REVIEW OF LITERATURE

It is well-known that the stabilization of native conformations of biopolymers is caused by the various non-covalent interactions such as hydrogen bonding, electrostatic, and hydrophobic interactions. In aqueous protein solutions, the amino acid residues of a polypeptide chain interact with each other and with the surrounding water by these non-covalent forces. Therefore, the characterization of the thermodynamic properties of hydration can assist in the understanding of the conformational stability and the functional properties of proteins in solution. However, since proteins are particularly complex macromolecules, it is difficult to resolve the various interactions that participate in protein hydration [1]. The solution behavior of model compounds such as amino acids and peptides are quite helpful in understanding the water-protein interactions in solutions. Thermodynamic properties like partial molar volumes, partial molar expansibilities, changes in enthalpy and free energy, viscometric properties like $B$-coefficients and $dB/dT$ of model compounds in water and in aqueous solutions of organic solvents or salts can provide valuable clues for comprehending the protein unfolding [2]. The second reason of studying viscometric and volumetric properties of amino acids is that many amino acids and their derivatives are known as compensatory (or compatible) solutes in stabilizing proteins and enhancing enzyme activity [3–5]. Therefore, the study of these properties has largely been undertaken by using low molecular weight model compounds like amino acids and peptides in order to investigate the molecular interaction taking place in solutions.

Yezdimer et al. [6] reported on the functional group additivity scheme for correlation of the partial molar volumes, compressibilities, heat capacities, hydration enthalpies, and hydration Gibbs energies, at infinite dilution of aqueous organic electrolytes and non-electrolytes. The results were used for predicting the chemical potentials of these solutes. The report included (-C) hydrocarbon, (-H) hydrocarbon, -COOH, -CONH$_2$, -NH$_2$, -OH, -COO$, -NH$_3^+$, and an amino acid functional group. An equation of state based on the Fluctuation Solution Theory was employed which allows predictions for numerous acyclic organic compounds composed of these functional groups to 623 K and 100 MPa. Although the uncertainty normally associated with a group additivity scheme is larger than the experimental uncertainty at ambient conditions, at high temperatures and pressures the two uncertainties become comparable. The functional group contributions were based on almost 1400 experimental points and are reported as a function of solvent density and temperature.
Yasuda et al. [1] determined the densities and speeds of sound in dilute solutions of amino acids; L-asparagine, L-glutamine, L-histidine, L-aspartic acid monosodium salt and L-glutamic acid monosodium salt, L-lysine monohydrochloride, L-arginine monohydrochloride and L-histidine monohydrochloride at (5, 15, 25, 35 and 45) °C. Partial molar volumes and partial molar isentropic compressibilities of these amino acids at infinite dilution were evaluated and discussed in connection with the electrostatic interactions between the charged groups of amino acids side chains and solvent water. The partial molar volumes of all the amino acids studied increase with increasing temperature, and furthermore their curves obtained are always concave downward. This feature is typical of electrolyte or hydrophilic non-electrolyte solutions. It is well known that ionic groups of solute attract strongly surrounding water molecules, so called electrostriction, which causes a large decrease both in volume and compressibilities of the solution. They also reported [1] that the standard partial molar volumes of Asp\textsuperscript{−}, Asp\textsuperscript{2−}, L-Arg\textsuperscript{+} and L-His\textsuperscript{+} are smaller than their zwitterionic amino acids and it has been suggested that there is no simple relationship between the $B$-coefficients of amino acid ions and their standard partial molar volumes. The standard partial molar volumes of L-Asp\textsuperscript{−}, L-Glu\textsuperscript{−}, L-Lys\textsuperscript{+}, L-Arg\textsuperscript{+} and L-His\textsuperscript{+} also increase with temperature.

Mishra and Ahluwalia [7] reported apparent molar volumes of 24 $\alpha$-amino acids, 6 N-acetylamino acids and 9 peptides in aqueous solutions at 298.15 K from precise density measurements. Using data for several homologous series of compounds reported in literature and the data of studied amino acids, the group additivity relations were examined. It has been shown that the presence of hydrophilic group in the close proximity in $\alpha$-amino acids and N-acetylamino acids decreases the functional group contribution as well as the contribution due to hydrophobic hydration to $V_2^\circ$ values relative to those observed in the mono-functional compounds. It has also been shown that the $V_2^\circ$ values of the constituent amino acids, with a proper consideration of change in the electrostriction volume due to separation of charged centers agree well with the experimental values. The influence of hydrophilic and charged centers on the $V_2^\circ$ contribution of other hydrophilic groups like -CONH and -CH\textsubscript{2}CONH has been discussed. It has been shown that $V_2^\circ$ values of peptide groups and other hydrophilic side chains are smaller that obtained from the additivity scheme. It has been suggested that for the prediction of the $V_2^\circ$ values of higher peptides, the side-chains and peptide-group contributions obtained from the $\alpha$-amino acids or N-acetylamino acids should be used.
Romero and Negrete [8] studied the effect of temperature on partial molar volumes and viscosities of aqueous solutions of DL-\(\alpha\)-amino butyric acid, DL-norvaline, and DL-norleucine and from the results they found that partial molar volumes increase with the temperature, while \(B\)-coefficients decrease with the temperature for these amino acids, showing hydrophilic hydration. From the hydrophobicity criteria, they found that hydrophilic interactions predominate over hydrophobic interactions.

