CHAPTER I

Introduction

The compound that will exerts a direct physiological effect on any type of living organism is known as biologically active compound.There is a diverse world of biologically active compound found in our daily life. Which include almost everything that would impact on the health and other biological phenomena that occurs in the living organism body. Some these are like vitamins, antibiotics, plant growth regulator(auxin, ethylene, etc), drug, extra cellular soil enzyme, siderophores, Humic substances, Natural insecticides or herbicides , Surfactant, different type of drug, Salt, ionic liquid, carbohydrates, acid, base etc. [1,7]

1.1. Biologically active molecule and living organism:

So a biologically active compound may be a compound that has a control on a living system, tissue cell. In case of nutrition, biologically active compounds are different from the essential nutrients. It is well known fact that nutrients are very much essential to our body, but the biologically active compounds aren't essential since the body will operate properly without them. Bioactive compounds will shows an Associate in nursing influence on health.[2-4] The branch Biochemistry define the biological activity of a substance incontestable in the living organisms. The biologically active substances area unit often from biological origin. Biological activity characterizes the biological effectiveness of a substance and describes the changes caused by biological material like hormones, vitamins, Enzyme and coenzyme, different type of drug molecule, etc.[5-7]

1.2. Technique for study the different types of interaction:

Different type of molecular interaction taking place between biologically active molecule and the living cell is our area of interest. Biological activity or molecular structure and physical properties will be investigated by viscometric volumetric method in aqueous medium. Some spectroscopic properties also done like infrared analysis, spectrofluorimetry, colorimetrical check, thermal analysis, UV-VIS spectrophotometry, negatron magnet resonance, catalyst activity, etc., area unit suggested for the quantitative and qualitative determination of chemical and organic chemistry compounds, their metabolites, and degradation product.[8-16] Biological activity (e.g., mutagenicity, cancerogenicity, teratogenicity, inhibitionof catalyst activity,toxicity) Each compound possesses varied biological activities. All the

actions and its participation within the biological, physiological and metabolically pathways despite the distinction within the experimental conditions are included in the the biological activity spectrum of a compound.

Provided that the changes in the gender, age, categorical species, and also the participation within the metabolic processes and pathways etc. area tumble down. Biologically active compounds will impart a net remarkable effect on the body whether it is suitable or harmful to our body, so within the body that will impact on the physiological condition in living system. Some of these type of compound are taken into research in medicinal chemistry in order to curing of cancer, heart diseases, gout, scurvy and many other different type of diseases. Our area of interest is focused on some biologically active compound that we come contact in in our daily life. Like numerous drug molecules, some food additive, food color, food preservative, surfactant present in detergent or soap or in tooth paste etc.[14-16] Since the study of interaction protein molecule with the bio active molecule in the living body is very much complicate. So the study of viscometric and volumetric, acoustic property, spectroscopic property, refractive index, conductivity measurement, surface tension value, rheological property etc. of these bioactive molecules with such amino acid in Aqueous media is a simple way to understand the all type interaction taking in between them. Water is taken as the sovent media in such cases, the logic is that water has high dielectric constant and human body (contain roughly around 60% water) or plants body mostly made up of water. So it is more justifiable that the interaction may be taking place in the aqueous media in the body. These type of study is very reliable and give us the deeper insight about the solute- solute or ion-ion, solute- solvent or ion-solvent, or solute-cosulte interaction.[17-24] In addition to this, it is also helpful for knowing the which type of interaction will predominate in the solution like Hydrophilic-hydrophilic or hydrophilic-hydrophobic or hydrophobic-hydrophobic. So the introductory part of my thesis mainly deals with the different type of amino acid interactions with ionic liquid, surfactant ,drug molecule, antioxidant, food additive ,some mild stimulating alkaloid present on the drinking beverages etc. In addition to this some application part and the solvation phenomenon including various type of interactions occurring in solution phase like solute-solute or ion-ion interactions and solute-solvent or ion-solvent interactions is discussed. In order to understand the different interaction takes place between the protein molecules with this biologically active substance we have to know about the amino acid and its function in living

organism and there after some of the biologically active molecules function and importance will be discussed later in this introductory chapter.[25-32]

1.3. Amino acid as a building block of the protein:

Amino acid is one of the most important and crucial substances for the all living bodies which made up of protein. Protein molecules have complex structural arrangement that contain four type of structure primary, secondary, tertiary and quaternary structure. Primary structure made up of specific sequence of various α-amino acid making the polypeptide chain. α- amino acid amino acid obtained from the primary structure by the hydrolysis of protein with enzymes or mineral acid by the following sequence.[32-38]

$$\boldsymbol{protiens \rightarrow Proteoses \rightarrow peptones \rightarrow polypeptides \rightarrow simple\ peptide \rightarrow \alpha - amino\ acid}$$

The secondary structure is consist of polypeptide chain form the H-bonded α-helix structure and means of some subunits (consist of polypeptide chain)and their spatial arrangement with respect to each other in an aggregate protein molecule. Best known example of a protein having quaternary structure is hemoglobin which transport oxygen from the lungs to the cell and carbon dioxide from cell to the lungs. Following figure 1.1 shows all types of structure of amines.

