ABSTRACT

The information about the origin of the stability of macromolecules like proteins in aqueous solutions is important for understanding of their structure and function. The stability of proteins is achieved through several non-covalent interactions such as hydrogen bonding, electrostatic and hydrophobic interactions. As proteins are complex molecules, the model compounds, amino acids, are considered by many authors in the determination of thermodynamic parameters in aqueous media.

The study of solute effects on the volumetric, acoustical and viscometric properties of amino acids is of great importance as biological fluids are not pure water after all. Several authors have reported the interaction study of amino acids in aqueous salts (such as Na$_2$SO$_4$, LiCl, NaCl, KCl, KSCN, CaCl$_2$ etc) and in aqueous organic solutes (such as ethanol 2chloroethanol, n-propanol, sorbitol, etc) as solutes have a significant impact on the protein (enzyme) stability and activity. Similarly, drug macromolecular interactions are an important phenomenon in physiological media, such as blood, membranes, intra and extra cellular fluids. The processes of drug transport, protein binding, anesthesia are some examples where drug and bio- macromolecules appear to interact in an important and vitally significant manner. The mechanisms of these molecular processes, are however not clearly understood. It has been shown that perceptible thermodynamic changes are associated with the processes of drug-protein binding, anesthesia
In the case of protein binding, anomalous behaviour has been noted with respect to certain drugs.

Drug action, i.e., drug reaching the blood stream, its extent of distribution, its binding to the receptors and finally producing the physiological action, all depend on various physio chemical properties chiefly detected by various interactions. A knowledge of the use of drugs involving physiological and biochemical effects and their mechanism of action at macro molecular / subcellular / organ system levels can be studied in pharmokinetics. All pharmokinetic processes involve transport of drugs across biological membranes which can be well understood by transport property measurements viz., ultrasonic speed, viscosity, diffusion and thermal conductivity. There are some reports available in literature on the molecular interaction study of some drugs in both aqueous and non-aqueous media.

A detailed literature survey shows that only a few authors have reported the interactions of amino acids in aqueous drug solutions. This has promoted us to investigate the interactions of some homologous amino acids and 4-Amino butyric acid in aqueous Metformin hydrochloride and Salbutamol sulphate solutions for the first time in literature. Metformin Hydrochloride is a white hygroscopic crystalline powder, with a bitter taste, has a molecular formula \( \text{C}_4\text{H}_{11}\text{N}_5\text{HCl} \). This drug belongs to the class of bigunamides and is chemically known as “1, 1-dimethyl bigunanide hydrochloride”. It is an anti-diabetic and anti-hyperglycemic agent that covers both basal and postprandial elevated blood glucose in patients with non-insulin dependent diabetes mellitus (Type-2 diabetes) whose hyperglycemic
cannot be satisfactorily managed by diet alone. Salbutamol sulphate on the other hand, a white odourless crystalline powder, is a beta adrenoceptor agonist used for the control of chronic bronchial asthma and acute broncospasm. Its molecular formula is \([(\text{C}_{13}\text{H}_{21}\text{NO}_3)_2\text{H}_2\text{SO}_4]\). In this thesis, the data on density, ultrasonic speed and viscosity of amino acids (AAs) belonging to homologous series such as like glycine, DL-\(\alpha\)-alanine, DL-\(\alpha\)-Valine, DL-\(\alpha\)-Leucine and 4-Amino butyric acid in aqueous metformin hydrochloride and salbutamol sulphate solutions at three different temperatures, viz., 308.15, 313.15 and 318.15 K, respectively are reported. The data at the studied temperature provide relevance to the drug macromolecular behaviour near physiological temperatures.

The measured data of density, ultrasonic speed and viscosity are used to estimate some important thermodynamic and transport parameters like apparent molal volume \(V_\phi\) and compressibility \(k_\phi\), partial molal volume \(V_\phi^0\) and compressibility \(k_\phi^0\), transfer partial molal volume \((\Delta V_\phi^0)\) and compressibility \(\Delta k_\phi^0\), hydration number \(n_H\), pair and triplet interaction parameters \(V_{AB}\), \(V_{ABB}\), \(K_{AB}\) and \(K_{ABB}\), second derivative of infinite dilute solutions of partial molal volume with temperature, viz, \(\partial^2 V_\phi^0 / \partial T^2\), isentropic compressibility \((k_S)\), change in isentropic compressibility \((\Delta k_S)\), relative change in isentropic compressibility \((\Delta V_\phi^0 / k_\phi^0)\), Viscosity B-coefficients, variation of B with temperature i.e., \(dB/dT\), free energy of activation per mole of solvent \(\Delta f_i^\sigma\) and solute \(\Delta f_2^\sigma\) of the amino acids. These parameters have been interpreted in terms of solute-solute and solute-solvent interactions and
structure making / breaking ability of solutes in the given solution. In addition
to this $V_0^0$, $\Delta V_0^0$, $k_0^0$, $\Delta k_0^0$, B-coefficient, $\Delta B$ and $\Delta \mu_2^{0^*}$ have been split into
group contributions ($NH_3^+, COO^-$) and CH2 of the amino acids using their
linear correlation behaviour and the results are discussed in terms of the
magnitudes of the group contributions to the above parameters.