Awasthi and Rastogi [9] reported that \(dB/dT\) is positive for acidic amino acids such as DL-aspartic and DL-glutamic acids implying structure-breaking, while negative for basic amino acids such as L-histidine and L-arginine implying structure making. The reason was explained as the protonation of water by acidic amino acids (protic behavior) causing the breakage of hydrogen bonds and deprotonation of water by basic amino acids (aprotic behavior) enhancing the hydrogen bonding [9]. However, arginine is well known as a perturbing (destabilizing) solute of proteins [3].

Chalikian et al. [10] observed that protonation of amino groups lead to a considerably larger volume contraction than ionization of the carboxylate groups of amino acids. From the temperature and pressure dependence of the partial molar properties of glycine and \(\alpha\)-alanine, [11] it has been concluded that the hydration of glycine is completely dominated by the electrostatic solute-solvent interactions, and the hydration of the methyl group in \(\alpha\)-alanine is influenced by the ionic hydration shell. Chalikian et al. [12] have also suggested that care must be exercised when the hydration properties of complex molecules such as proteins are modeled based on additive calculations using low molecular weight compound data.

Using additivity principle Lepori and Gianni proposed a contribution method [13, 14] for estimating the standard partial molar volumes of various \(\alpha\), \(\beta\), \(\omega\)-amino acids in aqueous solutions at 25 °C with relatively high accuracies. Millero and co-workers [15] also reported the partial molar volumes and adiabatic compressibilities of several amino acids in aqueous solutions at 25 °C and used group additivity scheme to calculate the group contributions towards the partial molar properties. The simplistic approach to relate the volume and compressibilities behavior with purely Coulombic interactions was successfully made to obtain credible values of properties like hydration numbers. Another simple group-contribution methozzd proposed by Hakin et al. [16] reported the densities and heat capacities of L-aspartic acid, L-glutamic acid and \(\alpha\)-amino-\(n\)-butyric acid in aqueous solutions at 288.15, 298.15, 313.15 and 328.15 K. Helgeson, Kirkham and Flowers
equations, for neutral organic species in water have been used to model the standard state volumes and standard state heat capacities of the amino acids as a function of temperature at constant pressure. The data [16, 17] have been used to estimate the temperature dependence of chemical group contribution to standard state volumes and heat capacities for aqueous amino acids systems.

Romero and Munar [18] determined the volumetric behavior of several amino acids at concentrations < 0.01m and found out the apparent molar volumes sharply deviate from the linear relationship. They observed that apparent molar volumes of α- and β-alanine dramatically decrease with the increase of concentration, while those of serine, phenylalanine, aspartic acid and α-amino-n-butyric acid increase with the concentration. According to this report, the standard partial molar volume extrapolated from the apparent molar volume may not be the ‘real’ value at infinite dilution.

Sandhu and Singh [19] observed positive values of $dB/dT$ for L-proline and L-hydroxyproline implying structure breaking. However, betaine and proline are known as two of the most important compensatory solutes (along with ornithine and N-acetylated ornithine/lysine) in nature with structure-making ability [3, 4, 20, 21]

Helgeson, Kirkham and Flowers (HKF) equation of state has found wide application in predicting the standard partial molar volumes and heat capacities of amino acids at different temperatures and pressures [22-24]. Using HKF equation a group-contribution model was developed to calculate several properties such as standard partial molar volumes, standard molar entropies, enthalpies of formation, Gibbs free energies of formation, compressibilities and standard heat capacities of biomolecules in their aqueous solutions over a wide temperature range [25].

Rao et al. [26] reported the partial molar volumes of several amino acids like Gly, Ala, Asp, Glu, Lys, Arg and their singly or multiply charged ions at 20 °C. He proposed the formula for calculating the partial molar volumes of amino acid cations and anions in acidic and basic solutions by considering the contributions made by H$^+$, and OH$^-$ ions. A good agreement was observed for volumes of cationic and anionic species of studied amino acids with the values calculated from amino acids salts reported in literature.

Schwitzer and Hedwig [27] reported the partial molar volumes $V_2^o$ and partial molar heat capacities $C^o_{p,2}$ at infinite dilution of two tripeptides; glycylasparylglucose (glyaspgly), glycylglutamylglucose (glyglugly) and also their salts K[glyaspgly] and Na[glyglugly] in aqueous solutions at 25 °C. Ionization constants for the aspartyl and glutamyl chains and the results have been combined with literature data for the electrolytes to obtain the volume and
heat capacity changes upon ionization of the acidic side chains of the peptides. The results are compared with those for other carboxylic acid systems. Side chain contribution of acidic amino acids side chains towards partial molar volumes and partial molar heat capacities have been reported. The $\Delta V^o$ values upon ionization for tripeptide, glyglugly (-11.36 cm$^3$ · mol$^{-1}$) was found to be more negative than that for glyaspgly (-10.2 cm$^3$ · mol$^{-1}$) and these trends are identical with trends for n-alkylcarboxylic acids i.e. 1-butanoic acid (-14.2 cm$^3$ · mol$^{-1}$) and 1-propanoic acid (-12.9 cm$^3$ · mol$^{-1}$). The $\Delta C_{p,2}^o$ values for ionization for tripeptides were reported to be less negative for glu side chain than that for the asp chain and similar trends are observed for corresponding n-alkylcarboxylic acids.

