2.1 Review of Literature

Any foreign agent (drug or vitamin) when introduced into the body fluid, interact with salts and other small biomolecules already present in the body fluids (intra and inter cellular), for its transportation and conversion into active metabolite. The study of physical processes like solute-solute, solute-solvent interactions, solubility and stability, are quite relevant from medical and pharmaceutical point of view, to determine the mechanism and hence the fate of these compounds in aqueous protoplasm. The thermodynamic properties: partial molar volume, partial molar isentropic compressibility (the first and second derivative of Gibbs free energy, respectively), and transport properties: viscosity B-coefficient and conductance being extensively used to elucidate various interactions occurring in the solution phase in vitro. In view of this, a brief review of literature on physicochemical properties of drugs belonging to different classes and vitamins in different solvent systems is presented here which has helped in formulating the research plan for the present study.

Iqbal et al.\textsuperscript{1,2} have measured the apparent molar volume, partial molar volume and isentropic compressibility of various drug compounds (sodium salicylate, methyl orange, L-tryptophan, phenol, ephedrine, cinchocaine HCl, lidocaine HCl, mepivacaine HCl, procaine HCl, propranolol HC1, tetracaine HCl) in aqueous and aqueous ethanol solutions at 298.15 and 308.15 K. The results have been discussed in terms solute-solute and solute-solvent interactions occurring in these solutions. The isentropic compressibility show strong correlation with the hydration behavior of solute molecules. The structure of solute like shape, size, branching and presence of aromatic ring also affect the hydration. The relative hydrophobicity has also been found from volume of transfer from aqueous to organic solvent.

Iqbal and Malik\textsuperscript{3} have measured the apparent molar volume of paracetamol in water and in aqueous solution of HCl and NaCl at different temperatures and at pressure 101.325 kPa. The apparent molar volume, partial molar volume, partial molar expansibility, isobaric coefficient of thermal expansion and interaction coefficients have been computed. The positive partial molar expansibility indicates that the hydration shell of
solute molecule increases with the change in solvent which may be due to increase in hydrogen bonding.

Iqbal and Chaudhry\textsuperscript{4-10} have measured the density and viscosity of drug compounds, belonging to different classes: anesthetic and antiseptic (phenyl salicylate)\textsuperscript{4,6}, non steroidal anti inflammatory drugs (salicyl amide, salicylic acid and acetyl salicylic acid)\textsuperscript{5,9,10}, anti depressant (notriptyline HCl and trimipramine maleate)\textsuperscript{7} and other drugs (diclofenac sodium, cetizine, doxyciline)\textsuperscript{8}, in aqueous solutions of various alcohols and aprotic solvents, at different temperatures. The partial molar volume, partial molar expansiblity, thermal expansion coefficient, viscosity $B$-coefficient and refraction coefficient have been calculated from density, viscosity and refractive index data. Strong solute-solvent interactions have been observed between the studied drugs and solvent system which are helpful for the prediction of absorption and permeability of drugs through biomembrane.

Jahagirdar et al.\textsuperscript{11, 12} have measured the density, velocity of sound and viscosity of four pharmacologically significant drugs (sulphamethoxazole, phenobarbitone, methyl paraben, isoniazid) in methanol at 298.15 K and caffeine in water at different temperatures. From the collected data apparent molar volume, apparent molar isentropic compressibility and viscosity $B$-coefficient values have been calculated. The apparent molar volume and apparent molar compressibility are used to find the solute-solvent interactions. The $B/V^2_o$ ratio, solvation number, relative association, and specific acoustic impedance, have also been calculated.

