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# Partial molar volume of ciprofloxacin in water, HCl and $FeCl_3.6H_2O$ at 298.15K and 308.15K

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## ABSTRACT

Partial molar volume, $V^0$, of Ciprofloxacin in water, 0.05 mol $Kg^{-1}$ hydrochloric acid and 0.05 mol $Kg^{-1}$, Iron (III) chloride solutions at 298.15 and 308.15 K was calculated from precision densities obtained from Density Sound Analyzer (DSA 5000). The data represent the smaller volume of drug in 0.05 mol $Kg^{-1}$ Iron (III) chloride solution than water and 0.05 mol $Kg^{-1}$ hydrochloric acid at constant temperature. The differences in volumes are interpreted as due to hydrophobicity of solutes. Relative hydrophobicities were estimated from volumes of transfer from one media to another media. The hydrophobicity of this compound also plays a key role in the drug action. The possible mechanism of drug binding with the membrane structure is also discussed.


## KEYWORDS

Ciprofloxacin;
Apparent molar volume;
Partial molar volume;
Partial molar expansivity;
Hydrophobicity.

## INTRODUCTION

In bio-physical chemistry, drug interaction is the subject of intensive studies, involving complex molecular mechanism and certain hormones, antibiotic and peptide actions, amphiphilicity in molecular structure are considered to be a key factor in the overall drug mechanism[1,2]. The knowledge of thermodynamic properties and properties of water and aqueous solutions in relations to ions or other types of solute molecules are of particular importance in biology[3]. The partial molar volume of a solute can be regarded as the sum of intrinsic volume, $V_i$, plus volumetric effects of solute-solvent interactions[4]. The partial molar volume and the related volumetric parameters of drug compounds in aqueous solutions at different temperatures and pressures have been investigated by several authors[5-9].

Since volume is an additive property therefore gross changes in the volume of a system can be assessed by comparing the volume of the system with those of its components hence volumetric data of drugs can provide clues to the interactions occurring in cellular fluids. Recent literature on the volumetric properties of drug and other materials of biological importance shows increasing interest by a number of workers in this area of study (6-10).

The fluoroquinolones are well-established broad-spectrum antibiotics with activity against clinically important uropathogens[10-13]. Ciprofloxacin is one of them which have been evaluated as single agents for the treatment of pneumonia. This fluorinated quinolone demonstrates excellent in vitro activity against

*Haemophilus influenzae, Enterobacteriacae,* including *Enterobacter cloacae,* methicillin-susceptible *Staphylococcus aureus,* and *Pseudomonas aeruginosa,* and moderate activity against *Streptococcus pneumoniae*[14-18]. Due to importance of ciprofloxacin as an antibiotic drug, the study of its volumetric properties in various aqueous solutions may be helpful in investigating the molecular phenomenon occurring in physiological media[18-22].

This work is part of a study of molecular interactions in drug-substrate systems using thermodynamic methods. Partial molar volumes of ciprofloxacin, is calculated from experimental densities in water, 0.05 mol $Kg^{-1}$ hydrochloric acid and 0.05 mol $Kg^{-1}$, Iron (III) chloride solutions at 298.15 and 308.15 K calculated from precision densities obtained from Density Sound Analyzer (DSA 5000). The data are discussed in terms of relative solvation of this compound in water, hydrochloric acid and Iron (III) chloride solutions. The hydrophobicity of drug and aspects of structural features along with drug action are also discussed.

## RESULTS AND DISCUSSION

The apparent molar volumes of ciprofloxacin ($V_\Phi$/ $cm^3.mol^{-1}$) have been calculated by the following equation

$$V_\phi = M/d - 10^3(d - d_o)/md_sd_o, \quad (1)$$

Where M is the molar mass of ciprofloxacin and $d_o$, $d_s$ and m are the solvent density, solution density and the solution molality, respectively. The constant $10^3$ is for recalculation of molality from mol/Kg into mol/g to be consistent with M in mol/g. The $V_\phi$ data obtained from equation (1) was fitted to the following equation[23].

$$V_\phi = V^0 + S_v m, \quad (2)$$

Where $V^0$ is the partial molar volume at infinite dilution, m is the molality of ciprofloxacin solution and $S_v$ is the impirical parameter which depends on solvent, solute and temperature[23]. The values of $V^0$ and $S_v$ are given in TABLE 1. The values of partial molar expansivity were then calculated from the partial molar volume by the relation:

$$E^0 = (\partial V^o/\partial T)_p \quad (3)$$

The isobaric coefficient of thermal expansion was determined, as defined by[23].

$$(\alpha)_p = (E^o/V^o)_p, \quad (4)$$

The values of $E^0$ and $(\alpha)_p$ are given in TABLE 2.