Chalikian et al. [28] reported the partial molar volumes, expansibilities and compressibilities of $\alpha,\omega$-aminocarboxylic acids in aqueous solutions at 18 to 55 °C. From the temperature dependence of partial molar volumes, the total electrostriction of the non-interacting amino and carboxylic groups at 25 °C was reported to be -26 cm$^3$ · mol$^{-1}$ and above 40 °C the value increases sharply and reaches to a value of -30 cm$^3$ · mol$^{-1}$ at 55 °C. It has been concluded that the hydration shells of the short $\alpha,\omega$-amino acids (glycine, $\beta$-alanine, 4-aminobutanoic acid and 5-aminopentanoic acids) are dictated predominantly by the solvation of the oppositely charged terminal groups to the near exclusion of the intervening methylene groups. By contrast, the aliphatic CH$_2$ groups participate in the formation of the hydration shells of the longer $\alpha, \omega$-amino acids. The independently hydrated CH$_2$ groups exhibited the same contribution to the partial molar properties of a substance that come from structurally different classes of organic compounds.

Chalikian et al. [29] also reported the partial specific volumes and adiabatic compressibilities of 15 globular proteins in the temperature range of 18 to 55 °C. The data were correlated with the intrinsic volumes and accessible surface areas of 12 proteins available from crystallographic data. By combining the studied macroscopic properties with microscopic properties a new model was proposed which allow the prediction of partial specific volumes and partial specific adiabatic compressibilities of a globular protein from the crystallographic coordinates of the constituent atoms.

Shahidi and Farrell [30] reported the partial molar volumes of $\alpha$-aminocarboxylic acid and contribution of side chains or their constituent parts to the volumes in water at 25 °C. Volumes of ionization of $\alpha$-amino acids with nitrogen containing side chains indicate the absence of any significant electrostatic effect by the terminal charged group.

On the basis of negative values of partial molar expansibilities, Banipal and Kapoor [31] suggested that, except L-proline, most amino acids (glycine, alanine, $\beta$-alanine, L-
valine, L-leucine, L-isoleucine, L-serine, L-phenylalanine, L-threonine, L-glutamic acid and α- amino-n-butyric acid) are structure-breakers.

Romero and Cadena [32] compared the thermodynamic behavior of the aqueous α,ω-amino acids with that reported literature for α-amino acids in water over the temperature 293.15-308.15 K through volumetric approach. It has been reported that the interaction volumes decrease with increasing surface area and number of methylene groups for 3-aminopropanoic, 4-aminobutanoic and 5-aminopentanoic acid, suggesting strong solute-solvent interactions. It has been considered that for α,ω-amino acids, the hydrophobic effect of the hydrocarbon chain decreases because of the strong electrostrictive effect of the charged groups. The behavior of the 6-aminohexanoic acid is different as compared to the other studied α,ω-amino acids.

Recently Dhondge et al. [33] reported thermodynamic properties based upon volumetric and compressibility studies on aqueous solutions of glycine, L-alanine and β-alanine at low temperatures (275.15-283.15) K. It has been concluded that the contribution of hydrophilic hydration predominates at low temperature and it increases with increase in the temperature. This is expressed by the total disordering action of the amino acids on the structure of water molecules. The partial molar expansibilities of glycine is positive (structure breaker) whereas for the L-alanine and β-alanine is positive (structure maker). β-alanine has small positive value of partial molar expansibilities as compared to L-alanine which shows that the effect of the position of the charged group in the structure of the amino acid molecule is the predominant factor for the feature of the temperature dependence of the partial molar volume.

Jamal and Iqbal [34] reported partial molar volume, partial molar expansivity and isobaric thermal expansion coefficient of twelve amino acids namely, glycine, alanine, arginine, asparagines, glutamic acid, histidine, leucine lysine HCl, proline, serine, threonine and valine in water over the temperature range of 283.15 K to 313.15 K. Using volumetric data the group contributions observed suggest increase in hydrophilic-hydrophobic group interactions with increase of side-chain length of the amino acids.

Very recently, Mansour and Haseib [35] reported partial molar volume and viscosity B-coefficients using densities and viscosities measurements for glycine, DL-alanine, L-valine, L-serine in aqueous solutions during the passage of alternating current at different voltages at 298.15 K. The viscosities of studied amino acids increase with concentration of solution, showing increase in solute-solvent interactions and decrease with alternating current showing decrease of solute-solvent interactions. It has been reported that the passage
of direct current does not produce this effect. Positive $S_v$ values for all the amino acids have been observed at different concentrations indicating that solute-solvent interactions operative in the solutions increase with increasing concentration.

By comparing with transfer volumes of some amino acids from water to aqueous sodium chloride solutions at 298.15 K reported by Bhat and Ahluwalia [36], it has been shown that for glycine, DL-alanine and DL-$\alpha$-amino-$n$-butyric acid from water to 1 mol · kg$^{-1}$ and 2 mol · kg$^{-1}$ aqueous solutions are smaller than those to the same concentration of aqueous sodium acetate and sodium butyrate solutions. This indicates that the interactions between carboxylate anion and amino acid are stronger than those between Cl$^-$ ion and amino acids.