Chauhan et al.\textsuperscript{13} have measured the viscosity of some narcotic analgesic drugs [(parvon spas containing paracetamol, dicyclomine HCl and dextropropoxyphene HCl), (Parvon fort containing ibuprofen and dextropropoxyphene HCl), (Parvodore containing dextropropoxyphene HCl) and (Tramacip containing tramadol HCl)] in aqueous-alcoholic mixture at 298.15K. From the data, viscosity $A$ and $B$-coefficients have been calculated, using Jones-Dole equation. An inference has been made from these studies that all the drug cations can be regarded as structure maker due to hydrophobic hydration of drug molecules.
Sinha et al.\textsuperscript{14} have measured the apparent molar volumes and viscosity $B$-coefficients of caffeine in aqueous thorium nitrate solutions at different temperatures. The corresponding transfer parameters (apparent molar volumes and viscosity $B$-coefficients) from water to thorium nitrate solutions have been calculated. Strong solute-solvent interactions have been found in the studied system, which further increases at higher temperatures. Caffeine acts as mild structure breaker due to hydrophobic hydration in the presence of thorium nitrate.

Baluja and Oza\textsuperscript{15} have measured the velocity of sound, density and viscosity of solutions of some derivatives of sulphonamides in dimethylformamide at 308.15 K. Various acoustical properties such as specific impedance, partial molar isentropic compressibility, Rao’s molar sound function, the van der Waals constant, intermolecular free length, relaxation strength, free volume, relative association, internal pressure, apparent molar volume etc. were calculated. The results have been calculated and interpreted in terms of various interactions occurring in these solutions.

Attwood et al.\textsuperscript{16-22} have measured and compared with literature the CMC values for promethazine, chlorpromazine, clomipramine, imipramine\textsuperscript{16, 18}, promazine HCl\textsuperscript{17}, clomipramine HCl and imipramine HCl\textsuperscript{19, 22}, trimeprazine tartrate\textsuperscript{20}, in the presence of electrolytes, drugs\textsuperscript{21} in aqueous solutions. The thermodynamic data were obtained by the use of vapor pressure osmometry, heat conduction calorimetry, density, velocity of sound, conductivity and dynamic light scattering techniques. It has been concluded that the presence of electrolyte effects greatly the self-association of these drug compounds. London dispersion interactions also play a vital role in the aggregation of these compounds.

Taboada et al.\textsuperscript{23-30} have studied the drug compounds from different classes like penicilline (cloxacilline, dicloxacilline, nafcilline\textsuperscript{23,24,28} and their salts\textsuperscript{25,26,27,29,30} and antidepressant drugs (amitryptyline and nortryptyline)\textsuperscript{25} in water and in aqueous solutions of electrolytes. The experimental techniques: surface tension, conductivity, calorimetry, light scattering (static and dynamic), NMR, density, velocity of sound and dielectric constant have been used to produce the required data. The CMC, surface properties, apparent molar volumes and apparent molar isentropic compressibility have been calculated. The modified law of mass action has been used to calculate the Gibbs
free energy, enthalpy and entropy of micellization. The variation of association behavior for these drug compounds, with temperature and concentration of electrolyte has been discussed.

Cheema et al.\textsuperscript{31-36} have studied phenothiazine drugs (thioridazine, promazine and triflupromazine and their salts)\textsuperscript{31,32,34-36} and anticoagulant warfarin sodium\textsuperscript{33} drugs, in aqueous and mixed aqueous media. The interactions of these drug compounds with proteins (horse myoglobin and human serum albumin)\textsuperscript{34-36} in buffer solutions of different pH have also been studied. The data have been collected by the use of density, velocity of sound, conductivity, surface tension, isothermal titration calorimetry, UV-visible spectroscopy, dynamic light scattering, fluorescence, and circular dichroism experimental techniques. The effects of temperature and co-solvent on the CMC values of these drug compounds have been observed and interpreted. Also the energetics of binding of drugs with protein has been discussed. The importance of London and van der Waal’s forces has been discussed in interpreting various interactions in solutions.

