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REFRACTIVE INDEX, MOLAR REFRACTION AND POLARIZABILITY OF CIPROFLOXACIN HYDROCHLORIDE IN AQUEOUS-GLYCINE SOLUTIONS

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ABSTRACT

Density and refractive index of binary {ciprofloxacin + water} and ternary {ciprofloxacin + aqueous-glycine} mixtures were measured as a function of drug (0.001-0.029 mol·dm^{-3}) and glycine (0.1, 0.25 and 0.45 mol·dm^{-3}) concentration at 26^{o}C. Molar refraction and polarizability of aqueous drug solutions was calculated from density and refractive index data. Polarizability effects with drug and glycine concentration have been studied.

Key words: Drug-amino acid interactions, Polarizability, Molar refraction.

INTRODUCTION

Refractive index along with density is used for understanding intermolecular interactions in solution. Refractive index is influenced by the polarizability of medium. More polarizable, the medium higher is the refractive index of medium. Valuable information on polarizability of solution can be collected from refractive index and molar refractivity[1-7]. Thermodynamic properties of {drug + aqueous – glycine} solution are very important for understanding different interactions between drug and glycine in aqueous medium. Two terminals of glycine are charged, positive charge (NH_3^+) and negative charge (COO^-) and it has zwitterionic properties[8]. Amino acids in solutions are somewhat between strong electrolytes and non-electrolytes due to hydrophobic alkyl groups and polar zwitterionic groups[9]. Amino acids in aqueous solutions are ionized and act as acids or bases due to formation of zwitterion like H_3N-CH(R)-COO^-.[10] Refractive index studies are being

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increasingly used as a tool for understanding molecular interactions in solution[11-14]. Ciprofloxacin (CFC) is second-generation fluoroquinolone and an antibiotic used for treatment of a number of bacterial infections. Refractive indices of aqueous solutions metoprolol succinate and duloxetine drugs are reported in our earlier papers[15,16]. An effort has been made here to study interactions in {CFC + aqueous – glycine} mixtures through density, refractive index, molar refraction and polarizability data.

EXPERIMENTAL

Ciprofloxacin hydrochloride monohydrate (CFC·HCl·H_2O; Fig. 1) was received as a gift sample from Godavari Drugs Ltd., Nanded (MS) India and it was used as received. Glycine (sd fine) was used for preparation of stock solution. Distilled water was used for preparation of drug solutions. Drug solution was prepared in stock solution of glycine. Weighing was done on single pan electronic balance (± 0.001 g). Densities were measured using calibrated single capillary pycnometer. Refractive index of solution was measured on thermostatically controlled Cyber LAB-Cyber Abbe Refractometer (Amkette Analytics, ± 0.0002, 1.3000 to 1.7000) by direct reading. Averages of three readings of density and refractive index are reported.

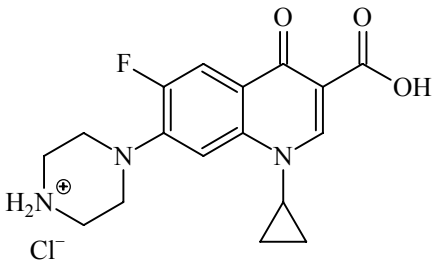


Fig. 1: Chemical structure of ciprofloxacin hydrochloride

RESULTS AND DISCUSSION

Measured density (ρ) and refractive index (n_D) of {CFC + water} and {CFC + Aqueous-glycine} solution are reported in Table 1.

It is seen that density increased with concentration of drug as well as glycine. Also, refractive index increased with concentration of drug as well as glycine. Concentration dependence of refractive index of {CFC + aqueous-glycine} solutions were studied using $n_D = K \times c + n^0_D$ equation and from the plot of n_D versus c, the refractive index at infinite

dilution (n^0_D) was obtained as an intercept and constant K as slope (dn_D/dc). Graphical values of n^0_D and constant K for are reported in Table 2. The n^0_D increased with increase in the relative amount of glycine in solution.

Molar refraction, R_M was calculated by using following Eq.[17-19]:

$$R_M = \frac{(n_D^2 - 1)}{(n_D^2 + 2)} \times \sum_{i=1}^{3} \frac{x_i M_i}{\rho_i} \quad \ldots(1)$$

Where, n_D = refractive index of solution, x_i = mole fractions of i-th component of solution, M_i = molecular mass of CFC (385.82 g·mol^{-1}), water (18.02 g·mol^{-1}) and glycine (75.07 g·mol^{-1}) and ρ = density of solution.