Bhat and Ahluwalia [37] reported the effect of 1M aqueous CaCl$_2$ on partial molar heat capacities $C_{p,2}^\circ$ and $V_2^\circ$ of some amino acids and peptides at 298.15 K. The transfer parameters were found to be significantly positive, indicating that strong interactions occur between the ions of calcium chloride and the charged centers of these compounds in the amino acids and peptides studied. A comparison had also been made with the similar transfer of these compounds to sodium chloride solutions. The transfer parameters for (-CONH) were found to be much more positive in CaCl$_2$ than in NaCl solutions.

Banerjee and Kishore [38] studied the interactions of glycine, L-alanine, DL-$\alpha$-amino-$n$-butyric acid, L-alanine and L-leucine with tetraethylammonium bromide (TEAB) at 298.15 K through volumetric approach. The results of standard partial molar volumes of transfer from water to aqueous TEAB solutions shows that ion-ion and ion-hydrophilic interactions are predominant in case of glycine and alanine whereas hydrophobic-hydrophobic group interactions are predominant in the case of DL-$\alpha$-amino-$n$-butyric acid, L-alanine and L-leucine. The increase in the hydrophobic content of the amino acids increases the number of water molecules hydrated to the charged centers of the salt, indicating the predominance of hydrophobic interactions between the amino acid and TEAB with increasing number of carbon atoms in the former.

Badarayani and Kumar [39] suggested that ions experiencing hydrophilic hydration have stronger effect on the amino acid hydration than those ions experiencing hydrophobic hydration.

Ogawa et al. [40] also noticed that the alkali chlorides have a dehydration effect on the amino acids, and the order of decreasing dehydration effect is: Na$^+$ > K$^+$ > Li$^+$. This sequence was explained by the difference in the interaction of the alkali cations with the amino acid; Li$^+$ ion has a stronger interaction with amino acids because of its smaller crystal
radius, causing higher electrostriction effect and thus a higher partial molar volume of amino acid [40]. However, a contradictory result reported by Basumallick et al. [41] suggested that for the same amino acid, the difference of volumes of transfer in solutions of various alkali halides is negligible.

Millero [42-43] reviewed the partial molar volumes of electrolytes both in aqueous and non-aqueous media. He also reported the partial molar volumes of aqueous NaCl solutions as a function of temperature (0 to 55 °C. He concluded that the ion-ion interactions are strongly related to the effect of temperature on the structure of hydrated ions or structure of water between the interacting ions.

Edsall and Wyman [44] suggested that smaller ions produce greater electrostriction of the solvent due to the stronger electric field near the ions and thus the increased orientation and compression effects. They also indicated that the amino group causes more electrostriction than the carboxyl group does.

The \( \Delta \phi B \) values of glycine and L-alanine in 1 mol \( \cdot \) kg\(^{-1} \) electrolytes at 25°C were observed in an increasing order for cations: \( \text{Mg}^{2+} < \text{Na}^+ < \text{K}^+ \) and for anions: \( \text{Cl}^- < \text{Br}^- \) [45]. One conclusion drawn from these data is that, the strongly hydrated ions (kosmotropes) have less effect on the \( B \)-coefficients of amino acids than weakly hydrated ones (chaotropes).

Based on the hydration numbers of amino acids in salt solution, Yan et al. [46, 47] concluded that caproate has larger dehydration effect on the amino acids than butyrate and acetate.

The \([\text{Et}_4\text{N}]\text{Br}\) salt is known to destabilize proteins such as lysozyme [48], and it was explained that the denaturing action of tetraalkylammonium halides was due to the binding of the denaturants to the protein being stronger than the exclusion of cosolvent from the protein surface [38, 49]. The above phenomena indicate that larger tetra-n-alkylammonium cations cause more dehydration of amino acids, which is consistent with the fact that large hydrophobic cations are more kosmotropic due to the hydrophobic hydration [50].

Sinha et al. [51] have reported partial molar volume and viscosity \( B \)-coefficients of L-alanine in aqueous solutions of \( \text{Ag}_2\text{SO}_4 \) at 298.15, 308.15 and 318.15 K. The \( \phi \) and viscosity \( B \)-coefficient values indicate the presence of strong solute-solvent interactions, which further strengthen at higher concentration of \( \text{Ag}_2\text{SO}_4 \) in ternary solutions, but decrease at higher temperatures. The trends of partial molar expansibilities, hydration numbers and free energy of activation of the viscous flow for L-alanine in aqueous solutions suggest L-alanine to be a net structure promoter in aqueous \( \text{Ag}_2\text{SO}_4 \) solutions.
Banipal et al. have reported the partial molar volumes, adiabatic compressibilities and viscosity $B$-coefficients of glycine, DL-$\alpha$-alanine, DL-$\alpha$-amino-n-butyric acid, L-valine and L-leucine in aqueous CdCl$_2$ [52] and MnCl$_2$.4H$_2$O [53] solutions over the temperature range of 288.15-318.15 K. The transfer parameters, $\Delta V^o$ and $\Delta K_{s,2}^o$ increase with concentration of cosolutes and temperature but that of $\Delta B$ values increase with concentration and decrease with temperature in both cosolutes. The variation of $K_{s,2}^o$ values for glycine, DL-$\alpha$-alanine and DL-$\alpha$-amino-n-butyric acid suggests that the cosphere of hydrophilic groups (-COO$^-$ and -NH$_3^+$) overlap destructively with that of hydrophobic group of non-polar side-chain of amino acids and thus decrease their hydration ability. In L-valine and L-leucine, the hydrophobic effect of non-polar side chain starts dominating and it is reflected in large negative value of $K_{s,2}^o$. The negative values of $dB/dT$ for the studied amino acids in water and in aqueous CdCl$_2$ solutions indicate the structure breaking nature of studied amino acids except glycine. All the transfer parameters increase sharply at lower concentration of MnCl$_2$.4H$_2$O which indicate that the interactions of amino acids with cosolute are very large even at low concentration and starts relatively saturating with further increase of concentration.