Barbosa et al.\textsuperscript{37-39} have studied the interactions of penicilline drugs, cloxacilline, dicloxacilline\textsuperscript{37, 38} and their salts\textsuperscript{39} with protein, human serum albumin, by changing solvent concentration, pH and temperature. The various experimental techniques like: density, velocity of sound, isothermal titration calorimetry and dynamic light scattering were used to collect the data. It was observed that hydrophobic and electrostatic interactions play very significant role in drug-protein interactions. The volumetric studies show the dehydration and change in tertiary structure of protein. Energetics of binding between drug and protein has also been discussed.

Varela et al.\textsuperscript{40} have studied the self association behavior of penicillin V in aqueous solutions by measuring the density and velocity of sound, and provided the evidence for two stage self association process for the drug. They concluded that the self association of the drug compound is due to hydrophobic interactions which are confirmed from change in apparent molar volume and the apparent molar isentropic compressibility.
Pichel et al.\textsuperscript{41} have measured the density and velocity of sound to study the self association of two antidepressant drugs (imipramine and desipramine HCl) at different temperatures and pH values. The CMC and energy involved in aggregation process have been evaluated using isothermal titration calorimeter. The results have been discussed in terms of solvent – aggregate interactions.

Ruso et al.\textsuperscript{42} have studied the volumetric properties of structurally related Beta-blockers (propranolol and acebutolol HCl) in aqueous sodium chloride solutions at different concentrations and temperatures. Negative deviations of the apparent molar volume from the Debye–Hückel limiting law in dilute solutions indicate the absence of premicellar aggregation. Positive isentropic compressibility changes indicate the predominant role of hydrophobic hydration in association process.

Torres et al.\textsuperscript{43} have studied the apparent molar volumes of two local anesthetics, lidocaine HCl and procaine HCl, in water at (298.15, 303.15 and 310.15) K. The concentration dependence of apparent molar volume has been calculated using the Redlich and Meyer equation. The results have been interpreted in terms of competitive effects between electrostriction and hydrophobic solvation.

Delgado et al.\textsuperscript{44} have measured the apparent molar volumes of some sulfonamides (sodium sulfadiazine, sodium sulfamerazine and sodium sulfamethazine) in water as a function of concentration and temperature. The partial molar volumes and expansibilities have been calculated. The $S_v$ values are found to be negative, showing the dominance of hydrophobic interactions in these solutions.

Zhang et al.\textsuperscript{45, 46} have determined n-octanol/water partition coefficients and solubility of many sulpha drugs (sulfadiazine, sulfamethazine, sulfadimethoxine, sulfamethoxydiazine, sulfamonemethoxine, sulfamethoxazole, sulfachloropyrizine and sulfaquinoxaline) at different temperatures. The results showed that the n-octanol/water partition coefficients for each sulfonamide decrease with temperature. It has been concluded that the partitioning of sulfonamide compounds in n-octanol/water is mainly enthalpy driven process. Using a static equilibrium method, the solubilities of sulfa drugs in water have been determined experimentally from (298.15 to 333.15) K. The experimental data were correlated with the modified
Apelblat equation. The calculated results show good agreement with the experimental data.

Martinez et al.\(^\text{48-51}\) have studied the solubility properties of some sulfonamides (sulfanilamide, sulfapyridine, sulfadiazine, sulfamerazine, sulfamethazine, sulfacetamide, sulfathiazole) in octanol, water and mutually saturated solvents\(^\text{48,50}\), octanol-buffer and liposome system\(^\text{49}\) and in cyclohexane\(^\text{51}\) by using calorimeter, UV-visible spectrophotometer, density meter and solubility measuring apparatus at different temperatures. The experimentally measured solubility data have been compared with the theoretically calculated one. The enthalpies of transfer from aqueous media to organic systems were positive in liposomes but negative or positive in 1-octanol, whereas the entropies of transfer were positive in almost all cases. The results have been interpreted in terms of solute-solvent interactions occurring in these systems.

