
11	100	20.75	20.1	19.38	18.66

Table No.3: (d_o) of (AN-H_2O) mixed solvents at different temperatures

S.No	AN (vol. %)	(d_o)			
		293.15K	298.15K	303.15K	308.15K
1	0	0.9991	0.997	0.9942	0.9912
2	20	0.9876	0.9792	0.9756	0.973
3	40	0.9577	0.9565	0.954	0.9511
4	60	0.9265	0.9214	0.919	0.9165
5	80	0.8751	0.8691	0.8681	0.8648
6	100	0.778	0.7766	0.7751	0.7731

Table No.4: (d) of saturated solution of OTC in (AN-H_2O) mixed solvents at different temperatures

S.No	AN (vol. %)	(d)			
		293.15 K	298.15 K	303.15 K	308.15 K
1	0	1.115	1.13	1.143	1.159
2	20	1.008	1.057	1.07	1.094
3	40	0.9695	0.971	0.999	1.029
4	60	0.943	0.951	0.0957	0.985
5	80	0.916	0.919	0.921	0.925
6	100	0.82	0.833	0.84	0.89

Table No.5: (V), (V_w), (V_e) and (r_o) of OTC in different (AN-H_2O) mixed solvents at 293.15 K and 398.15K. ($Cm^3.mol^{-1}$)

S.No	AN vol. %	V	V_w	V_e	r_o	V	V_w	V_e	r_o
		at 293.15K				at 298.15K			
1	0	445.42	294.42	-150.99	4.7385	439.48	290.49	-148.98	4.7175
2	20	492.87	325.78	-167.08	4.9006	469.71	310.47	-159.23	4.8237
3	40	512.49	338.75	-173.73	4.9646	511.69	338.22	-173.46	4.9621
4	60	526.84	348.24	-178.59	5.0107	522.31	345.24	-177.06	4.9966
5	80	542.13	358.35	-183.78	5.0595	540.30	357.13	-183.16	5.054
6	100	603.71	399.05	-204.65	5.2497	593.98	392.62	-201.35	5.2222

Table No.6: (V), V_w), (V_e) and (r_o) of OTC in different (AN-H_2O) mixed solvents at 303.15 K and 308.15K ($Cm^3.mol^{-1}$)

S.No	AN vol. %	V	V_w	V_e	r_o	V	V_w	V_e	r_o
		at 303.15K				at 308.15K			
1	0	434.47	287.18	-147.28	4.6995	428.44	283.20	-145.24	4.6778
2	20	463.94	306.66	-157.27	4.8041	453.68	299.88	-153.79	4.7687
3	40	497.16	328.62	-168.53	4.9153	482.50	318.93	-163.56	4.8670
4	60	525.12	347.10	-178.01	10.742	504.08	333.19	-170.88	4.9385
5	80	539.12	356.35	-182.76	5.0503	536.74	354.78	-181.95	5.0430
6	100	588.85	389.23	-199.62	5.2077	554.28	366.37	-187.90	5.1083

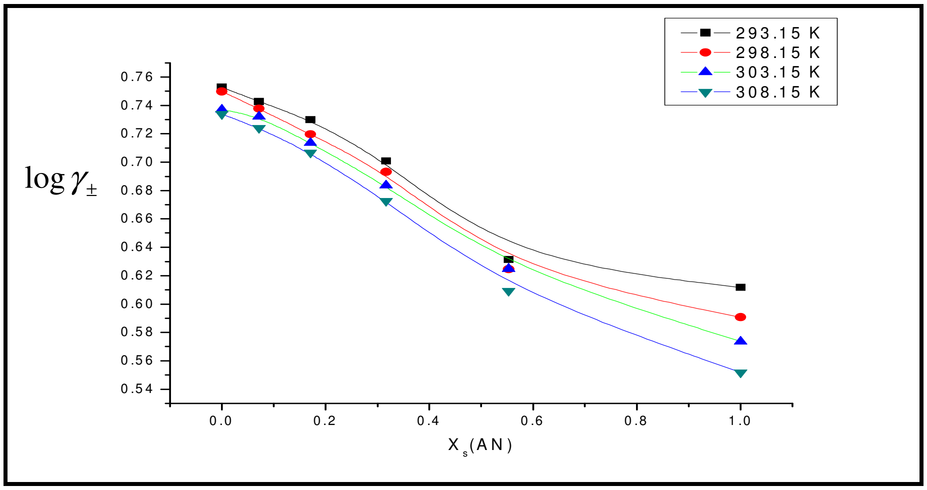

Figure No.1: Relation between ($\gamma\pm$) of OTC and (X_s) of AN in (AN-H_2O) mixed solvents at different temperatures

CONCLUSION

In this work we calculate ion-ion interaction, dielectric constant, density of organic-aqueous mixtures of AN-H_2O solvents, density of saturated solutions of OTC, salvation volumes (Van der Waals volume V_W, molar volume V_M and electrostriction volume Ve) and solvated radii from solubility experiments. It was found that values of the log $\gamma_{\pm}$ of OTC in (AN-H_2O) mixture were decreases by increasing in the content of the organic solvent used (AN). The values of the log ($\gamma_{\pm}$) found to decrease with the increase in temperature. The densities of the saturated solutions of OTC decrease by increasing ratio of AN and also increases by increasing in temperature. The values of the molar volume of AN mixtures with water are increased by increasing the organic solvents content in the mixtures due to the increase in the volume of organic solvent compared to water. All the electrostriction volumes calculated for OTC having negative values. The electrostriction volumes increase in negativity on increasing the percentages of the organic solvent. The solvated radii of OTC was increased as the organic solvent content increase and as the temperature increase.