Kumar et al. [54] have recently reported the volumetric and viscometric studies on glycine and L-valine in aqueous tripotassium citrate over the temperature range 308.15 and 318.15 K. The values of transfer partial molar volumes are positive and increase with concentration of cosolute suggesting that in tripotassium citrate the ion-hydrophilic and hydrophilic-hydrophilic group interactions are predominant over the hydrophobic-hydrophobic group interactions. The magnitude of transfer volume also increases from glycine to L-valine which means the glycine-tripotassium citrate interactions are weak as compared to L-valine-tripotassium citrate interactions. Large and positive values of $B$-coefficients also indicate the strong ion-solvent interactions and thus supporting the volumetric data.

Rajagopal and Gladson [55] have reported the volumetric and compressibility studies on four amino acids namely, glycine, L-alanine, L-valine and L-leucine in aqueous NaF solutions at different temperatures. It has been observed that ion-ion interactions are much stronger than ion-hydrophobic interactions over the entire studied concentration range of NaF and also the cosolute has strong dehydration effect on the amino acids.

Riyazudddeen and Afrin [56] studied the effect of NaCl and NaNO$_3$ on the partial molar volumes and partial molar isentropic compressibilities of L-phenylalanine, L-leucine,
L-glutamic acid and L-proline at different temperatures. The large partial molar volumes of amino acids in studied cosolutes have been attributed to the possible formation of ‘zwitterionic-Na⁺/Cl⁻/NO₃⁻-water’ and Na⁺/Cl⁻/NO₃⁻-water, dipole entities in solutions.

The effect of ionic liquids on the thermodynamics of amino acids and peptides has also been the topic of interest recently. A number of recent studies are available in literature on the volumetric, viscometric and compressibilities of amino acids and other model compounds of proteins in aqueous ionic liquids. Shekaari and Jebali [57, 58] reported the volumetric, compressibility, viscometric, conductometric and refractive indices studies in 1-propyl-3-methylimidazolium bromide and in 1-butyl-3-methylimidazolium bromide for glycine, L-alanine and L-valine. The values of $V_2^o(-\text{NH}_3^+, -\text{COO}^-)$ are larger than those of $V_2^o(-\text{CH}_2)$ indicating that the zwitterionic group has stronger interactions than hydrophobic group with both ionic liquids. The values of $B(-\text{NH}_3^+, -\text{COO}^-)$ increase, while that of $B(-\text{CH}_2)$ decrease with concentration of ionic liquids in solutions, indicating that the zwitterionic group break while CH$_2$ group promotes the structure of ionic liquids solution.

Gao et al. [59] reported the volumetric properties of binary mixtures of benzyl alcohol and amino acid ionic liquids; 1-butyl-3-methylimidazoliumglutamic acid, [bmim][glu] and 1-butyl-3-methylimidazoliumglycine, [bmim][gly] over the temperature range 298.15-313.15 K. The values of excess molar volumes increase slightly when temperature rises from 298.15 to 313.15 K. It has been concluded that the effect due to the ion-dipole interactions and packing between the organic molecular liquid (benzyl alcohol) and [bmim][glu] or [bmim][gly] are dominating over the disruption of dipolar order in benzyl alcohol. In other words, there is formation of liquid clathrate in mixed solution by small organic molecules.

Some reports [60-63] on the effect of carbohydrates on the thermodynamic behavior of amino acids and peptides are also available in literature. Das and Dash [60] studied solute-solvent interactions of amino acids (glycine, α-alanine and β-alanine) with glucose in aqueous solutions at different temperatures. Acoustical parameters like isentropic compressibility, acoustic impedance, solvation number, partial molar volume and partial molar expansibility have been reported. The results show that the amino acids have poor ion-solvent interactions with glucose and moreover the structure making effect is not very much favored. The isentropic compressibility also decreases with solute concentration due to occupation of interstitial spaces of water by the solute molecules thus making the medium less compressible. The decrease of relative association values with concentration of solutions indicate the breaking of associated solvent molecules on addition of amino acids in solution.
Ali et al. [61] studied the volumetric and viscometric properties of amino acids; glycine, L-alanine, phenylalanine, and dipeptide (glycylglycine) in D-glactose solutions at different temperatures. The results show the dominance of the hydrophilic-ionic group interactions between the –OH groups of D-glactose and zwitterionic centers of amino acids; and peptide over hydrophilic-hydrophilic and hydrophobic-hydrophobic group interactions. The large positive values of \( B \)-coefficients as compared to the values of \( A \)-coefficients suggest the predominance of solute-solvent interactions over solute-solute interactions, thereby supporting the results of volumetric data. Jha and Kishore [62] reported the combination of densimetry, compressibility measurements and isothermal titration calorimetry studies on aqueous glycine, alanine, \( \alpha \)-amino butyric acid, valine and leucine in sorbitol solutions at 298.15 K. The correlation of all the results suggest enhancement of the hydrophilic/polar group interactions operating in the ternary systems of amino acid-water-soritol. Zhao et al. [63] studied the partial molar volumes and viscosity \( B \)-coefficients of arginine in aqueous glucose, sucrose and L-ascorbic acid solutions at 298.15 K. The results indicate that the partial molar volumes of transfer and viscosity \( B \)-coefficients of arginine increase with concentration of sugar or L-ascorbic acid and the hydration number decreases owing to the interactions of sugar or L-ascorbic acid with zwitterionic groups. It has also been concluded that the magnitude of the enhancement effect on the volume and hydration number is related to the number of OH groups and the structure of mixture solvent.