Hanaee et al.\(^\text{52}\) have determined the solubility of various sulfonamides (sulphamethoxazole, sulphisoxazole and sulphasalazine) in methanol, ethanol, 1-propanol, acetone and chloroform at different temperatures. Two models derived from the Hildebrand solubility approach are proposed for solubility prediction at different temperatures using a single determination. The experimental data from present work and from literature have been employed to investigate the accuracy and prediction capability of the proposed models. It was found that the proposed models are much superior to the classical predictive models.

Raevsky et al.\(^\text{53}\) have measured the octanol/water partition coefficients of 38 sulfonamides by isothermal saturation method. Two approaches were applied to calculate log \(K_{\text{ow}}\) values: (i) direct correlation with molecular polarizability and H-bond acceptor ability and (ii) application of an analogous equation obtained for simple chemicals containing one functional group. Both methods ensure good estimation of octanol/water partition coefficients with statistic parameters close to program KOW-WIN and demonstrate the possibility to predict log \(K_{\text{ow}}\) values of complex organic compounds with few functional groups.
Li et al.\textsuperscript{54} have determined the densities and viscosities for the binary mixtures of cefodizime sodium + water and the ternary mixtures of cefodizime sodium + 0.9 mass % normal saline at the different temperatures. From the data, apparent molar volumes, partial molar volumes and the viscosity $B$-coefficients of cefodizime sodium were calculated. The positive values of apparent molar volume indicate that the solute–solvent interactions decrease with temperature. Positive values of the viscosity $B$-coefficient suggest the structure-breaking tendency of cefodizime sodium. The positive values of $dB/dT$ manifest that cefodizime sodium behaves as structure breaker, and solute–solvent interactions destroy structure of solution, which is consistent with the volumetric properties of systems studied.

Chen et al.\textsuperscript{55} have measured the densities and viscosities of the pseudo binary system 7-hydroxy-4-methylcoumarin + (ethanol or 1-propanol) + water at different temperatures and refractive indices of this system at 298.15 K. The observations and conclusions are: (i) the partial molar volumes and $B$-coefficients are positive and pass though a maximum with increasing solvent concentration, (ii) the partial molar volumes and $B$-coefficient decrease with temperature, (iii) the partial molar volumes and $B$-coefficient in aqueous 1-propanol solutions are larger than that in aqueous ethanol solutions at the same temperature and the molar refractions increase with the molality of solvent. The parameters and their variation have been interpreted in terms of solute–solvent interactions.

Kaulgud et al.\textsuperscript{56} have measured apparent molar volume, apparent molar isentropic compressibility and viscosity $B$-coefficient for ascorbic acid in dilute aqueous sodium chloride solutions at 298.15 K. Hydration numbers have been calculated from both $B$-coefficient and compressibility data. These properties are compared with those of glucose and results are discussed in terms of effect of ascorbic acid on the structure of water.

Shamim and Khoo\textsuperscript{57} have measured the densities, viscosities and refractive index of aqueous ascorbic acid solutions at different concentrations and at 298.15 K. They assumed that ascorbic acid remains undissociated in aqueous solutions and provided the equation to calculate apparent molar volume at infinite dilution.
Hakin et al.\textsuperscript{58} measured the volumetric and thermochemical properties of L-ascorbic acid in water at 288.15, 298.15 and 308.15 K. The apparent molar volume and the apparent molar heat capacity have been calculated. The volume of ionization and heat capacity of ionization for L-ascorbic acid have been calculated by a method that does not require volumetric and thermochemical data for the sodium salt of the ascorbic acid.

Kundu and Kishore\textsuperscript{59} have determined the apparent molar heat capacities and apparent molar volumes of aqueous nicotinamide, using microdifferential scanning calorimetry and digital density meter, at different temperatures. The results are discussed in terms of the changes in the packing of nicotinamide molecules in the crystal, interactions in the aqueous form, and its structure promoting ability with rise in temperature.

Changwei and Peisheng\textsuperscript{60} have measured and correlated the viscosity $B$-coefficient and apparent molar volumes of ternary system of L-ascorbic acid D-glucose and sucrose solutions, at different temperatures. $B$-coefficient values increase with the concentration of glucose or sucrose and with temperature. L-ascorbic acid behaves as structure breaker and structure maker in aqueous solutions of glucose and sucrose respectively.