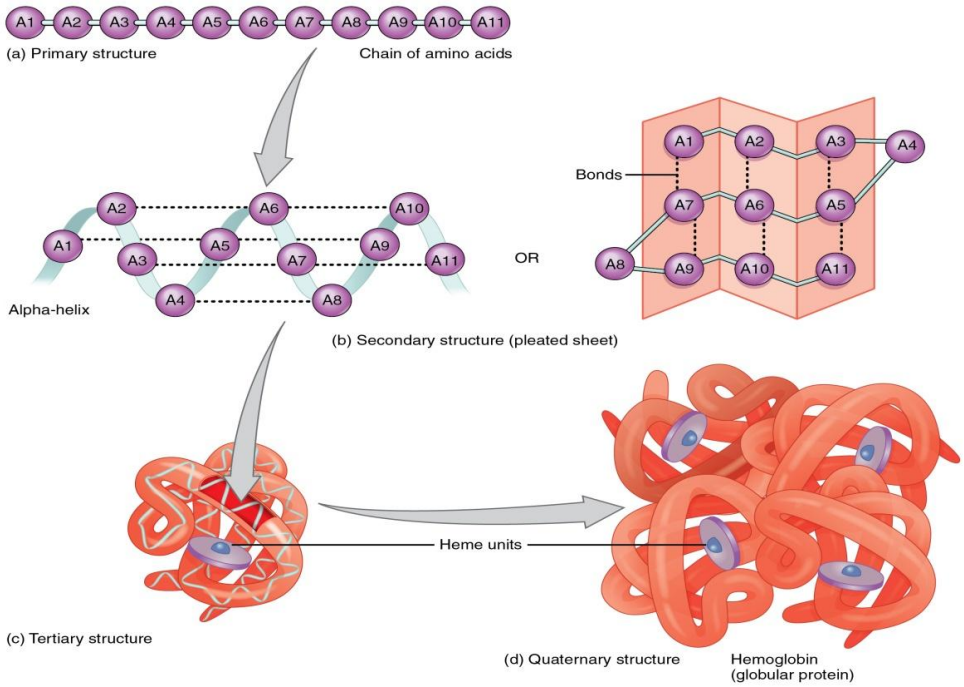

Figure 1.1. *3d view of four type of structure exist in the amino acid*

So it can understood from the above information that if we examine the interaction of amino acid in the aqueous solution with other cosolute of biologically active molecule it will provide us overall idea about the interaction taking place in between proteins with the such bioactive molecules in more simpler way . Because proteins are very much sensitive towards temperature and change in the *p*H which result into denaturation of protein. However in denaturation of protein all the structure collapsed but primary structure remain intact and protein lost it biological activity. This is reason why we take amino acid as a representative of the living organism and considered that the interaction taking place in between amino acid and bio active molecules are supposed to be same as like in living body. This is the main fundamental of the study.[33-40]

1.3.1. Types of amino acid and their need for living body

Our body desires as a net twenty completely different amino acids to grow and perform the biological activity. These all are square measure vital for our living human body, Among which only nine amino acids categories as essential amino acid. These are listed as leucine, isoleucine, valine, methionine, tryptophan, threonine, lysine, histidine and phenyl alanine. Non essential amino acids are produce in our body but the essential amino acids not produce by living body. So there should be only one option that it must consumed through our diet. Animal proteins like meat, eggs and poultry are the best sources of essential amino acids.[51,84]

Histidine: This essential amino acid is employed to provide aminoalkane, a neurochemical that's very important to response, digestion, sleep-wake cycles. It have a crucial role for maintaining the sheath, a protecting barrier that surrounds our nerve cells. Histidine metabolizes in Living body into histamine, which is play a vital role in case of body immunity build up, reproductive health, and digestion.

Valine: It is one amongst 3 branched-chain amino acids that helps to stimulate muscle growth and regeneration and is concerned in energy production.

Threonine: This essential amino acid may be a principal a part of structural proteins like albuminoid and scleroprotein, that square measure vital parts of the skin and animal tissue. It conjointly plays a task in metabolism and immune system . It metabolize fat of our body and may be beneficial for people who suffering from indigestion, anxiety, and mild depression.

Tryptophan: This essential amino acid has several alternative functions. It's required to keep up correct balance and may be a precursor to monoamine neurotransmitter, a neurochemical that regulates your appetence, sleep and mood.

Phenylalanine: This essential amino acid may be a precursor for the neurotransmitters amino acid, dopamine, adrenaline and monoamine neurotransmitter. It also plays vital role within the structure and performance of proteins and enzymes and also the production of alternative amino acids. Phenylalanine facilitate the body to use other amino acids as well as proteins and enzymes. The body converts phenylalanine to tyrosine, which is necessary for specific neuro-function.

Phenylalanine deficiency, though rare, can lead to poor weight gain in infants. It may also cause eczema, fatigue, and memory problems in adults. In diet sodas Phenylalanine is often used as artificial sweetener. If excess amount of aspartame consumed then it can increase the levels of phenylalanine in the brain which may results into anxiety and jitteriness and insomniac disorder .

Phenylketonuria (PKU) is genetic diseases where patient unable to metabolize phenylalanine. So they should avoid consuming diet that contain high levels of this amino acid.

Leucine: Leucine may be a branched-chain organic compound that is crucial for macromolecule synthesis and muscle repair. It conjointly helps regulate blood glucose levels, stimulates wound healing and produces growth hormones.

Methionine: essential amino acid plays a vital role in metabolism and detoxification. It's conjointly necessary for tissue growth and also the absorption of metallic element and chemical element, minerals that square measure very important to your health . Methionine keeps the nails strong of our body. It will help in absorption of selenium and zinc and the excretion of heavy metals, like lead and mercury.

Isoleucine: This branched-chain amino acids, is helps us in muscle metabolism and is heavily focused in muscle tissue. It's conjointly vital for immune system, hemoprotein production and energy regulation. It will shows it activity during healing of wound, blood sugar level maintain to optimum, and in hormone production. It is primarily present in muscle tissue and regulates energy levels. Older adults are found to be more isoleucine deficiency than younger people. This will results into muscle wasting and shaking.

Lysine: Lysine plays major roles in macromolecule synthesis, internal secretion and catalyst production and also the absorption of Calcium. It's conjointly vital for energy

production, immune system and also the production of albuminoid and scleroprotein.[31-34]

Though amino acids play versatile role in our body but moslty it recognized as a muscle developer and repairing the muscle in the body. That's why deficiencies of these amino acid will negatively impact our whole body as well as our central nervous system, procreative, immune and biological process systems. Tryptophan is required for the assembly of monoamine neurotransmitter, a chemical that acts as a neurochemical in living body.Serotonin is a vital regulator of mood, sleep and behaviors. Except thsese many other non essential amino are present which are contribute their role in order to sustain and growth of life in the living organism.

In this research work interaction of the drug molecules are also studied since without it living body can`t survive the diseases. So the Interaction as well as side effect and how to minimize the side effect by using some techniques so called "control drug realize" is very important. The net effect of the drug molecule on the living body can be understood by using some spectroscopic technique and conductometric or volumetric study can be done in aqueous media. So in order to understand that how the drug molecule impact on the living body, it obvious to know about the importance of the drug molecule.[41-48]

1.4. Necessity of Drug for sustaining the life:

Chemical substances that occurred naturally or produced by the synthetic way have the ability to curing the diseases and reducing pain are known as medicine or drug. However, there is a distinction between the term drug and medicine. Medicine is a chemical substance that cures diseases is safe to use and has negligible toxicity and does not cause addiction whereas drug is a chemical substance which also cures the diseases but it habits forming causes addiction and has the serious side effect[48-56]

1.4.1. Classification of drugs:

Drugs may be classified in several different ways some of these are discussed below.

1) Based on pharmacological effect 2) based on drug action 3) based on chemical structure.4) based on molecular targets.

1) Based on pharmacological effect: Every drug molecules have a specific effect on the human body. Like analgesic reduce or kill pain while antiseptic either kill or arrest the growth of microorganism. in this way different types of drugs are classified in this category.

2) Based on drug action: Drug molecules have a specific action on a particular biochemical process based upon this fact the drug molecules classified in this category. Like antacid reduces the acidity and antihistamine stop the secretion of histamine.

3) Based on chemical structure: Drugs that have some type of structure will show the same type of physiological effect.

