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Densiometric Study of Chloroquine Diphosphate in Aqueous Solution of Acetic Acid at 293.15K

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Authors' contributions

This work was carried out in collaboration between all authors. Author SPD designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MD and AKP managed the analyses of the study. Author SKP managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The apparent molar volume (V_ϕ), limiting apparent molar volume (V_ϕ^0) and solute-solute interaction parameter (S_v) of chloroquine diphosphate in aqueous solution of acetic acid at 293.15K were calculated. The apparent molar volumes had been computed to calculate the partial molar volumes of transfer (ΔV_ϕ^0) and excess molar volume (V_m^E). The excess values and other parameters such as density, apparent molar volume, limiting apparent molar volume, solute-solute interaction parameter, and transfer volume have been interpreted in terms of different interactions present in the mixture.

Keywords: Apparent molar volume; limiting apparent molar volume; transfer volume; excess molar volume; solute-solvent interaction.

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1. INTRODUCTION

The studies of volumetric and excess parameter are responsible for interpreting ion-solvent interaction in solution phase. Among the various physical parameters apparent molar volume at infinite dilution has been recognised as a quantity that is sensitive to structural changes in solutions. The apparent molar volume of a solute is associated with a combination of intrinsic volume and volumetric effect of ion-solvent interaction [1]. The partial molar volume and related volumetric parameters of drugs in aqueous solutions have been reported [2-6]. Hemmes et al. [7] have reported the dependence of ion-solvent interaction on chemical structure of nucleic acid derivatives in an aqueous solution. The excess molar volume $\left(V_m^E\right)$, excess viscosity $\left(\eta^E\right)$ and excess Gibb's free energy of activation of flow $\left(\Delta G^{*E}\right)$ have also been discussed in terms of molecular interactions [8]. Treszcznowicz et al. [9] and later Aminabhavi et al. [10] reported that V_m^E may be discussed in terms of physical, chemical and geometrical contributions. The binding of apolipoprotein to lipid surface [11] is considered as a subject of overall drug mechanism [11]. Most of the drugs containing certain groups responsible for their acidic, basic and amphoteric properties. Pharmacological properties of many drugs show colloidal behaviour and aggregates in the body lowering the transport rate of drug consequently detorating the health [12]. These properties are highly dependent upon solution behaviour [13-14]. The density and partial molar volume measurements of aqua-organic liquids at infinite dilution [15] have been found to be highly useful in understanding the structure of molecular interaction between water and organic molecules. But few have been reported the solution behaviour of drugs. Parmer et al. [16] have reported the partial volume of citric and tartaric acids in water and binary aqueous mixture of ethanol. The main aim of this present work is to study the effect of concentration of chloroquine diphosphate and mole fraction of acetic acid on the apparent molar volume of chloroquine diphosphate in aqueous solution of acetic acid. Ion-solvent interactions have been interpreted based on volumetric behaviour.

2. MATERIALS AND METHODS

Chloroquine diphosphate supplied by sigma Aldrich was taken to prepare solutions under study. Doubled distilled water was prepared by distilling water over alkaline potassium permanganate in all glass distillation flasks which was stored at room temperature. Acetic acid was Anal R grade. The solutions were prepared in different concentrations varying from 0.001-0.01 M. The density of solutions was determined accurately using single capillary pyknometer of 10 cm^3 capacity (Borosil glass) and electronic balance of accuracy (±0.1 mg).

The solutions of chloroquine diphosphate were prepared at different mole fractions of acetic acid. The molar concentration (c) was calculated by using the standard expression,

$$c = md\left(1 + 0.001\,mM_{\ 2}\right)^{-1} \quad (1)$$

From the density data, the apparent molar volume $\left(V_\phi\right)$ was calculated from the relation of the type Harned and Owen [17],

$$V_\phi = 1000(cd_0)^{-1}(d_0 - d) + M_2 d_0^{-1} \quad (2)$$

where c is the molar concentration of the solution, M_2 is the molecular mass of the solute, d_0 and is the density of water and acetic acid and d are the density of mixture respectively.