Terekhova et al.\textsuperscript{61, 62} have measured thermodynamic parameters for ascorbic acid in various mono and disaccharides, and nicotinic acid in saccharides and cyclodextrin at 298.15 calorimetrically. The results have been interpreted in terms of the influence of structure and the solvation of the solutes on the thermodynamic parameters and their interactions in aqueous solutions. The presence of hydrophobic cavity of cyclodextrin, makes interactions with nicotinic acid, enthalpically favorable. It was found that the complex formation of $\alpha$-cyclodextrin with nicotinic acid is stronger as compared to the complex between $\beta$-cyclodextrin and saccharides.

Orekhova et al.\textsuperscript{63} have measured the electric conductance and density of aqueous solutions of nicotinic acid and sodium nicotinate at different temperatures. The limiting equivalent conductance of the nicotinate ion, dissociation constant of nicotinic acid, apparent molar volumes, the cubic expansion coefficients and the
change in isobaric heat capacities with respect to pressure have been calculated and
were qualitatively correlated with the structural changes in water on dissolution of
nicotinic acid.

Zhao et al.\textsuperscript{64} have measured the densities and viscosities of arginine in (glucose +
water), (sucrose + water) and (L-ascorbic acid + water) at 298.15 K by an oscillating-
tube density meter and viscometer, respectively. Standard partial molar volumes and
viscosity \(B\)-coefficients have also been calculated. Values of density and viscosity as
well as the corresponding parameters, in sucrose + water system are found to be
higher than those in glucose + water system at same concentration and temperature.

Ayranci et al.\textsuperscript{65} have determined the apparent molar volumes and apparent molar
isoentropic compressibilities of L-ascorbic acid and thiamine hydrochloride in dilute
hydrochloric acid and sodium chloride over the temperature range 283.15 to 313.15
K. The apparent molar expansibility values are positive for both the vitamins which
indicate their hydrophilic character. Apparent molar isentropic compressibilities of
ascorbic acid were positive in water and in sodium chloride solutions at low molalities
while those of thiamine hydrochloride were all negative. Transfer apparent molar
volumes at infinite dilution from water to sodium chloride solutions also suggest the
complex interactions in vitamin + sodium chloride + water system.

Apelblat and Manzurola\textsuperscript{66} have measured the vapour pressure and volumetric properties
of ascorbate ions in aqueous solutions. The partial molar volume, the cubic expansion
coefficient, and the change of heat capacities with respect to pressure, have been
evaluated from density data. Further these values were correlated qualitatively with the
changes in the structure of water in the presence of ascorbic acid, magnesium and
calcium ascorbates.

Sinha et al.\textsuperscript{67} have measured the apparent molar volumes and viscosity \(B\)-coefficient
of nicotinamide in aqueous solutions of tetrabutylammonium bromide, (TBAB)
solutions at different temperatures. The corresponding transfer parameters have been
calculated from partial molar volume and viscosity \(B\)-coefficient values, used to
rationalize various interactions occurring in these systems. Nicotinamide acts as
structure promoter due to hydrophobic hydration in the presence of TBAB.
Kant et al.\textsuperscript{68} have measured the densities, viscosities and conductance of some alkali metal chlorides in aqueous ascorbic acid solutions. Partial molar volumes, viscosity $B$-coefficients and limiting molar conductance have been calculated. The results show that alkali metal chlorides behave as structure breaker in aqueous ascorbic acid solution.

Pan et al.\textsuperscript{69} have measured the density, viscosity and electric conductance of ternary solution of (nicotinic acid + polyethanol + water) at different temperatures. The degrees of dissociation, partial molar volume and $B$-coefficient of viscous flow have been evaluated. The results show that polyethanol increases the viscosity, decreases the dissociation and impedes the motion of nicotinic acid at lower concentrations but promotes the solubility and molecular diffusion at higher concentrations.