4) Based on molecular targets: Drugs undergo interaction with the biomolecules for a biologically active compound like protein, carbohydrate, lipids, and nucleic acid. That is why are biologically active molecules are supposed to be targeted molecules for a drug.[57-60]

1.4.2. Drug interaction with biologically active molecules:

Drug molecules interact with the biologically active molecules by a different type of techniques and mechanisms. E.g. enzymes are made up of Amino acid is plays a crucial role to digest the food by a lock and key mechanism. Drug molecule Docking with the active site of the enzyme so the activity of such enzyme will be hindered. Some drugs do not bind to the active site of the enzyme but bind to a different site of the enzyme which is called the allosteric site. The binding of the drug at the allosteric site changes the shape of the active site of the enzyme in such a way that the natural substrate cannot recognize it and the function of the enzyme towards substrate will diminished. These are categorized as enzyme inhibitor drugs.[61-66]

Drug molecules are designed in such a way that they are combined with a specific target. Like there are two types of adrenergic receptors called Alpha-adrenergic receptors and beta-adrenergic receptors. These receptors differ slightly in the structure of their active site but still can bind epinephrine. Alpha-adrenergic receptors are present in large amounts in Tissue and beta-adrenergic present more in the heart. So a drug if designed for beta-adrenergic then it will cause more effect on the heart than tissue. Drugs show some side effect due to binding of it more than one type of receptors present in the body. Different type of drugs and their importance are discussed below.[66-72]

1) Antihistamine: Some people show hypersensitivity towards drugs dust pollen grains, far, fabric, it is known as an allergy that causes itching in the body and

sneezing by the release of histamine. Brompheniramine, terfenadine, promethazine, etc. use as an antihistamine drug to reduce allergic problems, vomiting, nausea, etc.

2) Tranquilizer: Iproniazid, phenelzine, Equanil, serotonin, etc are used for the treatment of stress fatigue coma mild and severe mental disease are considered as a tranquilizer. it is also known as an antidepressant drug.

3) Analgesic drug: Aspirin, Paracetamol is the most important example of a non-narcotic pain reliever. These drugs are quite effective in relieving skeletal pain such that due to arthritis.

Whereas morphine, Codeine, heroin are considered narcotic drug which may be addictive.

4) Antimicrobial: These types of drugs are used to cure a disease caused by microbes or microorganisms bacteria viruses fungi etc. Salvarsan, prontosil sulphanilamide are these types of drugs.

5) Antipyretic: Drugs that are used to reduce the body temperature during high fever are called antipyretics. This drug when applied to the patient, they get excess sweating. Paracetamol, Aspirin,novalgine are the well-known example of these type of the drug.

6) Antibiotics: This type of drugs in its low concentration either kill or inhibit the growth of microorganism by intervening their metabolic process. Penicillin Is a very effective drug for pneumonia, Bronchitis, sore throat. Another example is aminoglycoside ofloxacin.

7) Sulpha Drug: Those drugs which are derivatives of sulfanilamide are called sulfur drugs.

8) Antifertility drugs: Drugs that are used to stop the pregnancy in a woman are called antifertility drugs or oral contraceptives. this controls the female menstrual cycle and ovulation. Mifepristone is a synthetic steroid that blocks the effect of progesterone and is used as an antifertility drug. Others are Norethindrone,novestrol used for the same purpose.

9) Gastro-resistant: Rabeprazole, omeprazole, Lansoprazole, cimetidine, ranitidine are types of drugs that can restrict the secretion of pepsin and hydrochloric acid. The working function of these drugs is supposed to prevent the interaction of the histamine with the receptors present in the stomach wall.

10) Allopurinol is a remarkable drug that was used to cure gout of the mid of twentieth century to the present. It blocks the production of uric acid.[73-79]

1.5. Enzymes as biologically active substances:

A biological reaction like digestion takes that place in the stomach are catalyzed by some special catalyst these are known as enzymes. For every type of food, there is a specific enzyme are present in our body, e.g protease for protein, urease for urea, amylase for starch, etc. Chemically all the enzymes are found to be the globular type of protein. Some of the enzymes are also contained some non-protein components called cofactor for their activity. Factors are two types 1) inorganic ions such as Zn2+, Fe2+, Cu2+,Co2+, Mo3+, K+, Na+ ,etc.

2) organic molecules, these are again are also two types (i) coenzymes and (ii) prosthetic group. It can be easily separated from the enzyme by dialysis which is loosely bound to the protein molecules. Whereas prosthetic groups are tightly held to the protein by the covalent bond but can be separated by careful and controlled hydrolysis most of these are also derived from vitamins like biotin. Protein cofactor complex is called holoenzyme wilder inactive protein part that left after the removal of the cofactor is called apoenzyme. A small amount of the enzyme required for the body for perform specific functions in the body. For every biochemical reaction, there must be a certain specific enzyme required. A large number of enzymes functioning in the living system to sustain life.[67-69] A rough estimation of nearly about 3000 catalyzing different reactions present in a particular typical cell. Enzymes are also used in industry for the production of sweet syrup from corn starch, in the manufacture of wine from carbohydrate fermentation. The milk industry also uses enzymes to produce cheese from the milk. So the enzyme plays important role in our living system which cannot be ignored. The deficiency of different types of such enzymes causes diseases formed in the body in the human body. Like PKU(phenyl ketone urea) due to deficiency of an enzyme called phenylalanine hydroxylase which required for converting phenylalanine to tyrosine. Due to the deficiency of this enzyme, the other is ions present in the cell convert phenylalanine to phenylpyruvate in terms accumulated in the bloodstream can cause severe brain damage and mental retardation. Another type of deficiency is “albinism” due to the deficiency of the tyrosinase enzyme that Will impact the skin color of the human and animal. Because enough Melanine is not produced by the body in that time and the body turns into white.[80-86]

1.6. Vitamins and their importance for sustainable lives:

Vitamins are another type of biologically active compound that is required every day in our diet to sustain the biological process that takes place in the living body. Vitamins are biomolecules that cannot be produced by the body and must be intake through our diet to execute specific biological functions for the life growth and health of the Living Organism. Vitamins Never produced any type of energy in the cell nor build any tissue for the cell but still, it plays a key role to keep good health for living beings. Some of the vitamins like vitamin D vitamin A are produced in the human body but most of the vitamins cannot be synthesized by the body so they can be intake from the outside of the body through diet. But plants can synthesize all vitamins.[154]

vitamins are broadly classified into the following two categories one is called water-soluble (B1, B2, B3, nicotinic acid, Ascorbic acid or vitamin c, etc)and another as fat-soluble vitamins(A, D, K, E). Since our present work deals with water. So we take only water-soluble vitamins for investigation. some of the important vitamins are discussed below.[73-74]

1) Vitamin C: These water-soluble vitamins prevent different types of infections and contribute to a healthy immune system. It also helps the body to absorb the iron that a necessary component to carry oxygen through blood cells. Deficiency of these may cause scurvy diseases.