Sastry et al. [64] observed that the solute-cosolute interactions of amino acids with urea, butane-2,3-diol, and 2-butoxy are more favored at elevated temperatures and in presence of high concentration of sucrose. Otherwise the hydrophobic side chains facilitate the solute-solute interactions and also time induced hydrophobic hydration in the bulk water. Keswani and Kishore [65] reported the biophysical studies of some hydrophobic amino acids, peptides, and proteins (lysozyme) in aqueous 3-chloro-1,2-propanediol and 3-chloro-1-propanol at 298.15 K. The transfer volumes and isentropic compressibilities suggested that the interactions of the amino acids and peptides with 3-chloro-1-propanol are more polar interactions compared to that with 3-chloro-1,2-propanediol. The limiting enthalpies of dilution of the amino acids and peptides in alcohol and diol support the conclusion drawn from the volumetric and compressibility data. A comparison of the heats of dilution of the amino acids and peptides with that of hen egg white lysozyme along with the fluorescence and circular dichroism spectroscopic data in aqueous alcohol and diol solutions correlates well with the higher ability of 3-chloro-1-propanol in altering the thermal stability of the protein compared to 3-chloro-1,2-propanediol.
Nain et al. [66] measured densities, ultrasonic speed and viscosities of L-histidine in water + sucrose solutions at different temperatures and concluded the presence of strong solute-solvent interactions, which further increase with the concentration of sucrose in these systems. Also L-histidine acts as structure maker in these aqueous sucrose solutions.

Singh and Kishore [67] reported the volumetric studies of some amino acids (glycine, alanine, α-amino-n-butyric acid, valine, leucine and lysine monohydrochloride) and hen-egg white lysozyme in aqueous Triton X-100 (TX-100) solutions at 298.15 K. The results of transfer partial molar volumes, $\Delta_t V^o$ from water to aqueous Triton X-100 were found to be very small in spite of different hydrophobic content, indicating an overall balance in interactions of zwitterionic/hydrophilic groups of amino acids with hydrophilic groups of TX-100, and of hydrophobic groups of amino acids with hydrophobic groups of TX-100. The values of partial specific volumes of transfer of lysozyme from water to aqueous TX-100 solutions also indicate a balance of hydrophobic and hydrophilic interactions in protein-nonionic surfactant systems.

Chen et al. [68] studied unfolding of hen egg white lysozyme as a function of urea concentration at pH 2.9 by solution X-ray scattering. Using denaturant binding model, the thermodynamic parameters of denaturation for the intermediate and unfolded states were estimated. Iqbal and Verrall [69] from the partial specific volumes, adiabatic compressibilities and expansibilities of some proteins in water, studied the protein-solvent and protein-protein interactions. The results provide some information about the structural and dynamic features of these proteins and show a greater dependence of volumetric data on the hydrophobicity than on any other protein characteristics.

Palani et al. [70] also studied the acoustical and transport properties of L-glutamine, L-arginine, L-lysine in aqueous DMSO solutions at 303.15 K. From the magnitude of $\phi_k^o$ and the values of $B$-coefficients it has been concluded that L-lysine possess strong ion-solvent interactions than other two amino acids in aqueous DMSO solutions. The transfer volumes suggest the predominance of hydrophilic-hydrophobic interactions over hydrophilic-hydrophilic interactions.

Bhuiyan et al. [71] recently examined the partial molar volumes and specific heat capacities of glycine in aqueous solutions of formamide, acetamide, N,N-dimethylacetamide at 298.15 K. The positive values of transfer volume from water to amide solutions results from a decrease in volume shrinkage in the presence of amide molecules in aqueous solutions. The positive values of transfer volumes also indicate the presence of hydrophilic-
hydrophilic co-sphere interactions between the zwitterionic group of glycine (–NH$_3^+$ and –COO$^-$) and –CON< group of amides. The transfer heat capacities, $\Delta C_{o,2,p}$, are positive in formamide and acetamide solutions and negative in dimethylformamide solutions. The values of $\Delta C_{o,2,p}$ decrease in the order: formamide > acetamide > N,N-dimethylformamide. This trend suggests that the values of $\Delta C_{o,2,p}$ reflect not only the structural features of amino acid solutes but also the structural features of amide cosolutes. Liu et al. [72] investigated the volumetric properties of glycine, L-alanine and L-serine in aqueous solutions of N-methylacetamide (NMA) at 298.15 K. It has been observed that the hydrophilic-hydrophilic interactions between the charged group of amino acids and –CONH- group of NMA predominate for glycine and L-serine, but for L-alanine the interactions between side group (-CH$_3$) and NMA predominate. The (-CH$_3$) group of L-alanine has much more influence on the value of transfer volume than that of the (-OH) group of L-serine.

