SUMMARY

The importance of studying amino acids and their derivatives has long been recognised for an understanding of various characteristic features of complex macromolecular systems like proteins, hormones etc. The alpha-amino carboxylic acids, are of great biological as well as theoretical interest, because polypeptides may be regarded as simple models for a study of proteins.

Hydrochloride derivatives of amino acids are of both theoretical and practical importance. They are of great importance in the drug industry. Most of the drugs are in the hydrochloride form because in this form they are easily assimilated into the human body and are also least toxic.

Acetylated amino acids have their own importance as they are utilized by the body in the detoxication of amines, of drugs containing amino groups such as sulfanilamide and related compounds and in the synthesis of acetyl-choline. Acetylcholine is of particular interest because it plays an important role in the transmission of nerve impulses across synapses and from nerve endings to the muscles innervated. The body acetylates amine acids and aromatic amine groups which apparently precedes the substance to be detoxicated.
A vibrational study of various amino acid hydrochlorides such as D-glycine, L-alanine, L-valine, L-leucine, L-cystine dihydrochloride, L-methionine, L-tyrosine and di-L-alanine in relation to their crystal structure has been made. Complete vibrational analysis of glycyl-L-alanine hydrochloride and L-phenyl alanine hydrochloride has been made. In addition to this, vibrational studies on acetyl derivatives of L-glutamic acid, L-glutamine, L-methionine and L-cysteine and their N-deuterated derivatives have also been made.

It has been observed for a number of amino acids and peptides that their hydrochloride derivatives have quite a different hydrogen bonding scheme and hence a significantly different packing arrangement in the crystal form. It is observed that the hydrochlorides have a relatively planar backbone structure as compared to the non-planar structure in the corresponding zwitterionic form.

Glycyl L-alanine hydrochloride is the simplest dipeptide of the basic amino acids L-glycine and L-alanine. The conformation of glycyl-L-alanine hydrochloride is significantly different from that of glycyl-L-alanine e.g., the $\phi_1$, $\psi_1$ and $\psi_2$ angles for the two compounds are 100°, 11°, 359° and 120°, 240° and 240° respectively.
L-phenylalanine hydrochloride is the simplest aromatic amino acid. It is a nutritionally essential amino acid for all living beings to maintain nitrogen proportion in the system. A complete normal coordinate analysis has been carried out treating it as a twenty four body problem.

Vibrational spectra of acetylated amino acids and their zwitterionic forms have also been studied. The essential difference between the spectra is the appearance of amide group and protonized carboxyl group in the acetylated derivatives and consequently the disappearance of NH$_3^+$ and COO$^-$ group frequencies. The acetylated amino acids are generally of importance due to their detoxication properties.

A Chapterwise summary of the thesis is given below:

The first chapter is an introduction to the subject matter discussed in the thesis. It briefly deals with the structure of amino acids and its hydrochlorides. Various techniques utilized for molecular characterization of amino acid have been discussed. The work outlined in the thesis deals mainly with the experimental and theoretical infrared absorption studies of many biomolecules. Infrared spectroscopy is one of the most useful tools in probing
into the structure of many unknown compounds through their dynamical characteristics.

In chapter II is described the Wilson's GF matrix method for the molecular vibration of a finite molecule where G matrix is the inverse kinetic energy matrix and F is the potential energy matrix.

Chapter III is a study of some acetylated amino acids. Vibrational spectra of acetyl derivatives of L-glutamic acid, L-glutamine, L-methionine and L-cysteine and their N-deuterated derivatives have been discussed. Assignments of the vibrational modes have been made on the basis of a comparison of the spectra of acetylated amino acids with their respective zwitterionic forms. Amide group bands frequencies and amide characteristic of skeleton and side chain conformation have also been reported.

Chapter IV is devoted to the normal mode analysis of glycyl-L-alanine hydrochloride. Similar studies on glycyllglycine, L-alanyl glycine and dialanine have already been reported from our laboratory. It has been observed that the presence of HCl causes remarkable conformational changes in glycyl-L-alanine. It approaches a nearly planar
structure. A similar phenomenon is observed in dialanine hydrochloride and L-glutamic acid hydrochloride. In glycyl-L-alanine hydrochloride the peptide group is in the trans configuration as in any other linear peptide. However, a significant non-planarity in the peptide group is observed, torsion angle being 10.2°.

Glycyl-L-alanine hydrochloride molecule can be assumed to be made up of two units viz. COOH.CH.CH₃.NH.CO.CH₂\(\text{NH}_3^+\) and Cl⁻. The three protons at \(\text{NH}_3^+\) take part in intermolecular hydrogen bonding with three different molecules.