Roy et al.\textsuperscript{70} have studied the thermodynamic and transport studies of TBAB in aqueous solution of ascorbic acid at different temperatures. In the ternary solution of TBAB + ascorbic acid + water, it was concluded that their exist strong interactions which further increase with temperature and concentration of ascorbic acid. TBAB behaves as water structure promoter due to hydrophobic hydration and ascorbic acid has dehydrating effect on the hydrated TBAB.

Sahin and Ayranci\textsuperscript{71} have measured the density and velocity of sound for, binary (water + L-ascorbic acid) and ternary (water + L-ascorbic acid + polyethylene glycol 3350) systems at temperature 288.15 to 308.15 K and determined apparent molar volumes and apparent molar isoentropic compressibilities. It was concluded that the transfer parameters are positive and increase with weight percent of polyethylene glycol and decrease with temperature.

Yang et al.\textsuperscript{72} have studied the density, viscosity and electric conductance of nicotinic acid in aqueous dextran (40000) solutions at various concentrations. From the data of electric conductance it was concluded that dissociation of nicotinic acid is little affected by the addition of dextran. Eyring’s Transition state theory has been applied to the viscosity $B$-coefficient data. It was found that the dextran impedes the movement of nicotinic acid.
Kant and Kumar\textsuperscript{73} have studied the effect of alkaline earth metal ions on thermodynamic properties (density and velocity of sound) of ascorbic acid at different temperatures. The positive values of partial molar volumes, decrease of isentropic compressibilities, increase in inter-molecular free length and relative association, have been discussed in terms of ion-solvent interactions of magnesium chloride, calcium chloride and barium chloride in aqueous ascorbic acid solutions. Further these halides of alkaline earth metals behave as structure breaker in aqueous solution of ascorbic acid.

Goncalves et al.\textsuperscript{74} have investigated the influence of temperature and ionic strength on the stoichiometric acidity constant of nicotinic acid in aqueous solution by potentiometry. Acidity constants at zero ionic strength were derived by means of Debye-Huckel type formalism and their temperature dependence was obtained through Van’t Hoff analysis. The values were compared with previously reported data.

Srivastava and Shivdas\textsuperscript{75} have studied the conductance behavior of pyridoxine HCl and propanolol HCl in aqueous dimethyl sulphoxide (DMSO) solutions at 298.15 K. Both studied systems obey Walden’s rule upto 40 mass % DMSO. It was observed that DMSO preferentially solvate the cations of both the drug compounds in DMSO rich region and the presence of two $\text{–CH}_2\text{OH}$ groups in the pyridoxine cations make it less extensively hydrated.

Joseph et al.\textsuperscript{76} have measured the molar heat capacity of nicotinic acid (pyridine-3-carboxylic acid) by differential scanning calorimetry (DSC) and Calvet-drop microcalorimetry, over the temperature range 296 to 531K. From the experimental results and comparison with the previous reports, it was concluded that there exists an enantiotropic nature of the studied system of solid and liquid nicotinic acid.

Dhondge et al.\textsuperscript{77} have reported the experimental values of density, speed of sound, viscosity and refractive index for the binary systems, (L-ascorbic acid + water) and (sodium ascorbate + water) at different concentrations and temperatures. From these experimental results, apparent molar volume, isentropic compressibility, apparent molar isentropic compressibility and relative viscosity of solution have been
calculated. This study reveals that ascorbic acid and sodium ascorbate act as a water structure destroyer. Also the addition of sodium ascorbate has a similar effect on the structure of water to that of ascorbic acid.

Dev et al.\textsuperscript{78} have measured the specific conductivity of sodium dodecyl sulphate, cetyl pyridinium chloride and sodium nitrate in acetamide melt at 89 °C. The specific conductivity maxima have been observed for sodium nitrate as well as for the two ionic surfactants. In acetamide melt the concentrations of sodium dodecyl sulfate and cetyl pyridinium chloride corresponding to their conductivity maxima are found to be less than that of sodium nitrate, which may be due to micellization of ionic surfactants.