2) Vitamin D: This is fat-soluble vitamin promotes the absorption of calcium in the body and will make it important for bone health and development. It also helps to reduce inflammation and improve our immune system. Deficiency of it causes rickets diseases.

3) Biotin: It sustains health by increasing the absorption of carbohydrates with protein and fat from food. It helps to keeps our hair growing and makes bones healthy and strong.

4) Folic acid: It mainly helps us to produce fresh red blood cells, thus it stop the diseases called anemia.

5) Vitamin E: It has functioned as an antioxidant and helpful to protect the cells from different types of damage. Vitamin E plays a critical role in fights against critical diseases like cancer and Alzheimer's. It sustains the immune system by preventing different infections and fighting off viruses, bacteria.

6) Vitamin K: It is very much important for blood clotting. It also improves bone health. It can minimize the risk of osteoporosis and some heart diseases.

7) Vitamin A: This fat-soluble vitamin stimulates healthy eyesight and skin development. It also supports bone and tooth growth. In addition, vitamin A supports the immune system and is important in the reproductive process. It also enables the heart, lungs, kidneys, and other physiological organs to operate properly.

8) Vitamin B12: It improves the nervous system of the living body and thus helps our body to produce fresh cells. It also minimizes the risk of heart disease.[87-93]

1.7. The function of nucleic acid and its importance:

It is now an established fact that the nucleus of a living cell is primarily responsible for the transmission of genetic characteristics from one generation to the next . The chromosome that presents in the cell is responsible for heredity which is made up of protein and nucleic acid. Nucleic acid is two types deoxyribonucleic acid or DNA and ribonucleic acid or RNA. A nucleic acid that made up of a repeating monomeric unit of nucleic acid which is known as a nucleotide. nucleotides are consisting of three parts that are sugar molecule (heterocyclic nitrogenous base) and phosphoric acid.

Complete hydrolysis of DNA or RNA gives a mixture of three different compounds viz pentose sugar, nitrogen-containing pentose sugar heterocyclic compounds also called the nitrogenous bases, and phosphoric acid. Two pentose sugar have been isolated. In which DNA contains beta-2-D deoxyribose and RNA contains beta-D-ribose.In addition to this there are two different types of heterocyclic nitrogenous base isolated from the hydrolysis of the nucleic acid these are purine and pyrimidine. The most common Purines are adenine and guanine which is found in nucleic acid. The 3 most common pyrimidines are uracil, thiamine, and cytosine. Nucleoside contains only two basic components of nucleic acid that are a pentose sugar and a nitrogenous base. Nucleosides are classified into two categories depending upon the type of sugar present (i) ribonucleoside and (ii) deoxyribose nucleoside. There are five types of bases present in ribonuclease sites are Adenine, guanine, cytosine thymine, uracil. Whereas nucleotide contains all three basic components of nucleic acid, phosphoric acid group, a pentose sugar, and nitrogenous base.[94-100]

1.7.1. Structure of nucleic acid:

It has two levels of structure one is primary structure and the other is secondary structure. primary structures are the sequence of four nitrogen bases that are attached to the sugar-phosphate backbone of a nucleotides chain. secondary structure can be understood by the chargaff`s rule. It states that the base composition in DNA Varied from one species to other but in all cases, the amount of adenine was equal to that of

thiamine(A=T) and that of cytosine was equal to that of guanine(C=G). Watson et. al from their studies proposed a double-helical structure for DNA. According to this model, DNA consists of two right-handed polynucleotide strands or chains. These two helical chains are attached to each other by H-bonding taking place between adenine (A) with thymine(T) and guanine (G) with C(cytosine).

The biological function of nucleic acid: 1)Replication is the process by which a single DNA molecule produces two identical copies of itself,2) protein synthesis is another important function of DNA. Actually, proteins are synthesized by RNA molecules in the cell but the message for the synthesis of a particular protein is encoded in DNA there are three types of RNA molecules that take part in the protein synthesis. These are messenger RNA(m-RNA), ribosomal RNA (r-RNA), and transfer RNA (t-RNA).[131,101-103]

1.8. Carbohydrates and key role the as bioactive molecule :

I. Carbohydrates are considered as a main source of energy for functioning biochemical processes in the living system and act as a bio-fuel. Maintaining the blood sugar level is another important role of carbohydrate.

II. Since carbohydrates are present and act as the main source of energy it prevents the proteins not to burn for producing energy.

III. In the case of fat metabolism it shows its presence to metabolize the fat.

IV. Carbohydrates are also used as an artificial sweetening agent. Sucrose and Fructose are examples of such which used in our daily life.[4] Other examples are sucrose which the trichloro derivative of the sucrose is 600 times sweeter than sucrose. L- sugar is another type of carbohydrate that is sweet in taste. One Interesting fact is that they did not have any calorific value because our body does not have any such enzyme to metabolize these sugars.[50] So it is very much useful for or diabetes patient to maintain their blood sugar level. it is also used in making diet soda, diet food, diet sweet, etc. The role of carbohydrates as a dietary fiber cant be ignored.

VI. carbohydrates drive the biological process in the living body.[104-106]

1.9. Role and effects of Solvent on the physiochemical processes :

It was well known fact that most of the physiochemical and biological processes occur in solution phase. So the Solvation phenomenon plays a key factor in chemistry, biochemistry as well as in biology. The impact of the solvent in physiochemical reactions is very important and hence numerous researchers from

both experimental and theoretical grounds associated with chemistry or biochemistry has shown their interest from the last decade to present. The results of any chemical reaction is get altered by the addition of requisite amount of solvents through the different possible interaction taking place with the local surroundings. In addition to this this interaction also takes place with the individual reactants molecules that take part in the reaction. The physical barrier that associated with motion of such reactive species and the energy path that need to stabilize the energetic products yield in the respective reactions. These can be also understood by the interaction knowledge provided by the solvents. It was found that the solvent also distress the potential energy curves of these type of reactions. As the solvent species surrounding a solute molecule can form a solvated structure that can control the result of any biological or chemical phenomena, the solvent species play an key role in the chemical or biochemical reaction. In atmospheric phenomena and biological process the solvation has found to be a driving factor in diverse areas that is well established fact. In living body, solvated ions may also appear in larger amount where their absence or presence can fundamentally distorted the life functions.[107-109] Solvation of ions in aqueous mixtures or any organic solvents are also very common and the changing of solvent molecules which surrounded the ions in solutions is important to know about the reactivity of ions in related respective solution. Since conductivity of electrolytes is very much related to the ion-solvent interactions, so the solvated ions can govern the electrochemical applications ,such as in cell or battery industry, extraction of metal by electro chemical process, neuro chemical drug etc. It is obvious that maximum no. of the chemical reactions are proceeds in solution medium and so solvents can simply govern the reactions in a numerous way. In a reaction or any type of physiochemical process solvents can act as a reaction medium in which reactants molecules are solublize to proceed the reaction further. Solvent can act as one of the reactants and convey the dissoluted solutes to bring about the chemical components together in solution phase in the requisite amounts and make the reaction to becomes feasible.

