CHAPTER I

NECESSITY OF THE RESEARCH WORK

1.1. OBJECT, SCOPE AND APPLICATION OF THE RESEARCH WORK

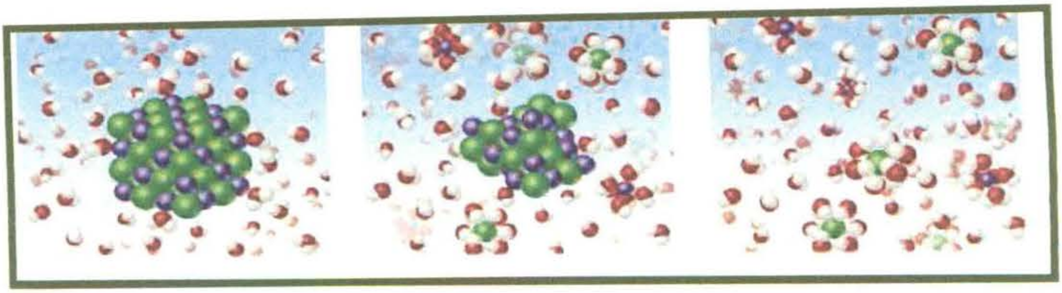
A material is said to be biologically active if it has an interaction or effect on living organism. Pharmacological activity is usually taken to describe beneficial effects, i.e. the effects of drug candidates. The main kind of biological activity is a substance's toxicity. "Bioactive compounds" are extra nutritional constituents that typically occur in small quantities in foods. They are being intensively studied to evaluate their effects on health. Bioactive compounds will reduce the risk of many diseases, including cancer, chronic diseases such as cardiovascular disease. Recent findings have established that cardiovascular disease is a disease of inflammation, and consequently is amenable to intervention via molecules that have anti-inflammatory effects. In addition, research demonstrating adverse effects of oxidants on atherogenesis raises the possibility that antioxidants can confer cardioprotective effects. This review provides an overview of research approaches that can be used to unravel the biology and health effects of bioactive compounds. Because of the number of bioactive compounds and the diversity of likely biological effects, numerous and diverse experimental approaches must be taken to increase our understanding of the biology of bioactive compounds. Recognizing the complexity of this biology, sophisticated experimental designs and analytical methodologies must be employed to advance the field. The discovery of novel health effects of bioactive compounds will provide the scientific basis for future efforts to use biotechnology to modify/fortify foods and food components as a means to improve public health. There is sufficient evidence to recommend consuming food sources rich in bioactive compounds. From a practical perspective, this translates to recommending a diet rich in a variety of fruits, vegetables, whole grains, legumes, oils, and nuts. In the body under physiological conditions, many vital functions are regulated by pulsed or transient release of bioactive substances at a specific time and site. Thus, to mimic the function of living systems, it is important to develop new drug delivery devices to achieve pulsed delivery of a certain amount of a bioactive compound at predetermined time intervals. The ability to deliver bioactive compounds and/or therapeutic agents to a patient in a pulsatile or staggered release profile has been a major goal in drug delivery research over the last two decades. Rice bran has been recognized as an excellent source of bioactive compounds, but only a small amount is consumed by humans. The limitation of using rice bran in a food industry is its rough texture and low concentration of bioactive compounds, when incorporated into food products. Various methods have been developed to enhance the level of bioactive components in food materials, including thermal, alkali, acid and chemical treatments. Many bioactive compounds have been discovered. These compounds vary widely in chemical structure and function. Many biologically active molecules are chiral, including the naturally occurring amino acids (the building blocks of proteins) and sugars. In biological systems, most of these compounds are of the same chirality: most amino acids are L and sugars are D. Typical naturally occurring proteins, made of L amino acids, are known as left-handed proteins, whereas D amino acids produce right-handed proteins. Amino acid serves as a buffering agent in antacids, analgesics, antiperspirants, cosmetics, and toiletries. It is used as a source of energy for muscle tissue, the brain, and central nervous system, in strengthening the immune system by producing antibodies. It has been used as a source for the production of glucose in order to stabilize blood sugar levels over lengthy periods. In sickle-cell disease, valine substitutes for the hydrophilic amino acid glutamic acid in hemoglobin. Because valine is hydrophobic, the hemoglobin does not fold correctly. Ascorbic acid, commonly known as vitamin C, is also able to regenerate other antioxidants as vitamin E. Vitamin C is required for the synthesis of collagen, the intercellular "cement" which gives the structure of muscles, vascular tissues, bones, and tendon. Vitamin C with Zn is also important for the healing of wounds. It is also needed for the metabolism of bile acids which may have implications for blood cholesterol levels and gallstones. Ascorbic acid and its sodium, potassium, and calcium salts are commonly used as antioxidants food additives.Vitamin C plays an important role for the synthesis of several important peptide hormones neurotransmitters and creatinine. It also enhances the eye's ability and delay the progression of advanced age related muscular degeneration [1]. Carbohydrates are an exceptionally important constituent of biological systems. They play an important role in animal and plant physiology. Carbohydrates are sources of energy for essential metabolic process. Water, the most abundant compound on earth, is widely used in chemistry as a universal solvent. The study of carbohydrates in aqueous solutions has become a subject of increasing attention because of the multidimensional physical, biochemical and industrially useful properties in addition to their significance in the food pharmaceutical and chemical industries [2, 3]. Understanding the behaviour of these effects in dilute solutions is of utmost importance in medicinal and biological systems. The pyridine-monocarboxylic acids are examples of amphiprotic electrolytes that are of considerable biological interest. Nicotinic acid (3-pyridine carboxylic acid), also known as niacin or pellagra-preventing factor, is an important compound which play a crucial role in various physiological effects, biosynthesis, metabolic reactions, and several drug preparations [4].