The V_ϕ data were fitted with an equation of the type Masson [18],

$$V_\phi = V_\phi^0 + S_v c^{1/2} \quad (3)$$

Where V_ϕ^0 is the limiting apparent molar volume and S_v is the solute-solute interaction parameter. The excess molar volume was calculated by the equation,

$$V_m^E = x_1M_1 + x_2M_2/\rho - x_1M_1/\rho_1 - x_2M_2/\rho_2 \quad (4)$$

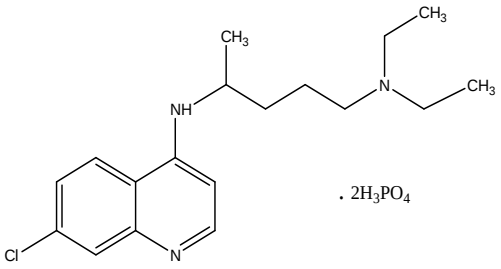
Transfer volume $\left(\Delta V_\phi^0\right)$ from chloquine diphosphate in water to chloroquine diphosphate in aqueous solution of acetic acid were calculated using the equation as,

$$\left(\Delta V_\phi^0\right) = V_{\phi(in\,aqueous\,acetic\,acid)}^0 - V_{\phi(in\,water)}^0 \quad (5)$$

3. RESULTS AND DISCUSSION

3.1 Drug Profile

Chloroquine diphosphate is used for the treatment of malaria [19], rheumatoid arthritis and also used for the systematic therapy of liver diseases caused by protozoa. It is also used as antibiotic [20-21]. Its IUPAC name is N^4-(7-chloro-4-quinolinyl-4-yl)-N^1, N^1-dimethyl- 1,4-pentadiamine diphosphate salt.



Structure of chloroquine diphosphate salt

3.2 Volumetric Parameters

The densities, apparent molar volume (V_ϕ), limiting apparent molar volume (V_ϕ^0) and its empirical parameter (S_v) of chloroquine in water and aqueous solution of acetic acid at 293.15K are recorded in Table 1.

Increase in density with concentration from Table 1 is due to the shrinkage in the volume which in turn due to the presence of solute molecules. In other words hydrophilic interaction results the increase in density of solutions. Apparent molar volume (V_ϕ) is a property of appropriate characteristic interaction and structural changes by the addition of solute. All the V_ϕ values are positive in aqueous solution of chloroquine diphosphate salt which decreases with concentration of chloroquine diphosphate salt in

Table 1. The data of concentration, density, apparent molar volume, limiting molar volume and solute-solute interaction parameter of chloroquine diphosphate in water and acetic acid-water at 293.15K

Mole fraction of acetic acid	Concentration of solution (c) mol dm^{-3}	Density (d) kgm^{-3}	Apparent molar volume (V_ϕ) x10^4 m^{3}mol^{-1}	Limiting apparent molar volume (V_ϕ^0) m^{3}mol^{-1}	S_v m^{3}kg$^{1/2}$mol$^{-3/2}$
Chloroquine diphosphate in water					
	0.001	0.9936	0.1183		
	0.003	0.9947	0.6226		
	0.005	0.9968	-0.3612	3.1289	-0.2072
	0.007	0.9983	-0.6295		
	0.01	1.0007	-0.6099		
Chloroquine diphosphate in acetic acid-water					
	0.001	1.0181	-1.1275		
	0.003	1.0290	-0.7483		
0.073	0.005	1.0235	-0.4565	-1.0878	0.0591
	0.007	1.0249	-0.2835		
	0.01	1.0261	-0.2285		
	0.001	1.0347	-1.4776		
	0.003	1.0381	-1.2842		
0.174	0.005	1.0409	-0.8661	-1.7461	0.6348
	0.007	1.0421	-0.4995		
	0.01	1.0446	-0.4144		
	0.001	1.0469	-2.5198		
	0.003	1.0485	-1.2583		
0.321	0.005	1.0491	-0.8734	-2.3909	0.8727
	0.007	1.0505	-0.6049		
	0.01	1.0516	-0.4847		
	0.001	1.0523	-2.3822		
	0.003	1.0604	-2.0308		
0.558	0.005	1.0679	-1.3485	-3.1231	1.5912
	0.007	1.0784	-0.9552		
	0.01	1.0839	-0.8091		

water. Maximum value of V_ϕ occurs at 0.001 and 0.003 M of chloroquine diphosphate in water in Table 1 which suggest ionic and hydrophobic interactions indicating the presence of solute-solvent interaction. The negative values of V_ϕ further indicate electrostrictive solvation of ions [22]. This may also support the possibility of stacking interaction between chloroquine diphosphate and acetic acid. Such values of V_ϕ increase with increase in mole fraction of chloroquine diphosphate and decrease with increase in mole fraction of acetic acid indicating the solvent-solvent interactions which may be due to existence of hydrogen bonding in acetic acid molecules.