A study of infrared absorption bands of glycyl-L-alanine hydrochloride shows the following characteristics:

The carboxylic group is unionized and a mode at 1722 cm⁻¹ is observed. This mode is the characteristic of the CO link in a COOH group. This mode is absent in the corresponding zwitterions and a new mode is observed at 1635 cm⁻¹ which is due to COO⁻ asymmetric stretch.

The amide I is observed at 1622 cm⁻¹, in contrast to a value of 1685 cm⁻¹ for its zwitterion. The carbonyl oxygen takes part in strong hydrogen bonding in glycyl-L-alanine hydrochloride and may be responsible for the frequency shift observed in it. This is supported by the
fact that the corresponding mode appears at 1690 cm$^{-1}$ in L-alanyl glycine, which has an unbonded carbonyl oxygen. Amide VII, which arises from the C=O-N torsion is of special interest from the conformational viewpoint. For glycyl-L-alanine hydrochloride which has a significantly non-planar amide group, this mode appears at a relatively higher value (253 cm$^{-1}$) than glycyl glycine (217 cm$^{-1}$) which has a relatively planar peptide group.

Chapter V deals with the structure and spectral correlation in some amino acid hydrochlorides. Hydrochloride derivatives of amino acids are of importance in the drug industry.

In this chapter a study of the spectroscopic correlation in various amino acid hydrochloride derivatives based on known structures and then extrapolated to unknown ones are reported. The basic approach is based on the fact that even though the molecular species are different yet it is the hydrogen bonding scheme which dictates their three dimensional packing arrangement. This enables one to make reasonable predictions regarding the structure of unknown biomolecules. The molecules having known structures are L-glycine hydrochloride, L-valine hydrochloride,
L-cystine di-hydrochloride, L-phenyl alanine hydrochloride, L-tyrosine hydrochloride and di-alanine hydrochloride and the ones with unknown structures are L-alanine hydrochloride and L-leucine hydrochloride.

The difference in vibrational spectra of zwitter-ionic amino acids and their hydrochloride derivatives is that the frequencies of all those groups which take part in the hydrogen bonding are altered. The groups which are effected are carboxylic, ammonium and the charged groups in the side chain. Appearance of a mode at 1720 cm
-1 is a typical characteristic mode of amino acid hydrochloride. This is the (C=O) stretching mode of an unionized carboxyl group. On the basis of a comparison of amino group and carboxyl group frequencies and hydrogen bond lengths and angles an effort was made to correlate the carboxyl and ammonium group frequencies with the known crystal structures and thus a possible prediction of the crystal structure of unknown amino acid hydrochloride could be made wherever possible.

Molecular packing is considerably effected by the nature of the side chain. A comparison of spectroscopic data have thus been made between similar natured side chains. A comparison of spectral data of L-phenyl alanine hydrochloride with L-tyrosine hydrochloride and
that of L-glycine hydrochloride with L-valine hydrochloride has been made.

On comparing the vibrational spectra of hydrochlorides of amino acid along with their bond lengths and bond angles we find that generally compounds having comparable vibrational spectra and having similar natured side groups usually have the same crystal structures. On the basis of the above comparison we predict that both L-alanine hydrochloride and L-leucine hydrochloride have orthorhombic crystal structure.

Chapter VI includes the vibrational analysis of L-phenyl alanine hydrochloride. It is an essential amino acid for all living beings to maintain proportional nitrogen in the system. There are layers of L-phenyl alanine molecules connected by chloride ions via a system of hydrogen bonds. Each chloride ion joins three molecules of one layer via $H^1$, $H^2$ and $H^3$ (see figure VI2) and connects these via $H^3$ to a fourth molecule in a second layer, thus forming a system of double layers. This kind of molecular arrangement is characteristic of structures containing both polar and non-polar groups together.
A comparison of vibrational group frequencies of L-phenyl alanine hydrochloride and L-tyrosine hydrochloride has been made. In the ammonium group frequencies we find that the stretches in case of L-phenyl alanine hydrochloride are at a higher frequency as compared to L-tyrosine hydrochloride. This may be interpreted as due to the fact that L-tyrosine hydrochloride has a longer hydrogen bond associated with the ammonium group.

The asymmetric bend and the symmetric bend and rock frequencies are nearly at the same frequency. This is not very surprising and only shows that the transverse force constants involved in out of plane motions are not significantly different in the two cases. The carboxyl group frequencies of the two compounds are nearly at the same frequency.

In Chapter VII a modification of Tobolsky - Gupta model for a semi-crystalline polymer chain with orientation in both crystalline and amorphous parts are presented. Mathematical methods of Markoff-chains are used to obtain expressions for molecular dimension of the chain.

The VIII chapter is devoted to the limitations for the normal mode calculations while treating the molecules as isolated systems and the possibility of a more general treatment of three dimensional system is discussed. The relative merits of various force fields and the harmonic approximation included in these calculations have also been discussed.