The word "salt" is a general chemical term that refers to ionic compounds formed when an acid reacts with a base. Salt became an essential part of commercial transactions and was often used as money or barter. Today, salt continues to be of major economic importance, with thousands of uses in addition to flavoring and preserving food. Sodium chloride occurs naturally as the mineral halite, commonly called rock salt, in large underground deposits on every continent. Seawater contains about 3.5 percent dissolved minerals, of which 2.8 percent is sodium chloride and the other 0.7 percent is primarily calcium, magnesium, and sulfate ions. Table salt is pure salt that has been ground into fine particles. Because salt tends to cake in humid climates, an anti-caking agent such as magnesium carbonate or calcium silicate is often added. Salt is used to cure meat and fish by soaking them in brine, rubbing salt onto them, or injecting them with a salt solution. Bacon and cured ham are examples of meats preserved by the use of salt. Salt is also used to make pickles by soaking cucumbers in brine. Both sodium chloride and potassium chloride are essential to the electrolyte balance in body fluids. Good health depends on the proper ratio of potassium ions to sodium ions. Typical values are greater than one. Natural, unprocessed foods have high K^+/Na^+ weight ratios. Calcium salt is also the fifth-most-abundant dissolved ion in seawater by both molarity and mass. Calcium is essential for living organisms, in particular in cell physiology, where movement of the calcium ion Ca^{2+} into and out of the cytoplasm functions as a signal for many cellular processes. As a major material used in mineralization of bones and shells, calcium is the most abundant metal by mass in many animals. Lithium salts are chemical salts of lithium used mainly in the treatment of bipolar disorder as mood stabilizers. They are also sometimes used to treat depression and mania. Lithium carbonate, Lithium sulfate, Lithium orotate, Lithium citrate are the most common salts used in this purpose. Lithium is widely distributed in the central nervous system and interacts with a number of neurotransmitters and receptors, decreasing noradrenaline release and increasing serotonin synthesis. Lithium and its compounds have several industrial applications, including heat-resistant glass and ceramics, high strength-to-weight alloys used in aircraft lithium batteries, and lithium-ion batteries. Lithium salt is used in lithium-ion batteries because of its high electrochemical potential. Lithium batteries are not to be confused with lithium-ion batteries, which are high energy-density rechargeable batteries. Other rechargeable batteries include the lithium-ion polymer batteries, lithium-iron phosphate batteries, and the nanowire batteries.

To date, most chemical reactions have been carried out in industrially important solvents. For two millennia, most of our understanding of chemistry has been based upon the behavior of molecules in the solution phase in molecular solvents. Recently, however, a new class of solvent has emerged—ionic liquids. An ionic liquid (IL) is an electrolyte in the liquid state/phase having melting point below some arbitrary temperature, such as 100°C (212°F), which consists of a combination of organic-organic or organic-inorganic cation/anions. Ionic liquid consists of only ions exhibiting non-volatility, high ionic conductivity and catalytic activity. Room temperature Ionic liquids (RTIL) are salts which are already liquid below room temperature [5]. Because of their insignificant vapour pressures, low melting points, good solvent characteristics for organic, inorganic and polymeric materials, adjustable polarity, selective catalytic effects, chemical and thermal stability, non-flammability and high ionic conductivity, ionic liquids have generated significant interest for a wide range of industrial applications [6]. It use as the solvent for extractions and electrolytes for batteries is attracting increasing attention. Ionic liquid is an environmentally friendly reagent for organic synthesis reactions. ILs finds a variety of industrial applications. Ionic liquids are used in Chemical industry, Pharmaceuticals, Cellulose processing, Gas handling, Gas treatment, Solar thermal energy, Nuclear fuel processing, Food and bi-products, waste recycling, Batteries etc.

In addition to having a wide range, ionic liquids have the ability to dissolve in both polar and non-polar compounds and perhaps most importantly, they do not evaporate due to their extremely low vapour pressure and thus, cannot lead to fugitive emissions. The chemical and physical properties of ILs can to some extent, be customized by proper selection of the type of cation and anion that compose the ILs, as well as any substituent groups. Because of their insignificant vapour pressures, low melting points, good solvent characteristics for organic, inorganic and polymeric materials, adjustable polarity, selective catalytic effects, chemical and thermal stability, non-flammability and high ionic conductivity, ionic liquids have generated significant interest for a wide range of industrial applications.

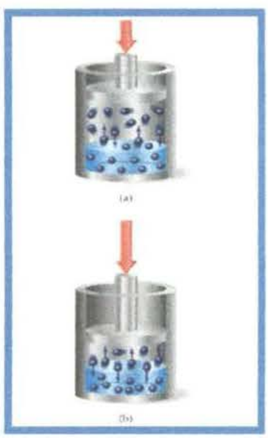
A 'solution' is a homogeneous mixture of two or more substances, consisting of ions or molecules, i.e. when a small amount of substance, called solute (solid, liquid or gas), dissolves to a certain limit in a liquid or solid substance (pure, or a mixture itself) called the solvent. In a solution the solute is dispersed uniformly throughout the solvent and substances must have similar intermolecular forces to form solutions. When a soluble solute is introduced into a solvent, the particles of solute can interact with the particles of solvent. In the case of a solid or liquid solute, the interactions between the solute particles and the solvent particles are so strong that the individual solute particles separate from each other and, surrounded by solvent molecules, enter the solution. The relative force of attraction of the solute for the solvent is a major factor in their solubility.



Solution chemistry is an important branch of physical chemistry that studies the change in properties that arise when one substance dissolves in another substance. It investigates the solubility of substances and how it is affected by the chemical nature of both the solute and the solvent. The mixing of different solute or solvent with another solvent/solvent mixtures gives rise to solutions that generally do not behave ideally.

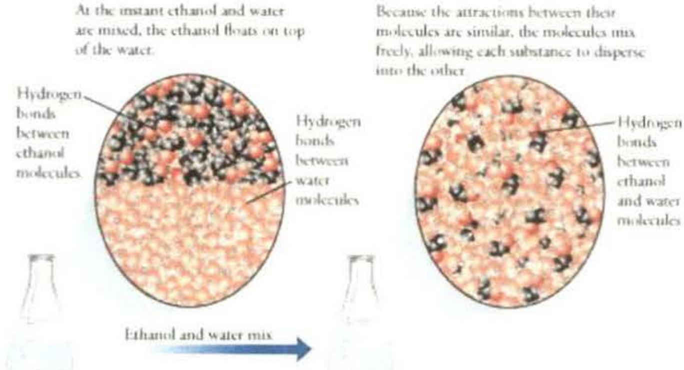
We know matter in three states of aggregation — solid, liquid, and gaseous. Matter in every one of these three states can be dissolved in matter of the same state of aggregation as itself and in both of the other states. Thus, we have solutions of gases in gases, or mixtures of gases which do not act chemically upon one another. The characteristic here is unlimited solubility, the properties of the mixture being the sum of the properties of the constituent gases.

Solutions of gases, liquids, and solids in liquids are the best and longest known types of solutions. Gases dissolve in liquids to only a limited extent, the amount, in keeping with Henry's law, increasing with the pressure to which the gas is subjected. The solubility of a gas in a liquid is directly proportional to its pressure.



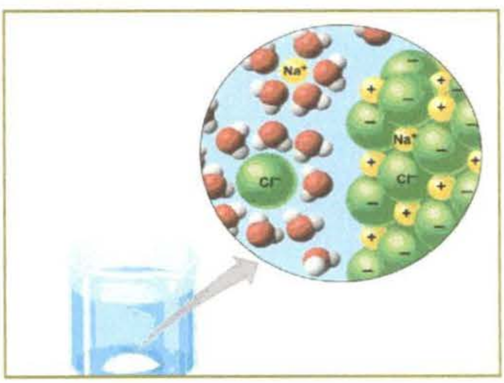
Dissolution of gas in liquid

The presence of intermolecular H-bonding in water and alcohol, after mixing new H-bonding prevails in the mixture due to solvent-solvent interaction. Liquids dissolve in liquids, many of them to an unlimited extent. Liquids which, at ordinary temperatures, have only limited solubility in other liquids, often become infinitely soluble at more elevated temperatures.



Solution of binary liquids

Solids dissolve in liquids to a limited extent, the amount for any solid being a function of the temperature. An ionic solid such as sodium chloride dissolves in water because of the electrostatic attraction between the cations (Na^+) and the partially negatively charged oxygen atoms of water molecules, and between the anions (Cl^-) and the partially positively charged hydrogen atoms of water.



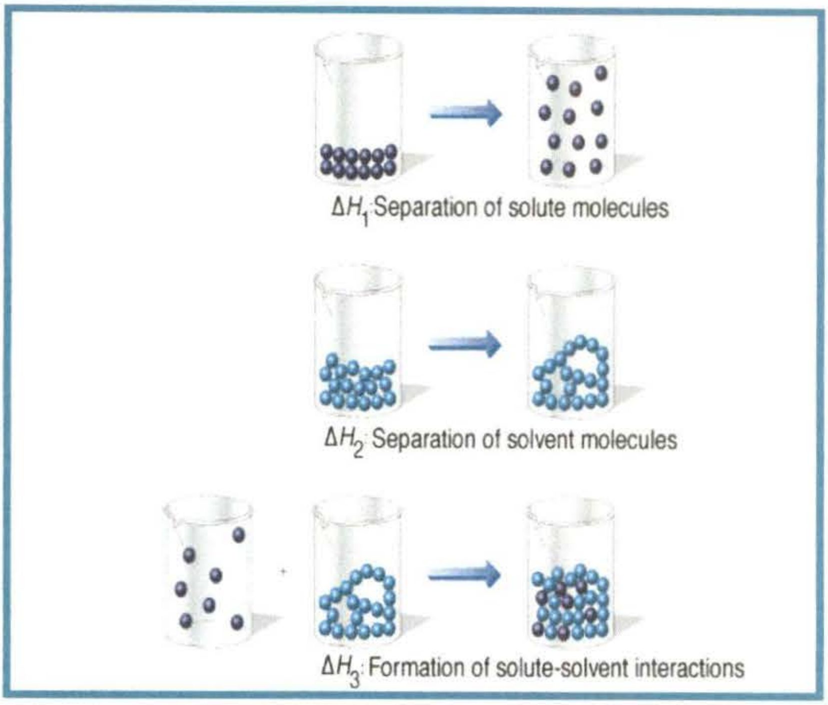
Solubility of solid in liquid

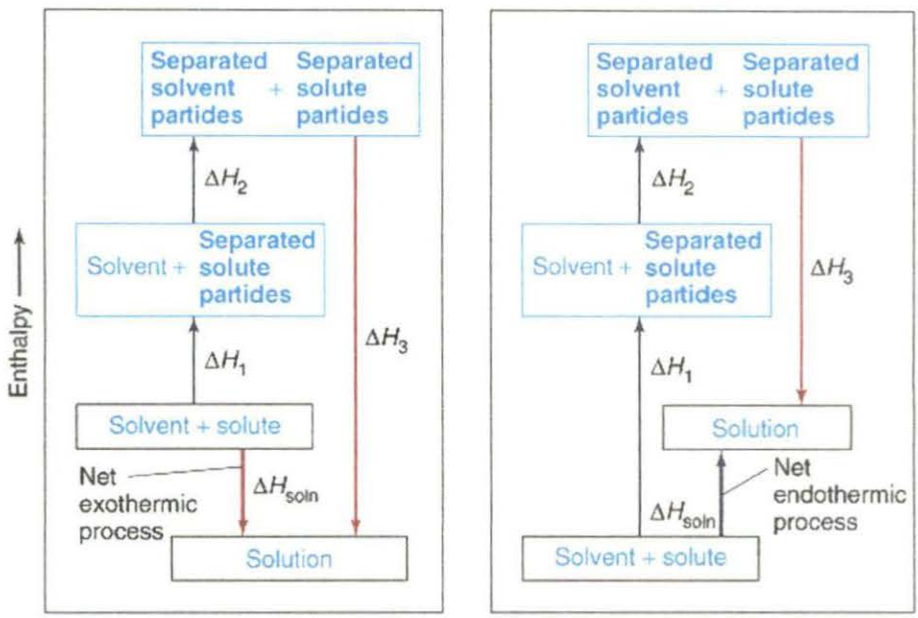
One of the newest and most interesting types of solutions is that of solid in solid. Solid-Solid solutions particularly of metals are sometimes called ALLOYS.

A Brass, a substitutional alloy

B Carbon steel, an interstitial alloy

The process of solubilisation involves the breaking of inter-ionic or intermolecular bonds in the solute, the separation of the molecules of the solvent to provide space in the solvent for the solute, interaction between the solvent and the solute molecule or ion. We understand much of the dissolution phenomenon through its energetic (thermodynamics).





In recent years there has been an increasing interest in the study of physicochemical properties of solvent-solvent [7, 8] and solute-solvent [9, 10] systems. The physicochemical properties play a pivotal role in interpreting the intermolecular interactions among mixed components and efforts in recent years have been directed at an understanding of such properties at microscopic and macroscopic levels. In order to gain insight into the mechanism of such interactions thermodynamic, transport and acoustic studies on binary and ternary solvent systems are highly useful. The excess thermodynamic properties of the mixtures correspond to the difference between actual property and the property if the system behaves ideally. Thus these properties provide important information about the nature and strength of intermolecular forces operating among mixed components. Also physico-chemical properties involving excess thermodynamic functions have relevance in carrying out engineering applications in the process industries and in the design of industrial separation processes.

The properties, both physical and chemical, of a solution (liquid) is a result of the strength of their intermolecular forces and the forces between molecules arises from the same source: differing charges on adjacent molecules that lead to electrostatic attractions and governed by coulombs law. Partial charges acquired by molecules results in dipole-dipole forces, dipole-induced dipole forces, hydrogen bonding, etc and are collectively termed as intermolecular forces. Intermolecular forces in a solution control their thermodynamic properties and the understanding of the solvation thermodynamics is essential to the characterization and interpretation of any process carried out in the liquid phase. These thermodynamic properties are quantities which are either an attribute of an entire system or are functions of position which is continuous and does not vary rapidly over microscopic distances, except in cases where there are abrupt changes at boundaries between phases of the system. Therefore, the studies on the thermodynamic along with the transport properties of a solution would give a clear idea about the nature of the forces existing within the constituents of a solution.

The object of this introductory chapter is to call attention to the significance of solvents and the study made on various interaction prevailing in liquid systems by studying their thermodynamic and transport properties.

The bearing of solution on natural processes was early recognized. It was clearly seen that without solution there would be no chemistry. This was summarized by the alchemists in the terse generalization, "Corpora non agunt nisi soluta,"or in the equally concise, "Menstrua non agunt nisifluida." These generalizations are a little too broad in the light of what was known about solutions at the time when they were written.

In solution chemistry the way for proper understanding of the different phenomena regarding the molecular interactions forms the basis of explaining quantitatively the influence of the solvent and the extent of interactions of ions in solvents. Estimates of ion-solvent interactions can be had thermodynamically and also from the measurement of partial molar volumes, viscosity B - coefficient and limiting ionic conductivity studies. Estimates of single-ion values enable us to refine our model of ion solvent interactions. Acceptable values of ion-solvent interactions would enable the chemists to choose solvents that will enhance (i) the rates of chemical reactions, (ii) the solubility of minerals in leaching operations or (iii) reverse the direction of equilibrium reactions. The importance and uses of the chemistry of electrolytes in non aqueous and mixed solvents are now well recognized.

The importance and uses of the chemistry of electrolytes in non-aqueous and mixed solvents are now well recognized. The applications and implications of the studies of reaction in non-aqueous and mixed solvents have been summarized by Meck [11] Franks [12] Popovych [13] Bates [14] Parker [15] Criss and Salomon [16], Marcus [17] and others [18].

In spite of vast collections of data on the different electrolytic and non electrolytic solutions in water, the structure of water and the different types of interactions that water undergoes with electrolytes are yet to be properly understood. However, the studies on properties of aqueous solutions have provided sufficient information on the thermodynamic properties of different electrolytes and non-electrolytes, the effects of variation in ionic structure, ionic mobility and common ions along with a host of other properties [12]. The behavior of electrolytes or solutes in non-aqueous and mixed solvents with a view to investigate solute-solute and solute-solvent interactions under varied conditions. However, different sequence of solubility, difference in solvating power and possibilities of chemical or electrochemical reactions unfamiliar in aqueous chemistry have opened vistas for physical chemists and interest in these organic solvents transcends the traditional boundaries of inorganic, physical, organic, analytical and electrochemistry [19]. Research on non-aqueous electrolyte solutions has manifested their wide applications in many fields. Non-aqueous electrolyte solutions are actually competing with other ion conductors, especially at ambient and at low temperatures, due to their high flexibility based on the choice of numerous solvents, additives and electrolytes with widely varying properties. High-energy primary and secondary batteries, wet double-layer capacitors and super capacitors, electro deposition and electroplating are some devices and processes for which the use of non-aqueous electrolyte solutions had brought the biggest success [20, 21].

Drug transport across biological cells and membranes is dependent on physicochemical properties of drugs. But direct study of the physico-chemical properties in physiological media such as blood, intracellular fluids is difficult to accomplish. One of the well-organized approaches is the study of molecular interactions in fluids by thermodynamic methods as thermodynamic parameters are convenient for interpreting intermolecular interactions in solution phase. Also the study of thermodynamic properties of drug in a suitable medium can be correlated to its therapeutic effects [22, 23].

1.2. CHOICE AND IMPORTANCE OF SOLVENTS AND SOLUTES USED

Nitromethane, formamide, N-methylformamide, 1,3-dioxolane, methanol, acetonitrile, N,N-dimethylformamide, N,N-dimethylacetamide, dimethylsulphoxide along with water, considered as a universal solvent, have been chosen as main solvent in this research work because these solvents are industrially very important and by mixing these solvents we could obtain a wide variation of viscosities and dielectric constants giving us an optimum environment for the study.

Amino acids viz., glycine, L-alanine, L-valine, carbohydrates (D-glucose, D-mannitol, D-sucrose), ascorbic acid (vitamin C), tetrabutylammonium tetrafluoroborate, tetrabutylammonium perchlorate, tetrabutyphosphonium tetrafluoroborate, tetrabutyphosphonium methanesulfonate, lithium hexafluoroarsenate were considered as solutes.

The study of these solutes is of great interest because of their wide use as solvents, solubilizing agents in pharmaceutical, cosmetics and medicinal industries.

1.3. METHODS OF INVESTIGATION

The existence of free ions, solvated ions, ion-pairs and triple-ions in aqueous and non-aqueous media depends upon the concentrations of the solvent systems. Hence, the study of various interactions and equilibrium of ions in different concentration regions are of immense importance to the technologist and theoretician as most of the chemical processes occurs in these systems.

It is of interest to employ different experimental techniques to get a better insight into the phenomena of solvation and different interactions prevailing in solution. We have, therefore, employed five important methods, namely, densitometry, viscometric, conductometric, ultrasonic interferometer and refractometric to probe the problem of solvation phenomena.

Thermodynamic properties, like partial molar volumes obtained from density measurements, are generally convenient parameters for interpreting solute-solvent/ion-solvent ad solute-solute/ion-ion interactions in solution. The sign and magnitude of partial molar volume (ϕ_V^0) also provides information about the nature and magnitude of ion-solvent interaction while the experimental slope (S_v^*) provides information about ion-ion interactions [24]. Viscosity B-coefficient obtained from the viscosity values indicates the extent of ion-solvent interaction in a solution. From experimental speed of sound values, limiting apparent molar adiabatic compressibility ($\phi°_K$) and the experimental slope (S_k^*) can be estimated. These parameters also give an idea about the ion-solvent and ion-ion interaction in the solution.

The change in viscosity by the addition of electrolyte solutions is attributed to interionic and ion-solvent effects. The *B*-coefficients are also separated into ionic components by the 'reference electrolyte' method and from the temperature dependence of ionic values, a satisfactory interpretation of ion-solvent interactions such as the effects of solvation, structure-breaking or structure-making, polarization, etc. may be given.

The transport properties in most cases are studied using the conductance data, especially the conductance at infinite dilution. Conductance data obtained as a function of concentration can be used to study the ion-association with the help of appropriate equations.

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