The volume behaviour of solute at infinite dilution is satisfactorily represented by V_ϕ^0 which independent of solute-solute interaction and provides information concerning solute-solvent interaction. It is also cleared from Table 1 that the values of limiting apparent molar volume, V_ϕ^0 are positive for aqueous solution of chloroquine diphosphate (Fig. 1) and negative in aqueous solution of acetic acid (Fig. 2).

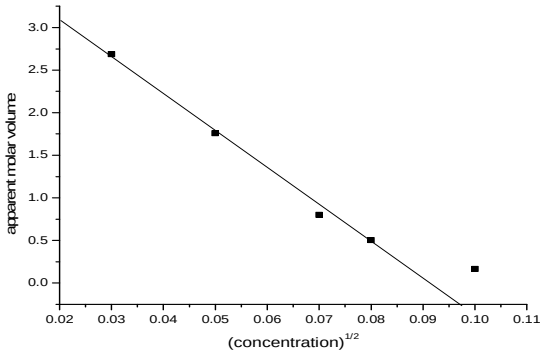


Fig. 1. Variation of apparent molar volume with $c^{1/2}$ for chloroquine diphosphate in water at 293.15K

The positive value of V_ϕ^0 indicates the strong solute-solvent interactions. This clearly indicates that the solute-solvent interaction is becoming more prominent in aqueous medium.

In Fig. 2 it is cleared that with increase in mole fraction of acetic acid the value of V_ϕ^0 is decreasing and becoming more negative leading to more solute-solute or solvent-solvent interaction in solution. The solute-solvent interaction is much weaker in chlororoquine diphosphate solution at higher mole fraction of acetic acid. This clearly indicates that the solvent-solvent interaction is becoming more prominent at higher mole fractions of acetic acid.

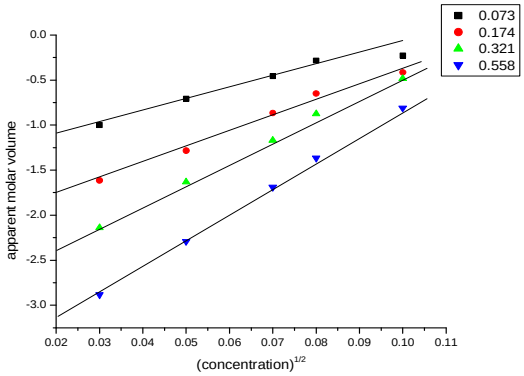


Fig. 2. Variation of apparent molar volume with $c^{1/2}$ for chloroquine diphosphate in different mole fractions of acetic acid in water at 293.15K

As observed the S_v values are negative in case of chloroquine diphosphate in water. The negative values of S_v indicate the presence of weak solute-solute interaction and more complex ion formation taking place in the aqueous solution. The positive values of S_v in acetic acid system indicate the existence of solute-solute interaction.

Ideal solution formation is accompanied with no change in volume. But due to molecular interactions between the components, there occurs real mixture with increase or decrease in volume. This increase or decrease in the volume on mixing known as excess molar volume V_m^E can be considered as a measure of molecular interaction. Mainly three important effects may contribute to the value of V_m^E.

(i) Breaking up of hydrogen bonding in acetic acid and dipolar interaction in chloroquine diphosphate and acetic acid.
(ii) Interstitial accommodation of one component into other.
(iii) Possible hydrogen bonding interaction between unlike molecules.