In some thermo chemical process both in exothermic and endothermic case, the vital parameter i.e. temperatures, are also affected by the solvents selection. In an endothermic reactions, heat is supplied by a external heated inert solvent having high heat capacity, while in exothermic reactions boiling the solvent or absorbing heat can minimize the surplus heat. Most of the solid reactants do not react in the solid phase it requires medium which will provide homogenous reaction phase (*i.e.*, solution).

Solvent in such case plays the role homogeneous medium to bring the solid reactants come into contact with each other to yield the product. So, it is very much important to select an appropriate solvent to get most fruitful outcome or expected yield of the products. The characteristics of a ideal solvent is that it can fulfill all the required criteria. Such as for any type of reaction conditions it is necessary to remain its presence as an inert and must have an appropriate boiling point , thereafter at the completion of the reaction there should not occur any kind difficulties during its removal. It must have the ability to dissolve all the reactant species and reagents. The reaction rate are also govern by the differential solvation taking place in the the starting materials and transition states made by the sovent. When the reactant molecules proceed towards to the transition state, the solvent molecules may arrange themselves in such way to stabilize the respective transition state. The reaction rate is high and are found to proceed faster if the transition state is seen to be stabilized to a greater extent in respect of the starting material. On the other hand, the reaction rate will be smaller and reaction may be slower if the transition state is stabilized to a lesser extent than the starting materials. However, re-orientation and quick relaxation of solvent is needed for such differential salvation to came back in the ground from the transition state and the results of a reaction is found to be impact by the equilibrium solvent effects.[110-114]

1.10. Solvation consequences of solute molecules

Solvation of solute molecules is the process in which solute molecules are surrounded by the layer of solvent and form a wrapper over the every dissolved solute molecules. These wrapper or shell of solvent molecules are may be tightly bound or may be it loosely bound the solute molecules depending upon the nature of the both solute and the solvent. Intermolecular forces between the solute molecules and the solvent molecules responsible for such formation of solvent shell or solvent wrapper. During the solvation process only small fraction of solute get dissolved in comparatively excessive amount of solvent. So formation of a homogeneous phase takes place by different type of intermolecular interaction or attraction such as solute-solute, solute-cosolute and solvent-solvent interactions in the respective solvent medium. When the dissolution of the solute in the solution going on then with the increase in concentration of solvent, it was found that solute-solute interactions disappear slowly. So the solute-solvent interactions will dominate over the solute-solute interaction. The solute molecules agitate the solvent structure when they

dissolved into the solution and this will out-turn into the emergence of some solvation wrapper or salvation shell (moderate order in nature) around them formed by the solvent molecules. It was found thermodynamically that the dissolving process becomes spontaneous if the decreasing in the free energy obtained from the salvation process of the solute is higher than the rising in free energy due to demolition of the different type of interactions among the solute the solvent molecules.[115-118] When the lattice energy is greater than release solvation energy then the overall process of dissolution is supposed to be endothermic and but if the lattice energy is smaller than the solvation energy then the overall process must evolve as exothermic.

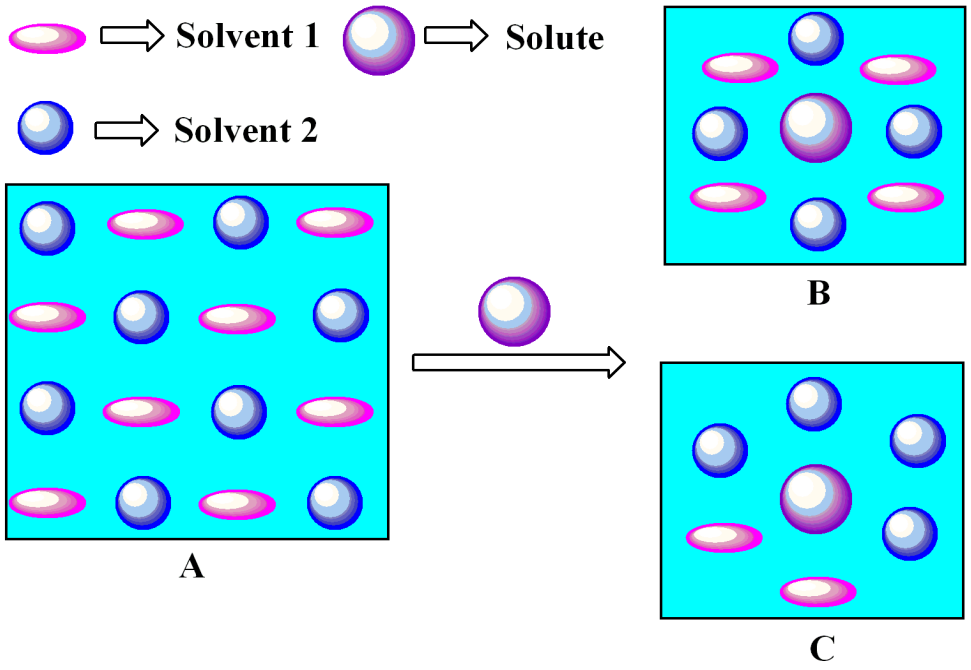

Fig. 1.2 Schematic representation of preferential solvation, A: binary solution mixture of solvent 1 and 2; B: ideal solvation; C: preferential solvation by solvent 1.

1.10.1. Preferential Solvation in solvent mixture:

The solvation mechanism for binary, ternary, etc, solvent mixtures is very much complicate in nature than that when taking place in pure solvents. The different types of interactions takes place in the solvent mixtures plays a significant role in the solvation phenomena, In addition to the different types of solute-solvent interactions. As a result there is a large deviation is perceived from the ideality according to the Raoult's law. Solute makes an remarkable difference in the composition of solvent mixture in sovaltion shell than that of the bulk composition.[119-122] This may referred as preferential solvation or selective solvation which diagrammatically represent on

the in Figure 1.2. Preferential solvation mostly found due to two type of solute-solvent interactions one is nonspecific (dielectric enrichment) and specific (hydrogen-bonding). It may be expressed as a outcome of solvent-solvent interactions in a solvent mixture.