Table 1: Density (ρ) and refractive index (n_D) of {CFC + Aqueous-glycine} solutions

c	ρ	n_D	ρ	n_D	ρ	n_D	ρ	n_D
	CFC + Water		CFC + 0.10 M Gly		CFC + 0.25 M Gly		CFC + 0.45 M Gly	
0.001	0.9965	1.3320	0.9995	1.3330	1.0035	1.3352	1.0097	1.3372
0.005	0.9970	1.3322	0.9999	1.3334	1.0040	1.3355	1.0101	1.3376
0.009	0.9975	1.3325	1.0003	1.3338	1.0044	1.3357	1.0104	1.3382
0.013	0.9979	1.3327	1.0006	1.3342	1.0048	1.3360	1.0107	1.3386
0.017	0.9982	1.3330	1.0009	1.3345	1.0052	1.3362	1.0110	1.3390
0.021	0.9985	1.3332	1.0012	1.3347	1.0056	1.3365	1.0113	1.3394
0.025	0.9988	1.3335	1.0015	1.3350	1.0060	1.3368	1.0115	1.3399
0.029	0.9991	1.3337	1.0018	1.3352	1.0063	1.3372	1.0118	1.3404

Note: c = mol·dm^{-3} and ρ = g·cm^{-3}

Table 2: Parameters of $n = K \times c + n^0_D$ plots for {CFC + Aq. glycine} solutions

System	n^0_D	K	r^2
CFC + water	1.3319	0.0619	0.9982
CFC + Aq. 0.10 mol·dm^{-3} Gly	1.3330	0.0786	0.9842
CFC + Aq. 0.25 mol·dm^{-3} Gly	1.3351	0.0688	0.9930
CFC + Aq. 0.45 mol·dm^{-3} Gly	1.3369	0.1250	0.9978

Polarizability is an important fundamental molecular property related with molar refraction. To gain the information regarding specific intermolecular interactions, polarizability of the studied systems were calculated using following Equation[20-21]:

$$\alpha = \frac{3}{4}\frac{R_M}{\pi N} \quad \ldots(2)$$

Where, N=Avogadro's constant (6.023×10^{23} mol^{-1}). Calculated molar refractions (R_M) along with polarizability (α) values are reported in Table 3.

Table 3: Molar refractions (R_M) and polarizability (α) of {CFC + Aq. glycine} solutions

c **(mol·dm^{-3})**	***R*$_M$ (cm^3·mol^{-1})**	**α (× 10^{-24} cm^3)**	***R*$_M$ (cm^3·mol^{-1})**	**α (× 10^{-24} cm^3)**
	CFC + water		**CFC + Aq. 0.10 mol·dm^{-3} Gly**	
0.001	3.710	1.471	3.730	1.479
0.005	3.716	1.473	3.738	1.482
0.009	3.722	1.475	3.746	1.485
0.013	3.728	1.478	3.754	1.488
0.017	3.736	1.481	3.762	1.491
0.021	3.742	1.483	3.768	1.494
0.025	3.749	1.486	3.775	1.497
0.029	3.756	1.489	3.782	1.499
	CFC + Aq. 0.25 mol·dm^{-3} Gly		**CFC + Aq. 0.45 mol·dm^{-3} Gly**	
0.001	3.769	1.494	3.807	1.509
0.005	3.775	1.497	3.816	1.513
0.009	3.781	1.499	3.826	1.517
0.013	3.789	1.502	3.835	1.520
0.017	3.795	1.504	3.842	1.523
0.021	3.804	1.508	3.852	1.527
0.025	3.809	1.510	3.862	1.531
0.029	3.817	1.513	3.871	1.535

Variation in molar refraction, R_M with concentration of CFC in different aqueous systems is graphically presented in Fig. 2. It is seen that, R_M increased with increase in concentration of CFC for all systems. R_M is calculated in additive manner and deviation in it is an indication of interactions between components[3]. R_M is a volume term and is directly proportional to molecular polarizability[3,22]. R_M is a measure of total polarizability of a mole of substance. R_M is highly used in QSAR studies for drug design[23]. Intermolecular forces between the solute and its surroundings reflect in molar refraction of solution.

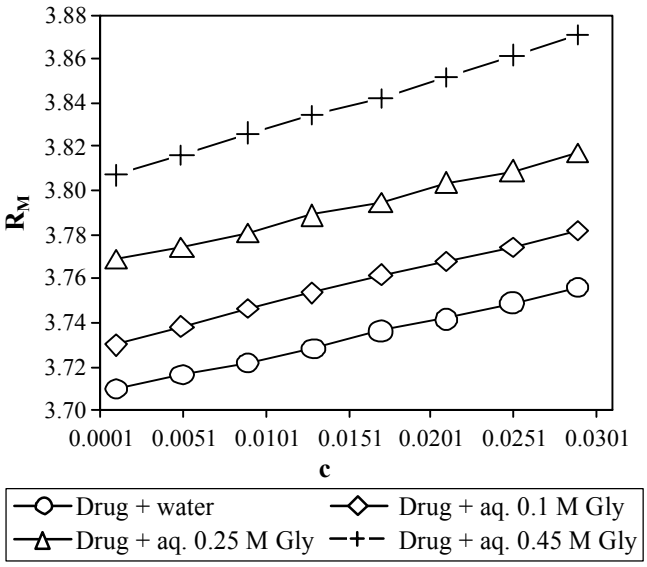
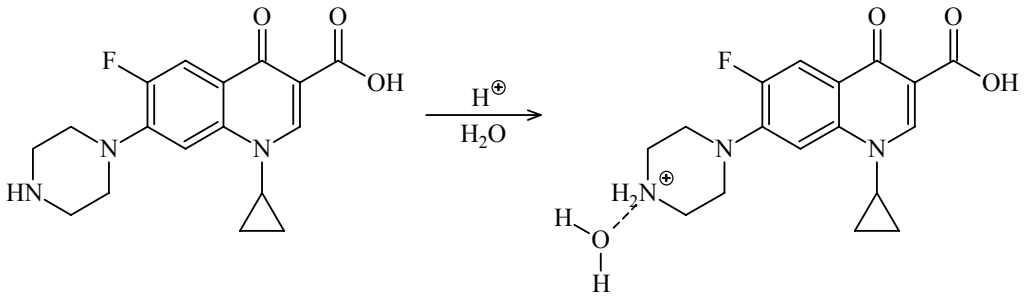


Fig. 2: Variation in R_M with drug concentration in aqueous-glycine solutions

In present investigation, R_M is found to be strongly dependent over concentration of CFC and glycine in each binary and ternary system. R_M increased with increase in concentration of drug as well as glycine. The dependence of R_M over the drug concentration is linear with $R^2 > 0.998$; Fig. 2, for each line. Trend of R_M indicate overall polarizability of solution become stronger with increase in the relative amount of drug and glycine in each system, which suggests existence of strong molecular interactions in solution.

CFC contains different interacting groups such as amide (-COOH), secondary amine (-NH), and tertiary amine (R_3-N). Up on protonation, -NH group get protonated and form cationic species through which the interaction with water molecule occurs. A dominant interaction of drug with water molecule is presented in **Scheme 1**.



Scheme 1: Protonated secondary amine showing interactions with water molecule

Polarizability (α) of solution increased with CFC concentration in each system and it further increased with increase in glycine concentration which is attributed to increasing CFC-glycine interactions between polar hydrophilic groups of drug and hydrophilic parts of glycine. Significant electrostatic types of interactions like hydrophilic-ionic interaction between polar groups of drug and zwitterionic centers of glycine, hydrophilic–hydrophilic interaction between polar groups of drug and polar groups of glycine and hydrophilic-hydrophobic interactions between polar groups of drug and hydrophobic parts of glycine exists in solution.

CONCLUSION

Molar refraction of binary {CFC + water} and ternary {CFC + aqueous-glycine} mixtures was increased and polarizability becomes stronger with CFC concentration, which indicates existence and improvement in the interactions between drug and water and drug and glycine. Modification in the structure of aqueous-glycine solution has been observed upon addition of drug. Interactions between CFC and glycine through polar hydrophilic groups of CFC and hydrophilic parts of glycine exits in solution.

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