The increase in partial molar volume $V^0$ with an increase in temperature (TABLE 1) is believed to be occurring due to the reduction in electrostriction. A decreasing trend is also observed in the values of $V^0$ as the solvent media changes from water to 0.05 mol/Kg HCl and 0.05 mol/Kg $FeCl_3.6H_2O$ solution at the same temperature. This can be explained by the disruption phenomenon of side-group hydration by that of the charged end. The values of the partial molar transfer volume $\Delta V_{tr}$ of ciprofloxacin in water and 0.05 mol/Kg HCl and water and 0.05 mol/Kg $FeCl_3$ solution are given in TABLE 3 and are calculated as;

$$\Delta V_{tr} = V^o \text{ (in water)} - V^o \text{ (in aq. HCl)} \quad (5)$$

$$\Delta V_{tr} = V^o \text{ (in water)} - V^o \text{ (in aq. } FeCl_3\text{)} \quad (6)$$

The positive values of $\Delta V_{tr}$ indicated that he hydration shell of the solute molecule increases in volume with the change of solvent due to increase in hydrogen bonding with the water molecules as discussed above. This leads to decrease to structure breaking tendency of the ion and then enhance the electrostriction of the water caused by hydrogen and chloride ion.

Partial molar expansibilities $E^o$, can be calculated using equation 2. $E^o$ values obtained in this manner are shown in TABLE 2. The positive values of $E^0$ indicate that the hydration shell of the solute molecules increases in volume with a change of the solvent due to increase in the water molecules and hence indicate the predominance of hydrophobic hydration over the electrostriction of water molecules around the solute molecules.

The compound studied in this work is a flouroquinolone antibiotic which exhibits minimal side effects and has broad antimicrobial spectrum, is being used frequently to treat various infections[24]. Figure 1 shows that an important structural feature of these compounds is the presence of hydrophobic and hydrophilic domains. The hydrophobicity of these compounds may well play a crucial role in the resulting drug reaction. It can be argued that the hydrophobic force supplements the structure-activity relationship in that these molecules tend to bind in a site-specific manner. The hydrophilic and hydrophobic parts of the drug match with the specific counter sites on the membrane. The hydrophilic part of the drug molecule be-

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ing anchored to the polar head group of the lipid chain (or at some suitable site on the imbedded protein), pushes the hydrophobic tail into the bilayer grease. The decrease of the bioavailability of ciprofloxacin due to interactions with drugs or food containing metal ions is known for a long time[25,26]. A marked rank order correlation between the extent of ciprofloxacin coordination with various metal cations and the reduction in ciprofloxacin oral bioavailability was observed. Thus, the reduction of bioavailability is somehow related to the formation of complexes between ciprofloxacin and metal ions[27]. The complexed species is different from the uncomplexed drug in size, geometry and charge. These factors could hinder the passive diffusion of ciprofloxacin through the cell membranes[27,28]. Thus the partial molar volume, $V^0$, of ciprofloxacin values (TABLE 1) in $FeCl_3$ solution was found to be decreased as compared with water and HCl which may be due to the complex formation.

## EXPERIMENTAL

Ciprofloxacin $C_{17}H_{18}FN_3O_3$, used in this study was supplied by Sigma (64K-661214). It is a faintly yellowish to light yellow crystalline substance and its chemical structure (Figure 1) The solvents used were water, conc. HCl (Riedel-231-595-7) and $FeCl_3.6H_2O$ (Merck, D6100). This compound was further purified by recrystallising from ethanol-water mixture. Water used in the experiments were doubly distilled and degassed. Solutions were prepared immediately prior to measurements by addition of stochiometric quantity ciprofloxacin to the solvents and were prepared by weight using Sartorious balance. The molality range studied was between $2.0 \times 10^{-2} \pm 10^{-5}$ mol $Kg^{-1}$ and $3.0 \times 10^{-2} \pm 10^{-5}$ mol $Kg^{-1}$. The density of Ciprofloxacin solutions of different concentrations at different temperatures were determined by DSA. Before measurements the DSA was calibrated using ultra pure water and air at each temperature.

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