Jolicoeur et al. [73] studied the solvation of 20 amino acids in water and 8M urea solutions by determining their partial molar volumes and heat capacities. The side chain contributions to $V_2^o$ and $C_p^o$ were obtained as the difference between the properties of the various amino acids and those of glycine, both in water and in urea. The solvent accessible surface area of the amino acid residues were obtained using a method developed by Herman [74], and the total surface areas were separated into their hydrophobic and hydrophilic components. In water, $C_p^o$ values for the various residues $C_p^o(R)$ values, in water yield a good estimate of side chain hydrophobicity, but the water-urea transfer heat capacities appear strongly affected by specific solvation effects in the urea solution.

Recently, Lee et al. [75] determined the partial molar volumes and adiabatic compressibilities of N-acetyl amino acid amide, N-acetylamino acid methylamides, N-acetyl amino acids and short oligoglycine as a function of concentration of urea. The data were analyzed within the framework of statistical thermodynamic formalism to determine the association constant, k for binding of the urea with glycyl unit and each of the naturally occurring side chains. A general equation that relates ‘k’ with change in free energy, $\Delta G_u$ accompanying the transfer of groups from water to urea was designed. The $\Delta G_u$ values correspond to the sum of the free energy of cavity formation, $\Delta \Delta G_C$ and differential free energy of solute-solvent interactions, $\Delta \Delta G_I$ in urea and water. The values of k correspond to values of $\Delta \Delta G_I$ ranging from highly favorable to slightly favorable. It has been denature that urea denature the protein by concerted action via favorable interactions with a wide range of protein groups. Similar type of studies [76] have been reported for the N-acetylamino acid.
amides and oligoglycines at different glycine betaine (GB) concentrations. It has been suggested that the transfer free energy $\Delta G_{tr}$ results from a fine balance between the large $\Delta\Delta G_C$ and $\Delta\Delta G_I$ contributions. The interplay between $\Delta\Delta G_C$ and $\Delta\Delta G_I$ results in pronounced maxima in the GB dependence of $\Delta G_{tr}$ for Val, Leu, Ile, Trp, Tyr and Gln side chains as well as glycyl units.

Recently, Misra and Kishore [77] carried out the volumetric and calorimetric investigations of molecular interactions in amino acids and peptides in combined presence of surfactants and glycine betaine. It has been concluded that glycine betaine primarily exhibit polar interactions with the zwitterionic centers of amino acids and peptide bonds of the peptides but might enhance the overall structure in the presence of amino acids with bulkier alky groups.

Harutyunyan et al. [78] reported the volumetric properties of DL-glycine, DL-alanine, DL-serine, L-aspartic acid, L-lysine and L-leucine in aqueous solutions of nonionic surfactant hexadecyl poly[oxyethylene(25)] alcohol at 303 and 333 K. It has been observed that glycine, alanine and aspartic acid in the transfer volumes in pre-micellar region are positive, while in post-micellar region these values are negative. Thus, in pre-micellar region hydrophilic-hydrophilic and ion-hydrophilic interactions are dominant while in post micellar region hydrophobic-hydrophobic interactions are dominant. For serine the transfer volumes are negative over the entire concentration range due to presence of –OH group. For leucine, the transfer volumes are negative in pre-micellar region and in post-micellar region the values become positive with temperature.

A number of studies [79-97] on the effect of organic solutes on the volumetric and viscometric behavior of amino acids have been reported. The type-1 solutes or non-compatible solutes like urea [79], DMF [80,81], 1,4-dioxane[82,83] and acetonitrile [84] increase the values of $B$-coefficients of amino acids with the concentration, whereas in type-2 or compatible solutes like methanol [19], 1-propanol [85] and propane-1,2-diol [86], the $B$-coefficients increase at low concentrations and decrease at high concentrations. Polyols and sugars [87-94] are also found to be compatible solutes and these stabilize the native conformation of globular proteins. The effect of methanol [19, 95] and ethanol [96] on $B$-coefficients of amino acids showed that a small amount of alcohols enhances or improves the three dimensional polymeric structure of water whereas high concentration tends to break the structure. Banipal et al. [97] have also reported that the non-hydrogen bonded 1,4-dioxane is weakly hydrated and may be considered as a weak structure-breaker.
Banipal et al. reported partial molar volumes and viscosities of amino acids (a) Glycine, DL-α-alanine, DL-α-Amino-n-butyric acid, L-leucine and L-phenylalanine having non-polar side chains [98], (b) L-serine and L-threonine having polar side chains [99] in aqueous magnesium acetate (MA) and sodium acetate (SA) solutions. The larger $\Delta_t V^o$ and $\Delta_t B$ values in aqueous MA reveals that the stronger interactions occur between MA and amino acids, which may be due to small size and high charge density of Mg$^{+2}$ ions as compared to Na$^+$ ions. Comparison of the volumetric properties of amino acids in aqueous NaCl, MgCl$_2$ and SA, MA shows that the stabilizing effect of these cations (Na$^+$ and Mg$^{+2}$) on the proteins also appear in the same order as in the Hofmeister series.