The actual volume change depends upon the relative strength of these three opposing effect. The values of V_m^E are positive for chloroquine diphosphate in acetic acid. The effect of

interaction between chloroquine diphosphate and acetic acid becomes less intense leading to decrease in V_m^E values. The decrease in V_m^E values with mole fraction suggest for interaction of acetic acid molecules. At lower mole fraction of acetic acid weaker dipole-dipole interaction exists due to decreased polarizabilities [23]. The positive V_m^E explains the predominance of dispersion forces due to declustering. The change in V_m^E with concentration of chloroquine diphosphate is shown by the Fig. 3.

At lower mole fraction V_m^E changes slightly but V_m^E decreases largely with increase in mole fraction of acetic acid. It may be due to the fact that chloroquine diphosphate interacts with acetic acid less strongly at higher mole fraction of acetic acid.

According to co-sphere model [24-25], hydrophilic-ionic group of interactions have positive contribution whereas ionic-hydrophobic group of interactions contribute negatively to the transfer volume studies (ΔV_ϕ^0) regarding ion-ion interactions. The value of (ΔV_ϕ^0) shown in Fig. 4 are negative which may be attributed to increase in electrostriction in the presence of acetic acid.

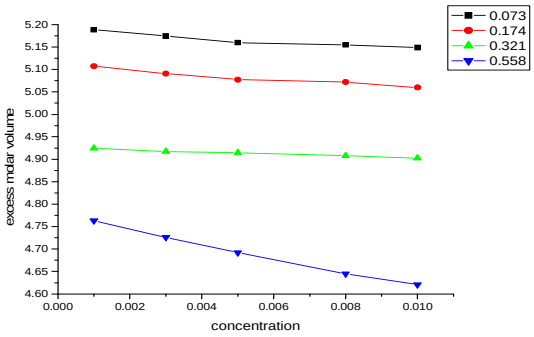


Fig. 3. Variation of excess molar volume with concentration for chloroquine diphosphate in different mole fractions of acetic acid in water at 293.15K

The electrostriction effect which brings about shrinkage in the volume of solvent is increased in aqueous solution of acetic acid.

Table 2. Results of excess molar volume and transfer volume of chloroquine diphosphate in acetic acid-water at 293.15K

Mole fraction	Concentration (c) mol dm^{-3}	Excess molar volume (V_m^E) x 10^2	Transfer volume (ΔV_ϕ^0)
	0.001	5.1885	
	0.003	5.1746	
0.073	0.005	5.1598	-4.2165
	0.008	5.1549	
	0.01	5.149	
	0.001	5.1072	
	0.003	5.0909	
0.174	0.005	5.0775	-4.8750
	0.008	5.0718	
	0.01	5.0599	
	0.001	4.9247	
	0.003	4.9172	
0.321	0.005	4.9144	-5.5192
	0.008	4.9078	
	0.01	4.9027	
	0.001	4.7635	
	0.003	4.7261	
0.558	0.005	4.692	-6.2520
	0.008	4.6449	
	0.01	4.6207	

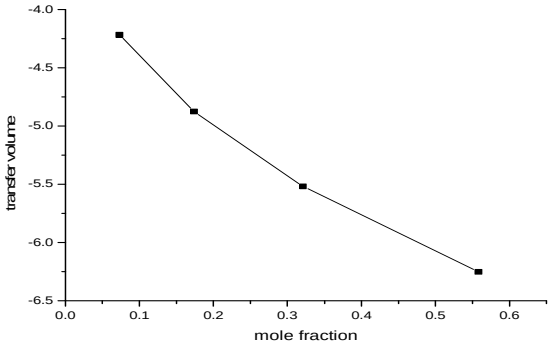


Fig. 4. Variation of transfer volume with mole fractions of acetic acid in water for chloroquine diphosphate at 293.15K

4. CONCLUSION

Interaction of solute with solvent plays a vital role in determining solute-solvent interactions. Measurement of physicochemical properties predicts the information regarding solute-solvent, solvent-solvent interactions. From the observed parameters it has been concluded that the interaction is much stronger in aqueous solution of chloroquine diphosphate. At low mole fraction of acetic acid, solute-solvent interaction predominates over solvent-solvent interaction which results due to hydrogen bonding between acetic acid molecules at higher mole fraction. Hence solute-solvent interaction is stronger in chloroquine diphosphate-water system as compared to chloroquine diphosphate -acetic acid-water mixture.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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