ACKNOWLEDGEMENT

The authors are sincerely thanks to the Department of Marine Pollution, Environmental Division, National Institute of Oceanography and Fisheries, Kayet Bey, Elanfoushy, Alexandria, Egypt for providing the facilities to complete this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBILIOGRAPHY

1. Rubino J T. Solubilization of Some Poorly Soluble Drugs by Co solvents, *Ph. D. Diss., University of Arizona, Tucson,* 1984.
2. Rubino J T and Yalkowsky S H. Solubilization by Cosolvents II: Phenytoin in Binary and Ternary Solvents, *J. Parent Sci. Technol,* 38(6), 1984, 215-221.
3. Rubino J T and Yalkowsky S H. Co solvency and Co solvent Polarity, *Pharm. Res,* 4(3), 1987, 220-230.
4. Yalkowsky S H and Valvani S C. Solubility and partitioning I. Solubility of nonelectrolytes in water, *J. Pharm. Sci,* 69(8), 1980, 912-922.
5. Yalkowsky S H and Valvani S C. Solubility and partitioning II. Relationship between aqueous solubility, partition coefficients, and Molecular Surface Areas of Rigid Aromatic Hydrocarbons, *J. Chem. Engin. Data,* 24(2), 1979, 127-129.
6. Jain N, Yang G, Tabibi E, Yalkowsky S H. Solubilization of NSC-639829, *Int J Pharm,* 225(1-2), 2001, 41-47.
7. Gomaa E A, Elleef E M A, Helmy E T. Conductance Studies on Complex Formation between $CaCl_2$ and Ampicillin as Ligand in Water and in Methanol Solvent at Different Temperatures, *RRJPPS,* 3(3), 2014, 55-64.
8. Gomaa E A, Bouelleef E M A, Helmy E T. Complexation of 2-Mercaptoimidazol with some Barium Salts Conductometrically in Various Solvent at Different Temperatures, *Int, J. Mod. Chem,* 7(2), 2015, 141-155.
9. Gomaa E A, Bouelleef E M A, Helmy E T. Solvent Effects on the Thermodynamics of Solvation of BARIUM DIPHENYLAMINE SULFONATE in Ethanol-Water Mixed Solvents, *South. Braz. J. Chem,* 21(21), 2013, 31-40.
10. Helmy E T, Gomaa E A, Elleef E M A, Negm A. Conductometric, Spectrophotometric and *in-vivo* Investigation of the Interaction of Ca (II) Ion with Oxytetracycline Hydrochloride, *IJPMBS,* 4(3), 2015, 197-203.
11. Helmy E T, Gomaa E A, Abou Eleef E M. Gibbs Free Energy and Activation Free Energy of Complexation of Some Divalent Cations with Ampicillin in Methanol at Different Temperatures, *American Journal of Applied and Industrial Chemistry,* 2(5), 2016, 29-32.

12. Aghaie M, Samaie E. Molecular dynamics study of $CaCl_2$ in liquid methanol, *J. Mol. Liq,* 126(1-3), 2006, 1-8.
13. Aghaie M, Ghaemi F. Giahi A M. Thermodynamic study of ion- association in KNO_3 solution in the mixed solvent (water +methanol), *J. Phys. Theor. Chem,* 11(3), 2014, 147-152.
14. Aghaie H, AliABA2di A, Sohrabi B, Aghaie M, Sohrabi M R. Binding Data Analysis for Interaction of n- Alkyl Sulfates with Insulin, *J. Phys. Theor. Chem,* 1(2), 2004, 25-28.
15. Aghaie M, Gafoorian S, Broojeni B S, Aghaie H. The effect of dielectric constant and ionic strength on the solubility of lithium carbonate at 25.0°C in thermodynamic view, *J. Phys. Theor. Chem,* 5(4), 2009, 223-227.
16. Malmberg C G, Maryott A A, Dielectric Constant of Water from 0^0 to 100^0C, *J. Res. Natl. Bur. Stand, U.S.A,* 56(1), 1956, 1-8.
17. Akerlof G. Dielectric constants of some organic solvent-water mixtures at various temperatures, *J. Am. Chem. Soc,* 54(11), 1932, 4125-4139.
18. El-Khouly A A, Gomaa E A and Abou El-leef S. Apparent association constants of HgCl2 in presence of kryptofix-22 in mixed aqueous-organic solvents, *Bulletin of electrochemistry,* 19(5), 2003, 193-202.
19. Jouyban Sh A, Soltanpour H K. Chan. A simple relationship between dielectric constant of mixed solvents with solvent composition and temperature, *Int. J. Pharm,* 269(2), 2004, 353-360.
20. Acree W E, Jr. Thermodynamic Properties of Nonelectrolyte Solutions; Harcourt Brace Javanovich, *Publishers: Orlando,* 1984, 1-211.
21. Padova J and Abrahamer I. Ion-solvent interactions. VII. Apparent and partial molal volumes of some symmetrical tetraalkylammonium halides in anhydrous methanol solutions, *J. Phys. Chem,* 71(7), 2112, 1967.

Please cite this article in press as: Elsayed T. Helmy *et al.* Ion solvation in biologically important antibiotic oxytetracycline with aqueous acetonitrile mixed-solvent systems, *Asian Journal of Research in Chemistry and Pharmaceutical Sciences,* 5(3), 2017, 98-105.