Yan et al. [100, 101] determined the densities and viscosities of glycine, DL-alanine, DL-α-amino-n-butyric acids, DL-α-valine and DL-α-leucine in aqueous sodium butyrate as a function of concentrations of amino acids and electrolyte at 298.15 K. These data have been used to calculate apparent molar volumes and viscosity $B$-coefficients of amino acids. The standard partial molar volumes and standard volumes of transfer and hydration numbers of the amino acids have been determined. It has been shown the above parameters vary linearly with increasing number of carbon atoms in the alkyl chain of amino acids, and they were split into contributions from the charged end group (NH$_3^+$, COO$^-$) and (CH$_2$) group of the amino acids. From the volumetric data, it has been found that sodium butyrate interacts strongly with the charged center of the zwitterionic group of amino acids and has a strong dehydration effect.

Wang et al. [102] reported the partial molar volumes and viscosities of some α-amino acids (glycine, DL-alanine, DL-α-amino-n-butyric acid, DL-α-valine and DL-α-leucine) in micellar solutions of sodium caprylate (NaC$_8$) as a function of amino acid and sodium caprylate at 298.15 K. These data have been used to calculate apparent molar volumes and viscosity $B$-coefficients of the amino acids. It has been shown that values of $V_2^o$ and the $B$-coefficients vary linearly with the increasing number of carbon atoms in the chain of the amino acids. From the volumetric data, it has been suggested that that the amino acids are solubilized in the palisade layer of sodium caprylate micelles. It has also been suggested that the $B$-coefficients of the amino acids and their groups in NaC$_8$ are larger than those in water and in NaC$_2$, NaC$_4$ and NaC$_6$ solutions and there is increased structure making tendency of the amino acids in aqueous NaC$_8$ solutions.

The thermal denaturation study of hen egg white lysozyme and α-lactalbumin in aqueous salt solutions further confirmed that the proteins are stabilized by osmotropic CH$_3$COO$^-$ and SO$_4^{2-}$, but destabilized by chaotropic SCN$^-$ as indicated by Singh and Kishore.
[103]. They also summarized the order of volumes of transfer ($\Delta V^o$) of amino acids and peptides from water to 1 M aqueous sodium salts ($\text{CH}_3\text{COO}^-$, $\text{SO}_4^{2-}$ and $\text{SCN}^-$) as two series: Series 1: glutamate $>$ serine $>$ glycine $\approx$ alanine $>$ valine $>$ leucine; Series 2: triglycine $>$ diglycine $>$ glycine. The salts impose stronger dehydration effect on the amino acids or peptides that are on the more left side of the above series. Series 1 is consistent with the hydrophobicity of amino acids: more hydrophilic an amino acid is, the higher the volume of transfer it has. It has been confirmed that more hydrophilic amino acids undergo more dehydration effect by sodium acetate. Glutamate is negatively charged and thus the most hydrophilic species than any others; serine contains a $-\text{OH}$ group and thus is more hydrophilic (due to H-bonding with water); other amino acids (from left to right in series 1) are more hydrophobic with the increase of alkyl chain length. Interestingly, series 2 indicates that peptides are more dehydrated by salts than the amino acid.

Recently, Hedwig and Hakin [104] have reported the partial molar volumes and heat capacities of aqueous solutions of N-acetylarginamide monotrifluoroacetate and sodium trifluoroacetate over the temperature range of 288.15 to 328.15 K. The data along with the relevant data taken from the literature have been used to calculate the contribution of the protonated arginyl side-chain to the thermodynamic properties. It has been concluded that the contribution of protonated arginyl side-chain towards $V_2^o$ obtained from amino acid data are smaller than those obtained using data for the $N$-acetyl amide derivatives.

Siddique and Naqvi [105] have reported the partial molar volumes of L-lysine monohydrochloride, L-histidine, and L-arginine in water and in aqueous sodium acetate, potassium acetate and calcium acetate over the temperature range of 303.15-323.15 K. The studies show that ion-ion interactions dominate for basic amino acids in the studied cosolute. Interactions of L-lysine monohydrochloride with cosolutes were found to be stronger as compared to L-histidine and L-arginine.

Recently, Korolev [106] analyzed the partial molar volumes of amino acids in aqueous urea solution. It was concluded that for a saturated urea solution the partial molar volume equals the molar volume of the amino acid, thus the amino acids dissolves without changing the system volume. Hydrophobic effects are manifested in the volumetric characteristics only in dilute solutions.

Zhao [107] has reviewed the standard partial molar volumes and viscosity $B$-coefficients of amino acids at different temperatures. The effect of salts, organic solutes, organic solutions and various ions on the viscometric and volumetric properties in terms of
their kosmotropic (structure-making) and chaotropic effects on the hydration of amino acids has been used to interpret their role on protein stability. He also reported the volumetric behavior of amino acid cations and anions, because these ions have been incorporated as a part of novel ionic liquids, which find wide applications in biocatalysts and protein stability. Relationship between $B$-coefficients and standard partial molar volumes of amino acids has also been discussed. Sharma and Kishore [108] determined the partial molar volumes and enthalpies of some amino acids in aqueous proline solutions at 298.15 K. They found that partial molar volumes of transfer, $\Delta V^0$ are positive for glycine, alanine, $\alpha$-amino-$n$-butyric acid and valine, whereas $\Delta V^0$ values are negative for leucine in aqueous proline solutions. The $\Delta V^0$ and enthalpies of transfer data are discussed in terms of various interactions operating in ternary mixtures of amino acids, water and proline.

References: