CHAPTER I

Introduction

Since most of the biochemical processes occur in aqueous media, investigation on the physico-chemical properties of biologically important molecules like amino acids, vitamins, carbohydrates, drugs, alkaloids, nitrogen bases, food additives and some electrolytes, *etc.*, in aqueous solutions impart useful information in understanding the complicated mechanism of molecular interactions,[1] because such interactions (*i.e.*, solute-solute and solute-solvent interactions) play vital roles in elucidating the complex behavior of different biochemical systems. The chemical, physical and biological nature of biologically important compounds like amino acids, nucleic acids, alkaloids, antibiotics, vitamins and carbohydrates, *etc.*, behave differently in various aqueous media, particularly in presence of different solutes and electrolytes. Therefore it is very interacting and necessary to understand various solute-solute or ion-ion and solute-solvent or ion-solvent interactions in order to understand the water-biomolecule interactions and how these interactions are altered in the environment of protein and other bio-molecules. These two areas remain almost mysterious for most of the biological and physical chemists. Therefore the introductory part of this thesis represents a brief discussion on the different important biological compounds, general application of important biological compounds and the solvation phenomenon including various interactions in solution phase, *viz.,* solute-solute or ion-ion interactions and solute-solvent or ion-solvent interactions.

1.1. Biologically important compounds

Most of the biologically important compounds have a core built of hydrogen and carbon. In addition, they may consist of oxygen, phosphorus, nitrogen, sulfur and some additional minor elements. The compounds differ in function and structure subject to presence of different functional groups. Some biologically important compounds are important for living cells and perform a large array of functions. Carbohydrates are one of the most useful biologically important compounds due to their various physical, biochemical, biomedical and industrially useful properties. Along with their importance in fields of food industry, chemical industry and pharmaceuticals, they are also able to protect biological compounds. When carbohydrates are located in cell surfaces, they act as very important receptors with respect to the structures of enzymes, hormones, antibodies and viruses.[2] Carbohydrates may interact with materials through several hydroxyl groups to form a vast number of metal carbohydrate complexes. Though these produced complexes are weak in nature, the associated interactions are found to be specific. Thermodynamic and volumetric properties of aqueous solutions of carbohydrates with metal ions thus give a lot of key information regarding solute-solvent as well as solute-solute interactions.[3,4]

It is well known that various non-covalent interactions such as hydrogen bonding, hydrophilic, hydrophobic and electrostatic interactions can stabilize the native conformation of the biological compounds (*e.g*., the amino acids).[5,6] Further the surrounding solvent and solute molecules may affect these interactions. Due to direct solute-solvent interactions or alteration of the structure of water, different properties of globular proteins including their activity towards enzymes, solubility, hydration, *etc*., are influenced by the addition of different solutes.[7-11] Therefore one worthy technique is to investigate different interactions of the model protein compounds, *i.e.,* amino acids or their peptides in mixed aqueous and aqueous solution.[7-9]

Amino acids are fundamental structural units of peptides, proteins, certain types of antibiotics and hormones and can participate in almost all the physiological processes of a living cell. Some essential amino acids are not components of living organisms but they affect the cellular fluid when used as cosmetics or medicine. Therefore, many physical and chemical studies have been carried out to elucidate mechanism of interaction between organic compounds and amino acids in cell fluids or compounds having same functional groups, as those exist in biomolecules of living organisms. Generally, peptides and amino acids can serve as useful models in estimating the properties of proteins and such approach is widely used in recent years.[7-9] Amino acids possess two characteristic functional groups- the amino group (-NH_2) and the carboxylic group (-COOH) and in aqueous solution they remain in zwitter-ionic form. The electrostatic field of zwitterions has a tendency to produce structural changes in the solution as it influences the structural orientations or assembly of the solvent molecules. This in turn has pronounced effect on compressibility of the solvent system. Thus compressibility and related parameters can provide significant information regarding the state of affairs in the solution on the background of solute-solvent or ion-solvent interactions. The investigation on some of the thermodynamic properties of proteins can easily be had from the behavior of their constituents, *viz.*, peptides and amino acids in solution phase in connection with various biochemical processes such as protein hydration, aggregation and denaturation and antigen-antibody reactions, *etc*. Hydration of proteins has an important role in the stability, dynamic, structural characteristic and fundamental activities of the biomolecules. Considerable works have been done to investigate hydration of amino acids through ultrasonic and volumetric studies during last few decades. It is necessary to study both the native and denatured state of protein to understand the effect of hydration in protein folding/unfolding transition. Hydration of amino acids and proteins can be investigated through ultrasonic and volumetric measurements, as these properties are very much sensitive towards the nature and degree of hydration.

Denaturation is defined as the types of reactions that lead to the changes in structure of a biological compound but don't change its molecular weight. During the denaturation process various structural changes occur in amino acid solutions. Knowledge of solute-solute and solute-solvent interactions is prerequisite to understand the denaturation process in solution phase. Most of the amino acids exist in aqueous solvent systems that contain many other organic substances. Again electrolytes have significant roles in different branches of science and engineering such as environment, chemistry and biology and hence transport and thermodynamic properties of electrolyte solutions are also of much interest. Enzymes catalyze various reactions in bio-fluids in cell metabolism. For catalyzing oxidation-reduction reactions and many types of group transfer processes, enzymes may require cofactors that can be a metal ion or an organic molecule (co-enzymes). Vitamins are the essential micronutrients for animal diet and act as precursors for various co-enzymes.[12-17] A vitamin is an essential micronutrient that is required for an organism in small quantities but the organism often cannot synthesize it. Therefore for proper functioning of its metabolism it is necessary to get it from the diet. They are classified by their chemical or biological activity, not by their structures. Human metabolism requires thirteen vitamins: vitamin A (carotenoids and retinols), vitamin B_{12}

(cobalamins), vitamin B_9 (folic acid or folate), vitamin B_7 (biotin), vitamin B_6 (pyridoxine), vitamin B_5 (pantothenic acid), vitamin B_3 (niacin), vitamin B_2 (riboflavin), vitamin B_1 (thiamine), vitamin C (ascorbic acid), vitamin D_3 (cholecalciferol), vitamin E (tocotrienols and tocopherols) and vitamin K (quinones). Structurally diverse vitamins are grouped together according to their solubility as fat-soluble and water-soluble. Many vitamins are precursors of different coenzymes and deficiency of vitamins may cause malfunctioning in the living world at high epidemic levels. This mechanism of vitamins is quite complex and this needs knowledge about the molecular interactions in fluids for better understanding. The action of these compounds is very difficult to understand. But some information can be had from the different interactions performed by biologically important compounds through various volumetric, transport and rheological properties.[18-37]

On the contrary in medicinal chemistry the chemist attempts to design a medicine or pharmaceutical agent that will benefit mankind, such a compound can be called as drug.[38] Generally a drug is any substance other than food and when it is injected, inhaled, absorbed through a patch on the skin, consumed, smoked or dissolved under the tongue may lead to physiological change in the bodies. Drugs can be classified based on the pharmacological action. *e.g.*, analgesics, antipsychotics, antihypertensive, antiasthmatics, antibiotics, *etc*.; by their chemical structure, *e.g.*, penicillins, catecholamines, barbiturates, steroids, opiates, *etc*.; by their target system, *e.g.*, antihistamines, cholinergics, *etc.,* and by their site of action. The blood stream carries the drug in the body. Liver contains certain enzymes that modify the drugs. This is called drug metabolism. The metabolized drug is then circulated in body through the blood stream to reach the sites wherein they work as medicine.[39] When the drug moves throughout the body by blood streams it interacts with amino acids, minerals, vitamins, hormones, carbohydrates, *etc*., present in the body. Most of the drugs are insoluble in water; they are administrated as hydrochlorides or other salt form. So they are amphipathic in nature due to presence of both hydrophilic and hydrophobic groups in the same molecular moiety. So their solvation is very much interesting as far as their structure and interactions in biological fluids are concerned. Physico-chemical measurements may be a useful tool for unveiling such interactions.[40-61] Thermodynamic properties are normally applied to study solute-solute and solute solvent interactions of the solution phase.

A nitrogen-containing base or nitrogenous base is defined as an organic molecule with a nitrogen atom that shows chemical properties like a base[62-65] due to the lone pair of electrons on their nitrogen atom. A biologically active nitrogenous base mainly binds nucleic acids together. Nitrogenous bases are classified into two types. It is done according to the derivatives of two mother compounds: purine and pyrimidine. They are planar and non-polar in nature due to their aromatic character. Both the pyrimidine and purine bases resemble pyridine and hence are weak bases and remain mostly unreactive towards aromatic electrophilic substitution reactions.

1.2. Importance of some biologically important compounds

A wide number of biologically important compounds are used in modern day depending upon the need. Such compounds are being used by human being from ancient times in different forms. Today medicinal chemistry is a field of interest due to its major applicability in mankind. Some important applications of some biologically important compounds are outlined here.

1.2.1. Importance of carbohydrates

I. They regulate the blood glucose level and provide energy to the body.

II. They prevent the use of proteins as energy source.

III. Carbohydrates help in fat metabolism.

IV. Carbohydrates are used as sweeteners to give sweet taste to the food.[65] High-intensity sweeteners are used as ingredients to sweeten and increase the flavor of foods. Because sweeteners with high-intensity are sweeter than sugar, *i.e.*, sucrose, smaller amounts of such sweetener show the same amount of sweetness as sugar in food. People may apply such high-intensity sweeteners instead of sugar since they contribute only a few calories to the diet. High-intensity sweeteners also control the blood sugar levels. Carbohydrates are used as sweeteners in soft drinks, baked goods, candy, dairy products, powdered drink mixes, canned foods, puddings, jams and jellies and scores of other beverages and food.

V. Carbohydrates act as a dietary fiber.

VI. Apart from dietary source carbohydrates helps in biological process in the body.

1.2.2. Importance of amino acids

I. Build Protein: Protein is generally found in the organs, glands and tissues of the body and works to repair and generate cells. When a protein is broken down, a chain of amino acids is left. Amino acids are essential for protein synthesis.

II. Lean Muscles: Amino acids are the main building blocks of protein. These build lean and strong muscles of body. These are most useful for growth in childhood and in the adolescent years. Pregnant women also need plenty of amino acids for proper development and growth of the fetus.

III. Waste removal: Body collects various waste products like ammonia over time from its natural processes. Some waste products are produced also from exercising. Amino acids then facilitate urea metabolism to excrete those waste products from the body.

IV. DNA Synthesis: When cells are reproduced in the body, they can pass along their unique DNA. In case of proteins, amino acids help the cells to successfully replicate this DNA.

V. Tissue Repair: Various tissues in the body like connective tissues, skins, and muscles, *etc.*, need amino acids for repairing when damaged or injured. They are very beneficial after difficult training or exercise, when muscles of the body can tear. If after exercise amino acid such as arginine is taken, it can help the muscles to quickly recover and properly heal.

VI. Arterial Health: Amino acids like arginine can retain elasticity of arteries of the body. It thus prevents them to stretch out and allow fluid to collect. Amino acids also support the contraction and expansion of the arteries with every heartbeat.

VII. Food Breakdown: Foods need to be properly broken down for their proper digestion of food so that the body can get the valuable nutrients out of them.

VIII. Immune Response: Amino acids protect the body by supporting a healthy immune system. Histidine helps to synthesize histamine and thus helps the body to become more particularly resistant to allergens.

IX. Relaxation: Theanine and tryptophan help the body to calm down in relaxation time. They can also be useful for people with sleeping issues and anxiety and are found in natural sleep aids.

X. Bone Loss: Amino acids like lysine prevent bone loss by absorbing calcium by the body that can cause osteoporosis and osteopenia.

1.2.3. Importance of vitamins

I. Vitamin A promotes healthy vision and skin and it also supports bone and tooth growth. In addition, vitamin A helps our immune system and is important in the reproductive process. It also enables our lungs, kidneys, heart and other organs to function properly.

II. Vitamin B_{12} can promote healthy nerve function and thus helps our body to produce new cells. It can also lower risk of heart disease.

III. Vitamin C prevents infections and promotes a healthy immune system. It also supports the body to absorb iron, a necessary component to carry oxygen through blood cells.

IV. Vitamin D promotes absorption of calcium in the body and thus it is important for bone health and development. It helps also to reduce inflammation and benefits your immune system.

V. Vitamin E is used as an antioxidant. It is helpful to protect cells from damage. Vitamin E fights against critical diseases like cancer and Alzheimer. It controls the immune system by preventing different infections and fighting off bacteria.

VI. Vitamin K is essential for blood clotting. It also promotes the bone health. It can reduce the risk of osteoporosis and coronary heart diseases.

VII. Biotin maintains the overall health by increasing absorption of protein, fat and carbohydrates from food. It keeps the hair growing and healthy and the bones strong.

VIII. Folic acid is mainly responsible for making new red blood cells, thus it prevents anemia.

1.2.4. Importance of drugs

Drugs are used to cure or prevent diseases. There are different types of drugs depending upon their actions. Few examples are given below:

I. Antipyretics are used to reduce fever.[66] Ibuprofen and aspirin are examples of this kind of drug.

II. Analgesics are used to reduce pain. Paracetamol and morphine are used as analgesic drugs.[67]

III. Chloroquine, amodiaquine, sulfonamides are used as antimalarial drug.

IV. Antibiotics like tetracycline, sulfacetamide, and erythromycin are used for the bacterial infections.

V. Boric acid, cetyl trimethylammonium bromide, bezalkonium chlorides are examples of antiseptic drugs. They prevent sepsis.

VI. Amphetamine, dextroamphetamine, epinephrine are used as stimulants. Generally they are psychoactive drugs that improve the mental condition.

VII. Metformin, glimepiride, pioglitazone, acarbose are few examples of antidiabatic drugs. They control the sugar level in body.

VIII. Ketamine, propofol, etomidate are used as anesthetic drugs.

IX. Zidovudine, retrovir are used as anti HIV drugs.

X. Bleomycin, epirubicin, etoposide, paclitaxel, irinotecan, carboplatin, cisplatin are some anti-cancer drugs.

XI. Lovastatin, fluvastatin are used as lipid lowering drugs.

XII. Sodium valporate, lamotrigine, carbapamazepine are used as anticonvulsant drugs or mood stabilizers.

1.2.5. Importance of nitrogenous base

In the field of biological sciences, nitrogenous bases have profound role in nucleic acids and thus termed as nucleobases. They play a crucial part as the building blocks of DNA and RNA and their flat shape is particularly important regarding this process. Normally five nitrogenous bases are used as set for the construction of nucleotides and then build up the two nucleic acids like RNA and DNA. These nitrogenous bases are classified into adenine (A), thymine (T), guanine (G), cytosine (C) and uracil (U). These nitrogenous bases show hydrogen bonding between opposing strands of DNA and thus form the double helix or "twisted ladder" of DNA. Thymine is always paired with adenine and cytosine is paired with guanine. These are commonly known as base pairs. Uracil replaces thymine in RNA. Pyrimidines are built of uracil, cytosine and thymine. They show a single ring structure. Purines are built of guanine and adenine. They show a double ring structure.[68]

1.3. Water activity

Water is omnipresent in biological systems, related materials and the surroundings. Therefore hydrophobic and hydrophilic interactions often control the behavior of certain products towards water. Its thermodynamic potential, *i.e.*, the water activity (a_w) signifies the equilibrium amount of water available for the solvation of further solutes or for their degradation reactions (chemical and biochemical). The presence of pure water is indicated by $a_\mathrm{w} = 1$, but $a_\mathrm{w} = 0$ means total absence of 'free' water. The understanding why certain products are more stable than others at the same water activity (a_w) requires knowledge of the water structure. Thus hydrophobic and hydrophilic interactions between water and the components of the materials like foodstuff, drugs, amino acids, *etc*., and the effect of such soluble molecules on the hydrogen bonds in water are very informative regarding their preservation and storage. As low water activity (a_w) hinders microbial growth, control of water activity (a_w) in food and related industries is inevitable. Effects of water activity (a_w) on the stability of bio-systems, biological macromolecules (*e.g*., carbohydrates), elongated proteins (*e.g*., myocin, gluten, collagen, *etc*.) and nucleic acids are well-documented [69].

The gradient of the chemical potential of water (μ_w) in a solution is related to its activity (a_w) through the expression[70]:

$$\mu_\mathrm{w} = \mu_\mathrm{w}^* + RT\ln a_\mathrm{w} \approx \mu_\mathrm{w}^* - RTV_\mathrm{w}^*(c/M + Bc^2 + \ldots) \qquad (1)$$

where μ_w^* and V_w^* are the gradient of the chemical potential and themolar volume of pure water, respectively. R, T, c, M and B are the universal gas constant, the absolute temperature, the solute concentration, the solute molar mass and the so-called second virial coefficient, respectively. The so-called second virial coefficient (B) reflects solute-solute and solute-solvent interactions due to non-ideal behavior of the solution. From the above expression it is evident why addition of a solute always lowers the water activity (a_w). Rearrangement of the above expression yields:

$$\begin{gathered}\ln a_\mathrm{w} = -V_\mathrm{w}^*(c/M + Bc^2 + \ldots) \le 0 \\ \text{or } B > -1/cM \end{gathered} \qquad (2)$$

If $B < 0$, water acts as weak solvent and if $B \approx 0$, the solute separates out as a precipitate. Obviously the so-called second virial coefficient (B) depends on pH of the solution. Biopolymers usually have small B-values; hence large changes of a_w-values produce minor effects on the B-values. But for real biological systems, most food products and certain polymers, *etc*., c is rather large and small changes in the moisture content results into a large drop in a_w -values. Such a large drop in a_w -values affects the overall structure and organization of the solution under investigation.

1.4. Solvent Effects

Most of the chemical and biological processes occur in solution phase. Solvation phenomena play a vital role in chemistry and biology. The solvent influences chemical reactions and hence it has gained the attention of researchers from both experimental and theoretical grounds associated with chemistry. The outcome of a chemical reaction is affected by the addition of solvents through the possible interaction of the local surroundings with the individual reactants undergoing the reactions. The physical barrier (associated with motion of the associated reactive species) and the energy path (required to stabilize the energetic products formed in the reactions) are also provided by the solvents. It is seen that the solvent also perturbs the potential energy curves that leads these reactions.[71] As the solvent species surrounding a solute can form a structure that can control the outcome of biological or chemical events, the solvent species play an important part in the chemical or biochemical processes. Solvation has been well established to be a driving factor in diverse areas like atmospheric processes and biological activities.[72] In living organisms, solvated ions may also appear in higher concentrations where their absence or presence can fundamentally change the life functions. Ions solvated in water mixtures or organic solvents and organic solvents are also very common[73] and the alteration of solvent molecules surrounding ions in solutions is essential to understand the reactivity of ions in related solution.[74] Solvated ions also govern the electrochemical applications generally because the conductivity of electrolytes is related to the ion-solvent interactions.[75] Most of the chemical reactions are performed in solutions and solvents can simply influence reactions in a number of ways. Solvents can act as a reaction medium to put reactants together. They can act as one of the reactants and carry the dissolved the solutes to bring chemical components together in solution phase in the required amounts and make the reaction feasible.

The temperatures, both in exothermic and endothermic processes, are also influenced by the solvents. In endothermic reactions, heat is supplied by a heated inert solvent with a high heat capacity, while in exothermic reactions boiling the solvent or absorbing heat can remove the surplus heat. In case of solid reactants, a homogenous reaction phase (*i.e*., solution) is created by the solvents to bring the solid reactants into contact. So, it is vital to select an appropriate solvent to obtain most fruitful results or favorable yield of the products. Any good solvent can fulfill all the necessary criteria such as for all reaction conditions it is necessary to be an inert solvent with an appropriate boiling point and at the completion of the reaction there should not occur any difficulties during its removal. It should also dissolve all the reactant species and reagents. In essence differential solvation of the transition states and the starting materials by the solvent govern the reaction rates. When the reactant species move forward to the transition state, the solvent molecules arrange themselves to stabilize the particular transition state. The reaction are seen to proceed faster if the transition state is found to be stabilized to a greater amount with respect to the starting material. On the contrary, the reaction proceeds slowly if the transition state is stabilized to a lesser amount than the starting materials. However, re-orientation of the solvent is required for such differential solvation and the outcome of a reaction is often governed by the equilibrium solvent effects.

1.4.1. Solvation

The term solvation is associated with the surrounding of every dissolved species by a shell of appreciably tight bound solvent molecules. Intermolecular forces, amongst the solute and the solvent, result in the formation of solvent shell. A relatively small amount of solute is dissolved in comparatively large amount of solvent during the solvation process. Thus a homogeneous phase is formed by a number of intermolecular forces such as solute-solute, solute-cosolute and solvent-solvent interactions. During the dissolving process, solute-solute interactions disappear slowly and altered by solute-solvent interactions. The solute molecules perturb the solvent structure when they pass into the solution and this results into the appearance of some solvation shell (more or less ordered in nature) around them created by the solvent molecules. If the lowering in the free energy arising from the solvation is greater than the increase in free energy due to annihilation of the various interactions among the solute the solvent molecules, the dissolving process becomes spontaneous. The overall process of dissolution is endothermic in nature when lattice energy is greater than liberated solvation energy and when the lattice energy is lower than the solvation energy then the overall process is exothermic.

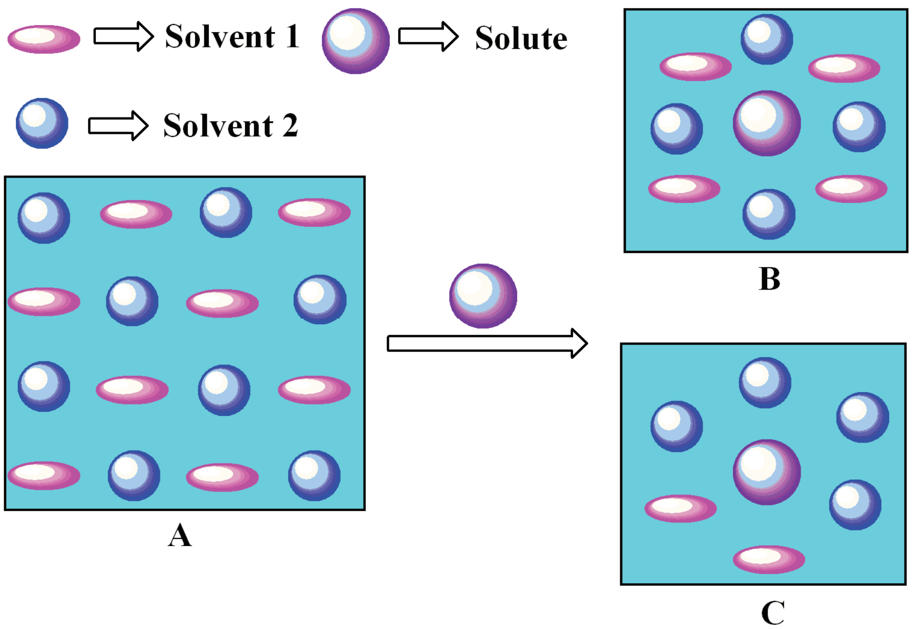

Fig. 1.1. A schematic presentation of preferential solvation, A: binary mixture of solvent 1 and 2; B: ideal solvation; C: preferential solvation by solvent 1.

1.4.2. Preferential Solvation

The solvation mechanism in solvent mixtures, *i.e.*, in mixtures of solvents (like binary and ternary, *etc*.) is more complex than that in pure solvents. The different interactions (occurring in solvent mixtures) take a pivotal role in the solvation process, besides the various types of solute-solvent interactions. Thus a large deviation is observed from the ideality as per the Raoult's law. Solute may lead an optimum change in the solvent mixture composition in solvation sphere than that in the bulk composition. This is commonly known as preferential solvation or selective solvation[76] as illustrated in Figure 1.1. Preferential solvation commonly occurs due to nonspecific (dielectric enrichment) and specific (hydrogen-bonding) solute-solvent interactions.[77] It can also be explained as a result of solvent-solvent interactions.[78]

1.5. Ion-Solvent or Solute-Solvent Interaction

Now–a-days many branches of chemistry deal with the solvation process of a solute by solvent molecules such as complex formation or chemical synthetic processes, *etc*. Solute-solvent or ion-solvent interactions is a governing factor that control the chemical equilibrium and the rate of chemical reaction, *etc*., that is why an important portion of chemistry is involved with the solvation of ions or solutes and its source discussed in terms of solute-solvent or ion-solvent and solvent-solvent interactions. To better understand if the structure of the solvent is distorted or modified by the added solute it is important to know their interactions.[79] It was shown that the reactivity of a chemical reaction is favored by preferential solvation of the reactant and transition state through specific and non-specific ion solvent or solute-solvent interactions. The changes in energy of the transition states are of critical importance in the process of solvation. To understand the solute-solvent or ion-solvent interactions, studies on the nature of solutions of non-electrolytes and electrolytes in binary mixtures of solvents and pure solvents have gained much interests.[80-81]

Solute (ion)-solvent interactions can be explained by the interactions among the solute (ion) and the solvent molecules during the solvation of the neutral (electrolytic) molecules. When a solvent with a power of influencing the inter-ionic forces in the ionic crystals is added, the inter-ionic forces may decrease to the extent that the mobile ions are produced in the solution due to freedom of transnational motion and considerable energy of such interactions, which are collectively termed as ion-solvent interactions. Figure 1.2 illustrates the dissolution of an ionic crystal by the action of a solvent.

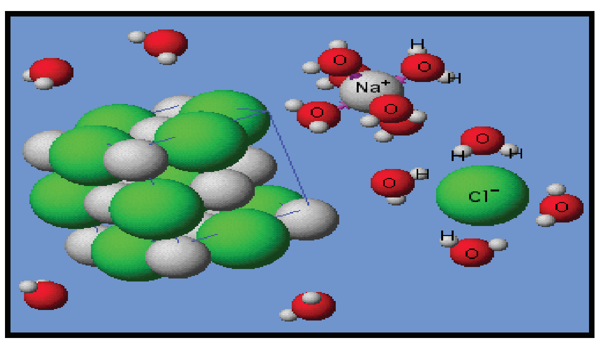

Fig. 1.2. Dissolution of an ionic crystal by a solvent.

Ions can influence the orientation of the dipoles. Solvent dipoles may be teared by the symmetrical and spherically electric field of the ion from of the solvent lattice and rearrange them with particular charged end towards the central ion. Thus, ion-dipole forces are one of the main sources of the ion-solvent interactions that consider the solvent molecules as electric dipoles and the ion as point charge. Most of the reactions in solutions are bio-chemical or chemical by nature. Earlier it was assumed that the solvent is only an inert medium in chemical reactions. But extensive studies in aqueous, non-aqueous and mixed solvents media suggests the importance of ion-solvent interactions.[81,82]

A variety of organic solvents can be differentiated based on their association through hydrogen bonding or acid base properties,[83] dielectric constants, donor-acceptor properties,[84] organic group types, hard and soft acid-base principles,[85] *etc*. Hence it is expected that the transport, thermodynamic and acoustic properties of such solvents are influenced by the presence of diverse electrolytes and non-electrolytes. Thus the determination of these above said properties of such solvation in presence of different electrolytes or non-electrolytes would provide valuable information regarding diverse solute-solvent and solute-solvent/ion-solvent interactions.

1.6. Ion-Ion or Solute-Solute Interaction

Ion-solvent interactions are commonly related to the surroundings and environment of the ions in solution. Not only the solvent molecules but also the other ions are seen by the ions through its surroundings. Thus their mutual interactions establish the key part 'ion-ion interactions' between these ions. The ion-ion interactions can influence the solution properties in different extent and are governed by the character of electrolyte under study. In general, ion-ion interactions are stronger than ion-solvent interactions. In dilute electrolytic solutions, ion-ion interaction is now well understood (at least theoretically) but ion-solvation or ion-solvent interactions still remains a complex phenomenon and often addition of solutes substantially modifies the structure of the solvent (such as water).

1.7. Object and Application of the Research work

In recent years the study of physico-chemical properties of solute-solvent systems has gained much attractions. To understand the diverse intermolecular interactions between mixed components the physico-chemical properties stand as a handy avenue. Hence efforts have been undertaken to elucidate such behaviors through various macroscopic and microscopic properties of the systems under investigation. Thermodynamic, acoustic and transport studies are highly useful in this regard. As most of the chemical and biological reactions occur in solution phase, chemical reactions is mostly dependent on the reactant behaviors in the solutions. Density, dielectric constant, refractive index and viscosity are useful solvent parameters in understanding various solvent properties to explain solvent effects in the chemical processes. The establishment of a valid model for solution is quite a hard task due to complex intermolecular interactions. Thus, models based on non-specific solute-solvent interactions (such as van der Waals interactions) are mainly used.[86] Biological processes like metabolism, signaling, transporting, *etc*., are also influenced by the solvation.[87, 88] Many theoretical considerations were used to elucidate how the solvent effects can influence the bulk solvent properties. Onsager[89] and Kirkwood[90] have developed a very simple model amongst those treatments. Several theories were suggested in the past years for determining the number molecules of solvents associated with ions and the number of those solvent molecules released to the bulk from the solvation sphere during ion-pair formation. At first cations of transition metal have well-defined first solvation shells geometrically.[91] But they undergo further solvation into a second concentric solvation sphere with no well-defined solvation numbers or solvation shell and geometries. However most of the ions are solvated in a much less well-defined manner beyond the closest surroundings of the ions due to non-directional electrostatic ion-induced dipole or ion-dipole interactions.[92] The basis of explaining the influence of the solvent quantitatively and the extent of ion-solvent interactions in solvents is required to properly understand the different phenomena in solution chemistry. Partial molar volumes, viscosity *B*-coefficient and limiting ionic conductivities, *etc*., are mainly used to estimate and understand the ion-solvent interactions thermodynamically.

The solute-solvent and solute-solute interactions have been the influencing factors in different fields of chemistry. These solute-solvent interactions lead to sufficient change in various chemical reactions associated with ions. These changes in ionic solvation are very useful in many practical problems in organic and inorganic synthesis, non-aqueous battery technology, studies of reaction mechanisms and extraction.[93] Knowledge of solute-solvent or ion-solvent interactions associated with aqueous solutions have major applications in wide areas like energy transport, mass transport, heat transport, fluid flow and reaction kinetics, *etc*. Therefore, over the past few decades a lot of focus has been thrown on the behavior of important biological compounds in different aqueous media to study solute-solvent and solute-solute interactions under various experimental conditions.[18-37, 40-61, 94-100]

Studies on solution thermodynamics of important biological compounds like amino acids, vitamins, carbohydrates, drugs, alkaloids, *etc*., in various aqueous media can impart valuable information on different interactions in solution, solution behavior and shelf life of different biological components.[18-37] Thermodynamic properties of such biological compounds in different aqueous media help in understanding of the solvation of these compounds.[40-61] From the physico-chemical properties, chemists choose different aqueous media that will increase the effect of these biological compounds and their solubility. Hence thermodynamic properties and transport properties studied for such compounds would provide valuable information about different molecular interactions occurring in their solutions. Actually, the aspect embraces a lot of topics but focus has only been given on the viscometric, volumetric, refractometric and spectrophotometric studies to unveil the physico-chemical behavior of the solvent systems (aqueous solutions), solute and cosolute structures and their specific or mutual interactions in solution phase.

1.8. Importance and Scope of the Physico-Chemical Parameters

Solvation of a solute in a particular solvent is a key factor that controls its solution behavior and thus solvation process, being a complex one, is governed by the nature of the solvent and solute, *i.e.*, their hydrophilic-hydrophobic properties[101] and molecular structure. Thermodynamic and thermophysical properties are better avenues to understand the non-ideal behavior of many complex systems, because the chemical and physical effects arise from the interplay of various molecular interactions/forces, amongst the unlike molecules.[102] Thus studies of the physico-chemical properties of the mixed components help to interpret the intermolecular interactions between the unlike molecules through a study of some physical properties like density, viscosity, refractive index and conductance, *etc*.[103, 104] From a practical point of view, these properties are of great importance for the pharmaceutical, chemical, petrochemical and food industries.[105] Solution densities and other related volumetric properties are necessary for physical and theoretical aspects. The density is essential for the conversion of the concentration units and also for investigation on the molecular interactions in solute-solvent systems. Density is used in different fields; it helps in quality control in the production of industrial liquids, it helps in concentration determination in the beverage and food industries, *etc*. The partial molar volumes and apparent molar volumes at infinite dilution can also be determined for the solute-solvent systems if densities of the solutions are known. Also density data is a must for the determination of the properties like viscosity, and molar refractions, *etc*.

Most engineering calculations need the knowledge of viscosity of the fluids where mass transport, fluid flow, heat transport are controlling factors. Viscosity mainly characterizes the flow behavior of a gas or a fluid or a liquid and it generally varies with temperature, for a liquid system it decreases as the temperature increases and *vice-versa*. Viscosity helps to understand the nature and strength of forces operating amongst the unlike molecules in a mixed system. Viscosity measurement is powerful tools for a physical chemist, because viscosity or the viscosity coefficient are dependent on the shape, size and orientation of the molecules in solutions and thus help to interpret ion-solvent or solute-solvent interactions through the calculation of free energy and the related thermodynamic parameters of transfer from one solvent to another for a single ion or solute.[106]

Acoustic properties has also proved to be a valuable tool for understanding the behavior of various solutes like amino acids, vitamins, carbohydrates and drugs, *etc*., in aqueous and non aqueous solutions. The propagation of ultrasonic wave in solutions help to reveal the changes in different physical properties at macroscopic level.[107, 108] As the structure and interactions present in the solution are highly influenced by speed of sound, molecular interactions can be estimated quantitatively in the solution in light of ultrasonic speed of sound.[109]

Refractive index determination is also helpful for the study of the various physico-chemical aspects of solutes in solution. Solute-solute or ion-ion, solute-solvent or ion-solvent as well as solvent-solvent interactions can be easily established from the refractive index studies.[110] Refractive index is therefore one of the key parameters of a solution and it can easily be determined almost accurately. Electronic polarization of ions can be understood by means of molar refractivity that depends on the electron shell arrangements of ions under the influence of the neighboring ions or surrounding environment.[111]

Moreover, a solute-solvent system is characterized by the presence of various electronically excited states of the solvent and solute with substantial electronic interactions. Solvents can alter intensities, shapes and positions of absorption bands of the solutes when solvents of different polarities are used to record the absorption spectra. Such effects arise from various intermolecular solute-solvent interactions in the solutions such as ion-dipole, dipole-induced dipole, dipole-dipole and hydrogen bond, *etc*. These interactions/forces may change the energy difference between excited and ground state of the absorbing species and thus solute-solvent and the solvent-solvent interactions can be studied from absorption spectra of the solutes in solutions. These facts, therefore, encouraged us to undertake studies on the solution thermodynamics of some biologically important compounds in various aqueous media.

1.9. Importance of Solutes and Solvents Used

The importance of solutes and solvents used in the works included in this thesis is outlined below.

1.9.1 Solutes and cosolutes

Ascorbic acid, commonly known as vitamin C, is a water-soluble, naturally occurring vitamin. It has antioxidant properties. It is not only essential for the metabolism of phenylalanine, folic acid, histamine, tyrosine, *etc.*, but it is also required in the synthesis of collagen required for the structure of muscles and bones.[112] It is used an anti-ageing agent as it protects the body tissues and cells against oxidative damage from free radicals and reactive oxygen derivatives. It has a key role in improving elasticity of skin as it decreases wrinkles through its involvement in lysine hydroxylation and proline in collagen biosynthesis. Deficiency of vitamin C in human body can cause several diseases like gum problems, scurvy, muscle degradation, neurotic disorders and anemia, *etc*. It is mainly applied to food and feed to increase product stability and quality. So before packing or during the processing, ascorbic acid is applied to different foodstuffs in order to retain its nutrients, characteristic aroma and other characteristic properties.[113]

Nicotinic acid has earned great attention because of its versatile nature in terms of biochemical, therapeutic and chemical applications.[114] This derivative of pyridine has a molecular formula $C_6H_5NO_2$ with a carboxyl group (-COOH) at the 3-

position and it is often called vitamin B_3 or niacin in combination with Nicotinamide.[114-116] It is water-soluble and colorless compound and it could be converted to NAD and NADP in pharmacological doses *in vivo*. It reverses atherosclerosis by reducing total cholesterol, triglycerides and lipoproteins. It plays an important role to repair DNA and to produce steroid hormones in adrenal gland. So it finds widespread uses as cosmetics, forage and as food additive.[117, 118] Paracetamol also known as N-acetyl-p-amino phenol or acetaminophen is an antipyretic, mild analgesic agent and also an anti-inflammatory non-steroidal drug.[119-121]

Among various organic salts sodium pyruvates has significance in body as it can provide energy into the cell by converting itself into acetyl coenzyme A. Sodium malonate is a disodium salt of an organic acid of relatively high charge density. It is high solubility in water and behaves as a cosmotrope in water. It also stabilizes protein structure and also conforms to water structure.[122, 123] It is generally applied in increasing the reproducibility of crystals and improving resistance to physico-chemical shocks. It is also found to be a good cryoprotectant. Uracil is an important nucleobase of the nucleic acid of RNA. It is very helpful to body in synthesizing many necessary enzymes for proper cell functioning. Uracil has also vast use as an allosteric regulator in the body. It is also finds applications in drug delivery.

Amino acids are the fundamental building blocks of proteins. Salt induced electrostatic forces often modify protein structure by affecting properties like denaturation, solubility and activity of enzymes, *etc*. The physicochemical properties of certain salts in aqueous phase and amino acids thus give valuable data on the solute-solvent and solute-solute interactions. These interactions are valuable to understand the proteins stability and informative for several physiological and biochemical process that occur in a living cell. Hence to get more insight into the hydration of protein and various non-covalent forces stabilizing the native structure of protein, it is important to measure the effect of such salts on the model compound of proteins, *i.e*., the amino acids.

Caffeine is a bitter alkaloid and white crystalline purine. It occurs as white, odourless, glistening needles of fleecy masses.[124] It is found in nuts, seeds, fruits and leaves of a number of plants like coffee, tea, beans, guarana and cola, *etc*. Caffeine has vital effect on vasoconstriction and other cardiovascular activities.[125, 126] It can inhibit DNA repairing[127] and it can lead to complications for pregnant woman[128] and it may be one of the causes of cancer, ageing and heart diseases.[129] In pharmacology this compound is often used as diet aids, analgesics, and flu/cold remedies.[130]

Gluconic acid is found in various natural products (*e.g.*, in honey up to 1%) and fermented foods and is often used as a food additive to impart a refreshing sour taste in many food items like wine, fruit juices, *etc*. Sodium gluconate tastes less salty than the table salt (NaCl) probably due to its large anion[131] and is often mixed with many processed foods, because it promotes the growth of *lactobacillus bifidus* in the intestine[132] and it has a property of inhibiting bitterness in foodstuffs.[133] Many sodium salts were reported to suppress bitterness of certain compounds.[134] For example sodium gluconate can be a better replacement[135] for reducing the uses of blood pressure enhancing preservatives (like NaCl in breads). The molecular structure of all the biologically important compounds used as solute and cosolutes in various chapters are illustrated in Fig. 1.3.

1.9.2. Solvents

Since water is ubiquitous, aqueous systems deserve special attention. Such systems are apparently very simple but they aroused a lot of questions from ancient times. Water should never be treated as an inert diluent. It has a unique cluster structure (through extensive hydrogen bonds in three-dimension), a high boiling temperature, a large heat capacity and a high dielectric constant and many anomalies in its specific volume. It has been considered as a universal solvent for its amazing roles in chemical, biochemical and cellular systems. For example, water ionizes and affords proton exchange between molecules to facilitate the affluence of ionic synergies in biological systems. Also it's unique hydration properties towards different biological macromolecules afford the three-dimensional structure of such macromolecules and thus water can influence their functions in solution. Regarding this, the preferential organization of its molecules around the non-polar and polar parts of the biopolymers (preferential hydration) is very fascinating and informative. Amid these fascinating water properties, studies on its behavior as a solvent and its interactions with different biologically important compounds deserve extensive attention. Therefore, in this dissertation different aqueous media were used as solvent

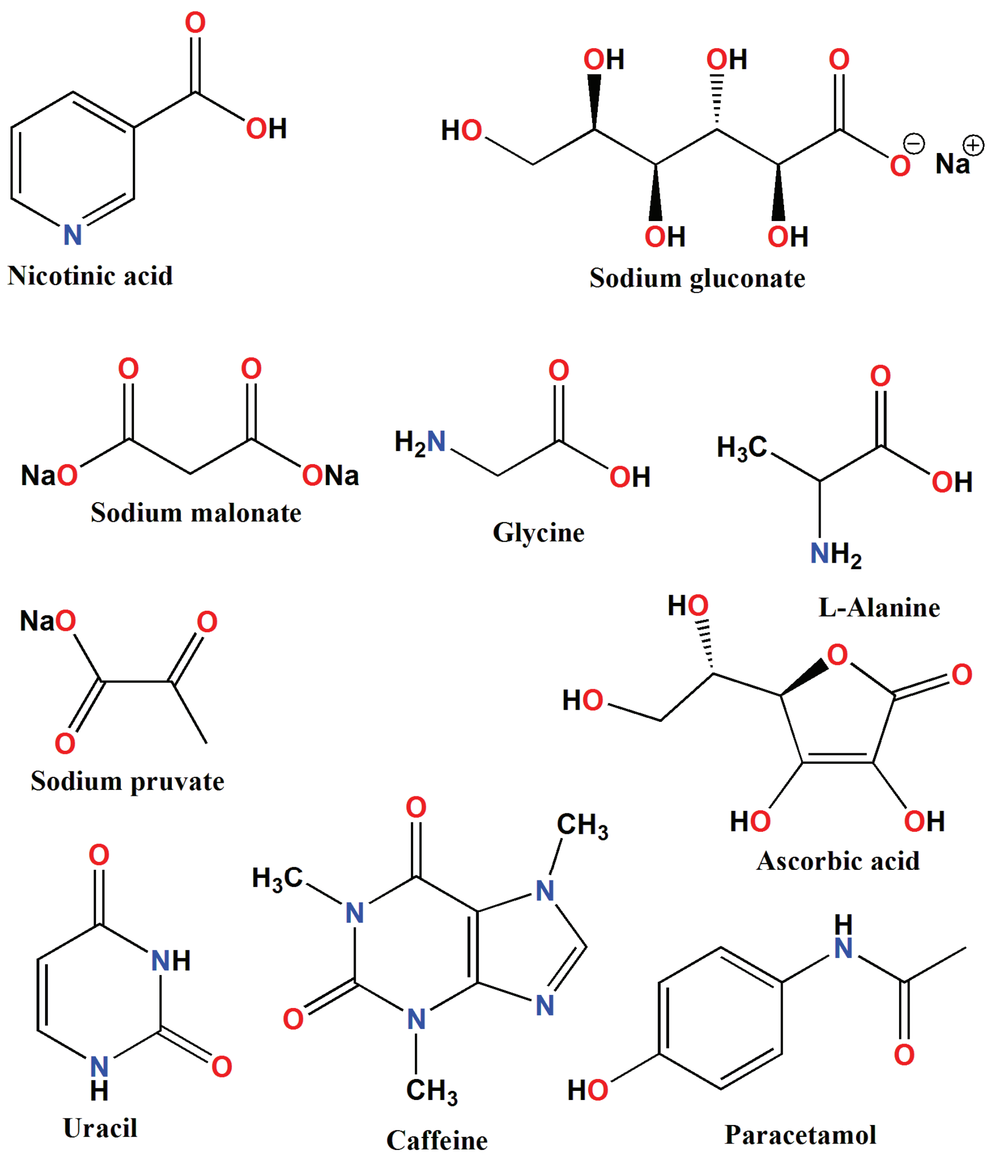

Fig.1.3. Structures of the biologically important compounds used as solutes and co-solutes.

systems. Sodium malonate, amino acids (*e.g.*, glycine and L-Alanine), RNA base like uracil were used as cosolutes for different aqueous solvent systems.

1.10. Method of Investigation

The phenomena of solute-solute, solvent-solvent and solute-solvent interactions are intriguing and these interactions can be explored by using different experimental techniques. For physico-chemical investigation important methods of densitometry, viscometry, Ultrasonic interferometry, refractometry and UV-visible spectroscopy were used in the research works embodied in this thesis. Thermodynamic properties of solutions are not only helpful in estimating feasibility of chemical reactions in solution phase but they also offer one of the best methods to investigate theoretical aspects of solution structure. Thermodynamic properties like apparent molar volume, partial molar volume and partial molar expansibility, *etc*., obtained from density measurements are generally convenient parameters for interpreting solute-solvent and solute-solute interactions in solution. The partial molar volumes and apparent molar volumes of electrolyte solutions are popular tools in elucidating structural interactions (*i.e*., ion-ion or solute-solute, ion-solvent or solute-solvent and solvent-solvent interactions) in solution. The viscosities of electrolyte and non-electrolyte solutions are also helpful properties to study their solution behavior. The compressibility, a second derivative of Gibbs energy, is an indicator that is very sensitive to molecular interactions and thus it can also provide useful information in studies when partial molar volumes alone suffice to provide an unequivocal and proper interpretation of such interactions. The concentration and temperature dependences of viscosities of electrolyte and non-electrolyte solutions are often used to study solute-solvent or ion-solvent (solvation) interactions and long-range ion-ion electrostatic interactions. Changes in solvent viscosity by the addition of electrolytes are due to inter-ionic and ion-solvent effects. The viscosity *B*-coefficients can provide a satisfactory interpretation of ion-solvent or solute-solvent interactions, *i.e*., the effects of solvation, preferential solvation and long range structure-breaking or structure-making capacity of the solutes. Refractometric studies also focus on the different molecular interactions that take place in solute-solvent systems (*i.e*., solutions) of varying compositions and thus such studies help in exploration of the behavior of the solutes in different solvent systems. UV-visible spectroscopy of such solutions can also help to elucidate or support the results obtained from density, viscosity, ultrasonic speed and refractive index measurements.

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