Silva et al.\textsuperscript{79} have studied the density, velocity of sound, surface tension and electrical conductivity of aqueous sodium dodecanoate solutions at various temperatures. The values for density, electrical conductivity and velocity of sound increase with surfactant concentration, but surface tension decreases. Also an increase in temperature produces a decrease in the value of critical micelle concentration of the surfactant in the studied range.

Alam et al.\textsuperscript{80-83} have measured the surface properties of amphiphilic drugs (amitriptyline, imipramine, chlorpromazine and promethazine)\textsuperscript{80-83} in water and in aqueous solutions of electrolytes, alcohols, surfactants, and polymers. The maximum surface excess concentration at air/water interface and minimum area per surfactant molecule at air/water interface, have been calculated. The additives which increase the micelle size, decrease the randomness of the system under study. On the other hand the additives which cause the breakdown of micelles and are water structure breaker show positive enthalpy and entropy values.

Kabir-ud-din et al.\textsuperscript{84, 85} have measured the cloud point and surface properties of drugs (promazine HCl, nortriptyline HCl, amitriptyline HCl and promethazine HCl)\textsuperscript{84, 85} in the presence of alcohols (ethanol to octanol), surfactants and sugars. It has been observed that long chain alcohols and cyclohexanol increases the size of micelle, results in the negative values of entropy. The CMC values are constant in the presence of short chain alcohols but sugar increases the hydrophobic interactions and thus
decreases the CMC values of the drugs. Maximum surface excess concentration at air/solution interface decreases for long chain alcohols and sugars but constant for short chain alcohols.

Yan et al.\textsuperscript{86} have investigated the effect of temperature on the interactions of glycyl dipeptides with SDS in aqueous solutions by density, conductivity and florescence methods. The volumetric studies conclude that dipeptides act as structure-maker in SDS solutions and, ion-ion and ion-peptide group interactions between dipeptide and SDS predominate. The standard enthalpy of micellization is found to be positive at lower temperatures and becomes negative at higher temperatures.

Liu et al.\textsuperscript{87} have investigated the solubilisation of valdecoxib in aqueous solution of ethanol and sodium lauryl sulfate at different temperatures. The analysis of valdecoxib is carried out by UV-visible spectral measurements. The aqueous solubility of valdecoxib could be enhanced significantly by using ethanol and by increasing the temperature of dissolution media. For sodium lauryl sulfate and water mixtures, the solubility of valdecoxib linearly increases with increasing mass fraction of sodium lauryl sulfate at all temperatures.

Ribeiro et al.\textsuperscript{88} have investigated the solubilisation of griseofulvin in aqueous micellar solutions of diblock copolymer E\textsubscript{m}B\textsubscript{n} (E = oxyethylene, B = oxybutylene) with lengthy B blocks. On comparison with the previous reports it was found that the amount of drug solubilised per gram of hydrophobe is essentially independent of B block length when this exceeds about 15 B units, suggesting that core size is not a major influence on solubilisation.

Waters et al.\textsuperscript{89} have studied the interactions between drug and surfactant (SDS) by employing isothermal titration calorimeter. The drugs were added to the SDS to a point at which they were saturated with drug. Analysis of the data using this method, has confirmed the suitability of the technique to acquire such data with saturation limit established in all cases. It is observed that micellar system can be disrupted by the presence of additional chemicals, such as drugs used here.
Harutyunyan et al.\textsuperscript{90} have studied the interactions between different types of surfactants and ascorbic acid in aqueous solution by measuring conductance, density, viscosity, and fluorescence. The addition of ascorbic acid in water increases the cmc values of both anionic (SDS) and cationic (CPBr) and decreases the cmc values of nonionic (E\textsubscript{16}A\textsubscript{20}). The values of enthalpy and entropy of micellization indicate that the entropy dominates over the micellization process. Also the ascorbic acid is solubilized in studied surfactants, especially at low concentrations. The observed partial molar volumes and partial molar volumes of transfer values of ascorbic acid also indicated the solubilization of ascorbic acid in surfactants and domination of hydrated ascorbic acid-hydrated surfactants interactions. The viscosity and fluorescence data further confirm the observed behaviour.