1.11. Ion-Solvent or Solute-Solvent Interaction takes place in salvation process

In the present day various branches of chemistry basically deal with the solvation process of a solute by solvent molecules like formation of complex or synthetic chemical processes, *etc*. Solute-solvent or ion-solvent interactions is playing a vital role to regulate the chemical equilibrium and the rate of chemical reaction, *etc*., So that a portion of chemistry get involved with the solvation of ions or solutes and its origin may explained in terms of solute-solvent or ion-solvent and solvent-solvent interactions. In order to understand more clearly that if the structure of the solvent molecule is distorted or changed by the added solute it is very much important to know their interactions in the solution. It was found that the reactivity of a chemical reaction is mostly increase by the preferential absorption of solute particle of reactant molecule and the transition state through a specific or non-specific solute-solvent or ion-solvent interactions. During the solvation process altering in energy of the transition states are very much important. In order to know the solute-solvent or ion-solvent interactions more appropriately, research on the nature non-electrolytes solution and electrolytes solution in their binary mixtures of solvents and pure solvents have drawn attention in nowdays.[123-129]

During the solvation of the electrolytic molecules having neutral charge, the Ionic Solute and solvent interactions can be expressed more appropriately by knowing the interactions between the solute (ion) and the solvent molecules. Solvent having a ability to govern the inter-ionic forces in the ionic crystals. The inter ionic forces may be decrease to a extent that the moving ions are formed in the mixture due to independent transnational motion and considerable energy of these interactions that are summarily termed as ion-solvent interactions. Figure 1.3 represents the solvation of an ionic crystal by the exertion of a solvent.

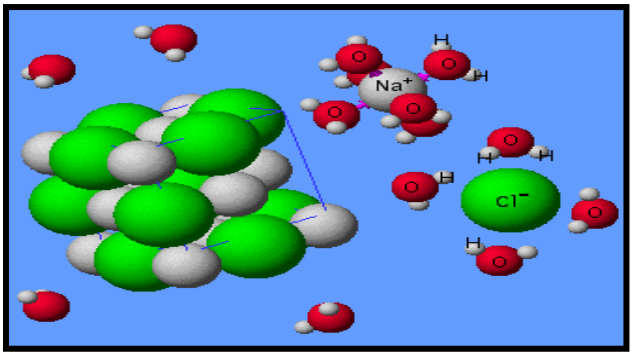

Fig. 1.3. Ionic crystal dissoluted by a solvent.

Ions can have the ability to orientate of the dipoles of respective solvent. Dipoles of the solvent may be rip up by the spherically symmetrical electric field of the ion from the solvent lattice and rearranged themselves with a specific charged end in direction of the central ion. For that cause ion-dipole interaction are considered as one of the main origin of the ion-solvent interactions takes place in the solution. In such cases the solvent molecules considered as electric dipoles and the ions are as point charge. Maximum no of reactions found in solutions are physiochemical or chemical or biochemical in nature. In past century it was considered that the solvent was behave as inert medium in any type of chemical reactions practically having no participation in reaction. But recent research work in aqueous medium found that non-aqueous and mixed solvents media can impart an affect on the ion-solvent interactions.[128]

Based on the association by the hydrogen bonding or acid base properties, numerous no of organic solvents can be differentiated from each other. Other properties like donor-acceptor properties, dielectric constants, organic group types, hard and soft acid-base(HSAB) principles, *etc* may be imply to differentiate organic solvent. Hence it is expected that thermodynamic the transport, acoustic properties, volumetric, viscometric properties of such solvents are very much affected by the existence of numerous electrolytes and non-electrolytes. Therefore the study of the affect of different electrolytes or non-electrolytes on the salvation process and also in their above said respective properties may give valuable information considering the numerous solute-solvent and solute-solvent/ion-solvent interactions.[130-135]

1.12. Ion-Ion or Solute-Solute Interaction in solution

The interactions between solvent and ions are usually associated with the vicinity of the ions in the mixture. It is here mentioned here that in addition to solvent

molecules the other ions are also studied through their surrounding environment. So mutual interaction taking place in between ion-solvent produce a key part of the "ion-ion interaction" between these ions. Ion-ion interactions can affect the properties of the whole solution to different degrees and are determined by the character of the electrolyte being examined. generally, ion-ion interactions are predominant over ion-solvent interactions.[135-138] In aqueous solutions of any electrolyte, ion-ion interactions are can be easily realized theoretically, but the interaction taking place between ion-solvent or ion-solvation very complex for study, and sometimes the small addition of a solute can remarkably changed the structural conformation of the solvent (e.g Water) .

1.13. Objective and application of the Research work

In present days researchers shows much more interest in the the study of physico-chemical properties of solute-solvent systems. In order to understand the miscellaneous intermolecular interactions taking place between components present in the mixture, the physico-chemical properties will provide a valuable information. So Endeavour to explore such behaviors through different type macroscopic and microscopic properties of the solution systems is investigated. Viscometric, acoustic ,volumetric, Thermodynamic, and transport studies are very much precise technique in this regard. Since maximum no. of the chemical and biological reactions found to takes place in solution medium, so the chemical reactions is depending on the behaviors of reactant present in the solutions mixture. Density, viscosity , dielectric constant, refractive index, etc are helpful solvent parameters in order to realization of different type of solvent properties to expressed the solvent effects in the chemical processes. The foundation model of solution is little bit a hard task due to complex nature of intermolecular interactions taking place in solution mixture. Therefore the main models centered on non-directional solute-solvent interactions (like Vander Waals interactions) are mainly applied. Various biological phenomena such as metabolism, transporting, signaling, *etc*., are also affected by the solvation process. Many theoretical considerations were also used to explore influence of the solvent effects on the bulk solvent properties. Onsager and Kirkwood have derived a simple model among all those treatments. There Several theories were proposed in the previous year for calculating the number molecules of solvents associated with respective ions and the number of those solvent molecules liberated to the bulk from the solvation shell during ion-pair development. At the beginning cations of transition

metal have geometrically well-defined first solvation shells. But they live through further solvation into a next concentric solvation sphere with no apparent solvation numbers or solvation sphere and geometries. However due to non-directional electrostatic ion-induced dipole or ion-dipole interactions maximum no. of the ions are get solvated in a marginally well-defined manner beyond the nearest surroundings of the ions. The theory of explaining the affect of the solvent quantitatively and the extent of ion-solvent interactions in solvent phase is needed to properly understand the different type of phenomena in solution thermodynamic chemistry. Partial molar volumes, isentropic compressibility, viscosity *B*-coefficient, refractive index and limiting ionic conductivities, *etc*., are basically used to calculate and realize the ion-solvent interactions takes place in solution thermodynamically.

The solute-solvent and solute-solute interactions have been found to influence in various fields of chemistry. Such type of solute-solvent interactions may guide the sufficient alteration in various chemical reactions accompanied with ions.[139-146] These type of change in ionic solvation are very helpful in various practical problems found in organic and inorganic compound synthesis, waterless battery technology, studies of reaction mechanisms and extraction of metal. Knowledge of such solute-solvent or ion-solvent interactions accompanied with the aqueous solutions have widest utility in diverse areas, such as energy transport, heat transport, mass transport, flow of fluid and the reaction kinetics, *etc*. Hence during the period from past to present a lot of attention has been drawn on the behavior of important biologically active compounds in various aqueous media under various experimental environment to study solute-solvent and solute-solute interactions.

Solution thermodynamics Studies on different types of important biologically active compounds like amino acids, alkaloids, drugs, vitamins, carbohydrates, *etc*., in various aqueous solution can proposed enriched information on various type of interactions in the solution, behavior of Solution and lifespan of numerous biological components. Solution thermodynamic parameters of such biological compounds in various aqueous medium help to understand the solvation process of solute. Researchers are chosen various type of aqueous media that will increase the net effect on these biologically active compounds and their solubility from their physico-chemical properties.[116-122] So the thermodynamic parameters and transport properties studied for such compounds would give us enriched information about different molecular interactions takes place in their respective solutions. Actually it can be said

that features covered a numerous topics but the main focus given towards on the viscometric, volumetric, spectrophotometric, and refractometric studies to explore the physico-chemical behavior of the solvent systems like aqueous media, Structures of solute and cosolute and their specific or mutual interactions in aqueous media or any other liquid phase.

1.14. Significance and span of the Physico-Chemical Parameters

Solvation process of a solute or ion in such a solvent plays an important role in proving solution character and thus solvation phenomena which complex nature, is influenced by the nature of the solvent and solute, *i.e*., their hydrophilic-hydrophobic behavior and molecular structure. Thermodynamic parameter and thermophysical properties are very much useful to know about the non-ideal behavior various complex solution systems. Because the physiochemical consequences evolve from the interplay of numerous molecular interactions or molecular forces amongst the different molecules.[146-148] In order to depict the intermolecular interactions between the different molecule through a study of some physical properties like, refractive index, density, viscosity and conductance, *etc*, helps us to investigate of the physiochemical behavior of the solution mixture. Regarding the practical point of view, these characteristics are very much important for the petrochemical ,pharmaceutical, and food industries chemical industries. Solution viscosity, densities and other related volumetric properties are important for physical and theoretical strands. The density is very much important for the changing of the concentration units and also for the study of the molecular interactions taking place in solute-solvent systems. Density measurement is applied in various fields; it found to be helpful to maintain quality in the production of industrial liquids, it helps in concentration determination in the beverage, soda and food industries, *etc*. Limiting Apparent molar volumes and the limiting partial molar volumes at infinite dilution can also be obtained for the solute-solvent systems provided densities of the mixtures are known. In addition to this the density data is very much important for the explain the properties like viscosity, and molar refractions, *etc*.

Chemical engineering calculations are required for gathering the knowledge of viscosity of the solution mixture where fluid flow, heat transport, mass transport, are the monitoring factors. Viscosity mainly provide info about the flow behavior of any gas and any liquid and it generally alter with the alteration of temperature. In case of solvent system it decreases as the temperature rises and *vice-versa*. Viscosity data helps to know about the nature and strength and extent of forces operating among the different type of molecules in a mixed solution system. Calculation of the viscosity data is very robust tools for a physiochemical researchers, since viscosity or the viscosity coefficient are dependent on the shape & size of molecule and also on the orientation of the molecules in solution phase. So it helps us to explain the ion-solvent or solute-solvent interactions through the measurement of free energy and the related thermodynamic parameters of transfer (like transfer of apparent molar volume) from one solvent to another for a ion or a solute.

Acoustic properties is another important valuable tool for gathering the knowledge about the behavior of various solutes like vitamins, carbohydrates, amino acids, and drugs, *etc*., in aqueous and non aqueous mixtures. At macroscopic level the changes can be understood from the propagation of ultrasonic sound measurement in solutions help to explore the changes in various physical properties. Since the structure and interactions between molecules present in the solution are highly affected by sound velocity, so molecular interactions can be determine quantitatively in the solution with the help of ultrasonic speed of sound.

Refractive index is another vital parameter for determination of the various physico-chemical phenomena of solutes in solution. Solute-solute or ion-ion, solute-solvent or ion-solvent as well as solvent-solvent interactions can be easily derived from the refractive index studies. Refractive index is supposed to be one of the key parameters of a solution and it can easily be measured somewhat more accurately. Molar refractivity helps us to know about electronic polarization of any ion present in solution that depends on the electronic shell arrangements of ions under the influence of the surrounding environment and neighboring ions.

In addition to this a solute-solvent system is more explained by the presence of different electronically excited states of the solvent molecule and solute molecule with considerable electronic interactions. When solvents of separate polarities are imply to record the absorption spectra Solvents found that it can changes the intensities, positions of absorption bands, shapes of the solutes. This effect arises due

to different types of intermolecular solute-solvent interactions present in the solutions, like ion-dipole, dipole-induced dipole, dipole-dipole and hydrogen bond, *etc*. These interactions/forces may lead to alter in the energy gap between excited and ground state of the absorbing species. Hence solute-solvent and the solvent-solvent interactions measured from the absorption spectra of the solutes present in the solutions. Due to this overall fact of discussion, research on the solution thermodynamics of some biologically active compounds in various aqueous medium have undertaken.[149-156]

1.15. Vital role of Solutes and Solvents used

The role of solutes and solvents in a solution mixture is included in this thesis is given below.

1.15.1 Solutes and cosolutes

L-Leucine performs numerous functions in the body. It helps to maintain blood sugar level, improves wound healing, and bring about the growth hormone. But leucine is best known for its role in the muscular system. It build up the muscle in the body and also supposed to repair it when required.

L-proline, is an amino acid. It is non-essential amino acid since body can synthesize it by the breakdown of L-glutamate. It is well known fact that Protein is disintegrate into amino acids the building blocks of protein. L-Proline is an important compound that responsible for repairing the damage tissue, collagen formation, arteriosclerosis prevention and blood maintenance pressure level of the body.

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.[156]

Allopurinol is a drug that is widely used for the treatment of the gout from mid of the last century to till now. It has shows accurate effectiveness towards the gout problem.

Uracil is an nucleobase found in nucleic acid of RNA. It is very useful to body in producing many necessary enzymes for proper functioning of cell in the living body. Uracil has also wide application as an allosteric regulator in the body. It is also found to operating in drug delivery.

Amino acids are the fundamental building blocks of proteins. Salt and some surfactant induced electrostatic forces often modify protein structure by changing the properties like denaturation, solubility and enzymes activity, *etc*. The physicochemical properties of certain salts and surfactant in aqueous solution of

amino acids thus provide valuable data on the solute-solvent and solute-solute interactions. These interactions are valuable to understand the stability of proteins and give information for several physiological and biochemical process that occur in a living body. Hence to get a deeper insight into the hydration of protein and various non-covalent forces that stabilizes the native structure of protein, it is important to detect the effect of such salts and surfactant on the model of proteins compound, simply the amino acids.[156-159]

Caffeine is a alkaloid which bitter in taste and state is white crystalline (purine). It occurs as odourless, glistening needles of fleecy masses. It is found in nature seeds, nuts, fruits and leaves of a number of plants like tea, beans, guarana, coffee, and cola, *etc*. Caffeine has put its role on vasoconstriction and other cardiovascular activities. It can have the ability to inhibit DNA reproduction and this can lead to serious complications for pregnant woman. It may be considered as one of the causes of cancer, ageing and heart diseases. In pharmacology this compound is often used as diet aids, analgesics, and flu/cold remedies.

Cyclodextrins found to protect the compounds from the effects of heat, and light, oxygen. It can be used to reduced volatility of compounds can be give rise the shelf life and reduced liberation of compounds into the environment. Cyclodextrins can be used to removal or isolation of specific compounds from their mixture.[160-162]

1.16. Solvents

Since water is considered as universal solvent system , so the aqueous systems draw the special attention. Such systems are comparatively very simple. Water is not an inert diluents. It possess a unique cluster structure through extensive hydrogen bonds in three-dimension, a large heat capacity and, a high boiling temperature, a high dielectric constant and found many anomalies in its specific volume. Due to its amazing properties it has been considered as a universal solvent in chemical, biochemical and cellular systems. Such as water ionizes and felicitate proton exchange between molecules to renders the affluence of ionic synergies in biological systems. In addition to this it's unique hydration properties towards various biological protein molecules afford the three-dimensional structure of such macromolecules and hence water can govern their functions in the solution.[145-150] Regarding that the preferential arrangement of water around the non-polar and polar parts of the biopolymers (preferential hydration) is very engrossing and informative. Except these interesting water properties, studies on its behavior as a solvent and its interactions

with different biologically active compounds draw extensive attention. Therefore, in this work different aqueous media were used as solvent systems. Cyclo dextrine, amino acids (*e.g.*, glycine and L-Alanine), RNA base like uracil were used as cosolutes for different aqueous solvent systems.[162-165]

1.17. Activity of water as a solvent

Water is universally present in biological systems and related materials and the surroundings. So the hydrophobic and hydrophilic interactions supposed to control the behavior of certain products in presence of water. Its thermodynamic parameter, *i.e.*, the water activity a_w depict that the equilibrium amount of water is available for the solvation of remaining solutes or for their degradation reactions which may be chemical or biochemical. Pure water is depicted by $a_w = 1$, but $a_w = 0$ means total skiving of 'free' water molecule. In order to understand comparison of stability of certain products have the similar water activity (a_w) in such cases knowledge of the water structure is important. Thus hydrophobic and hydrophilic interactions takes place between water and the bioactive molecule like drugs, foodstuff, amino acids, *etc*., and the influence of such soluble molecules on the hydrogen bonds present in the water are very valuable in order to preservation and storage of them. If water activity (a_w) value found to be lower then it stop the growth of the microbes. So by monitoring the water activity (a_w) in packaging food and its related industries is giving more life time to the food. Such effect of water activity (a_w) on the stability of bio-systems, protein, amino acid, carbohydrates, and nucleic acids are well defined.

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

$$\mu_w = \mu_w^* + RT \ln a_w \approx \mu_w^* - RTV_w^*(c/M + Bc^2 + \mathrm{K}) \qquad (1)$$

where μ_w^* = gradient of the chemical potential and V_w^* = the molar 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 second virial coefficient (B) shows the solute-solute and solute-solvent interactions because of non-ideal behavior of the mixture. From the above expression it is clear that why addition of a solute always minimize the water activity (a_w). By rearrangement of the above expression yields:

$$\ln a_w = -V_w^*(c/M + Bc^2 + \mathrm{K}) \leq 0$$
$$\text{or } B > -1/cM \qquad (2)$$

If $B < 0$, water behave as weak solvent and if $B \approx 0$, the solute will separated out as a precipitate from the solution. Hence the second virial coefficient (B) depends on pH of the solution. Biopolymers such biologically active molecules usually have lower value of B; so the large changes of a_w values produces minor effects on the B-values. But for existing biological systems, most of the food products and certain of polymers c is rather large and minor changes in the moisture content leads to a large drop in a_w -values. This type of a large drop in a_w -values affects the overall structure and arrangement of the solution taken under investigation.[163-165]

1.18. Method of Investigation

In order to investigate the solute-solute, solvent-solvent and solute-solvent interaction there are different experimental techniques are employed. Densitometry, Ultrasonic sound measurement, viscometry, volumetry, refractometry and UV-visible spectroscopy were used in the used in the present study and discussed in this thesis.Thermodynamic properties of solutions useful in determining the feasibility of chemical reactions in solution phase and also valuable to investigate theoretical phenomena of solution structure. Thermodynamic properties like apparent molar volume, limiting partial molar volume and partial molar volume of transfer, *etc*., obtained from density calculation which are more convenient parameters for depicting the solute-solvent and solute-solute interactions in the solution. The partial molar volumes and apparent molar volumes of electrolyte solutions are familiar tool in exploring structural interactions (*i.e*., ion-ion or solute-solute, ion-solvent or solute-solvent and solvent-solvent interactions) in solution mixture.[150-158] For electrolyte and non-electrolyte solutions, viscosities property explains their solution behavior. The compressibility factor, a second derivative of Gibbs energy, is reveal that it is very sensitive towards molecular interactions taking place in solution phase. So it can also provide valuable information regarding the partial molar volumes for such interactions. For the electrolyte and non-electrolyte solutions viscosity measure as function of concentration and temperature, in order to study solute-solvent or ion-solvent (solvation) interactions. In addition to this long-range ion-ion electrostatic interactions are also measured. Gradual addition of electrolytes may changes the

solvent viscosity due to inter-ionic and ion-solvent interaction. The viscosity *B*-coefficients will give appropriate explanation of ion-solvent or solute-solvent interactions, *i.e*., the net effects of salvation process, preferential solvation and long range structure-making or structure-breaking ability of the solutes. Refract metric studies also draw the attention on the different molecular interactions that taking place in solute-solvent systems of different compositions. Such studies useful in interpretation of the character of the solutes in various solvent systems. UV-visible spectroscopy also employed to of such solutions in order to explore the interaction and support the results obtained previously from viscosity, Acoustic, density, and refractive index measurements.

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