2.2 Research Plan

Biofluids contain small biomolecules like amino acids, peptides, proteins, sugars, nucleotides, nucleosides, nucleic acids etc. and various mineral salts in aqueous solution of definite composition. Biological functions like working, solubility, stability, transportation etc. of biomolecules across the biomembrane, are very well performed with the coordination of the ions of these mineral salts. Any foreign substance like drug or vitamin when entered into body fluid, have to interact with these small molecules and electrolytes at various biological barriers. The knowledge of physical phenomenon, the forces governing these interactions at various levels are quite important and interesting and many studies on variety of biomolecules in aqueous, non-aqueous and mixed aqueous solvent systems are in progress. The role of alkali and alkaline metal chlorides (sodium and magnesium chloride) in biological processes is well known and these salts are the first choice for any preliminary investigation in aqueous media. Vitamins, the essential constituents of human diet, are cofactor for various enzymes and also the precursor of nucleotides. Interaction studies of these vitamins with electrolyte in aqueous solutions are also important to explore and understand the functioning of various biological phenomenona. Any drug formulation contain various additives like sugars, surfactants, polymers etc. along with active drug, for its better shelf-life, stability and transport inside and outside the living system. The interactions between various additives and active drug should be properly balanced, in order to have required
effective drug concentration at the target site. These discussions further form the ground for the energetic studies of the interactions of additives (surfactant) and drugs in aqueous systems.

In the light of the above, the present research work contain the investigations of physicochemical parameters like partial molar volumes, $V_2^o$, partial molar isentropic compressibilities, $K_2^{o^S}$, viscosity $B$-coefficients, $B$, critical micelle concentration, CMC, etc. of different systems consisting of drug molecule: sulpha drugs (sulphanilamide, sulphanilic acid and sulphosalicylic acid dihydrate etc.) and vitamins (L-ascorbic acid, nicotinic acid, thiamine hydrochloride and pyridoxine hydrochloride) in water and in aqueous solutions of alkali and alkaline earth metal halides (sodium and magnesium chloride hexahydrate) at different temperatures. In order to study the drug-surfactant interactions, the CMC values for SDS have been determined in aqueous solutions of these sulpha drugs and vitamins at different concentrations and temperatures (288.15, 298.15, 308.15, 318.15) K. The above parameters have been obtained from the experimentally determined density, velocity of sound, viscosity and conductivity data. The data obtained have been used to calculate corresponding transfer parameters ($\Delta_n V_2^o$ and $\Delta_n B$), partial molar expansibility, $V_E^o$, second derivative, $(\partial^2 V_2^o / \partial T^2)_P$, $dB/dT$ coefficients and interactions parameters. The $B/V_2^o$ ratios have been calculated to discuss the solvation behavior of these solutes in aqueous solutions of electrolytes. The transition state theory has been applied to calculate the activation parameters ($\Delta \mu_1^{o^\pm}$, $\Delta \mu_2^{o^\pm}$, $\Delta H_2^{o\#}$, $\Delta S_2^{o\#}$ etc.) for viscous flow for these solutions which are interpreted in terms of interactions occurring in these systems. The free energy, $\Delta G_m^o$, enthalpy, $\Delta H_m^o$, and entropy, $\Delta S_m^o$, of micelle formation have been calculated. Also the solubility of these drug compounds and vitamins in aqueous solutions of sodium and magnesium chloride has been discussed in terms of salting-in/salting-out effect. These studies will further provide information about the hydration behavior for these drugs and vitamins in studied aqueous systems. These studies will help in understanding the various physical phenomena and the forces governing these interactions.
References:


