Proteins

Proteins are large biomolecules, or macromolecules, consisting of one or more long chains of amino acid residues. Proteins differ from one another in their sequence of amino acids. A linear chain of amino acid residues is called a **polypeptide**. A protein contains at least one long polypeptide. Short polypeptides, containing less than 20–30 residues, are commonly called **peptides**, or oligopeptides. The individual amino acid residues are bonded together by **peptide bonds**. The sequence of amino acid residues in a protein is defined by the sequence of a gene, which is encoded in the genetic code. In general, the genetic code specifies 20 standard amino acids.

Many proteins are enzymes that catalyze biochemical reactions. Proteins also have structural or mechanical functions, such as actin and myosin in muscle and the proteins in the cytoskeleton. Other proteins are important in cell signaling, immune responses, cell adhesion, and the cell cycle.

Proteins are polymers of amino acid molecules which are bonded with each other through peptide bond. Amino acids are organic compounds containing amine (-NH2) and carboxyl (-COOH) and a side-chain (R group) specific to each amino acid (Figure 4.1).

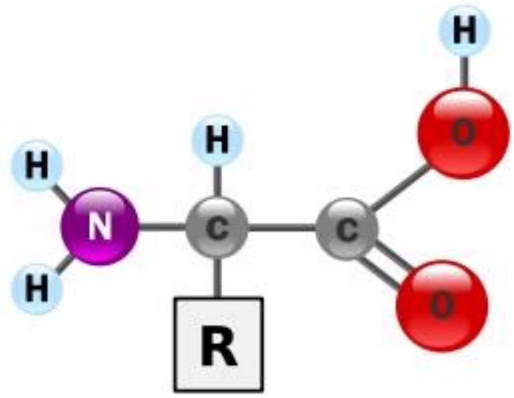

Figure 4.1: The structure of an amino acid.

The peptide (amide) bond is formed when the carboxyl group of one amino acid molecule reacts with the amino group of the other amino acid molecule, causing the release of a molecule of water (H2O). The end with a free amino group is known as the N-terminus or amino terminus, whereas the end of the protein with a free carboxyl group is known as the C-terminus or carboxyl terminus (the sequence of the protein is written from N-terminus to C-terminus, from left to right) (Figure 4.2).

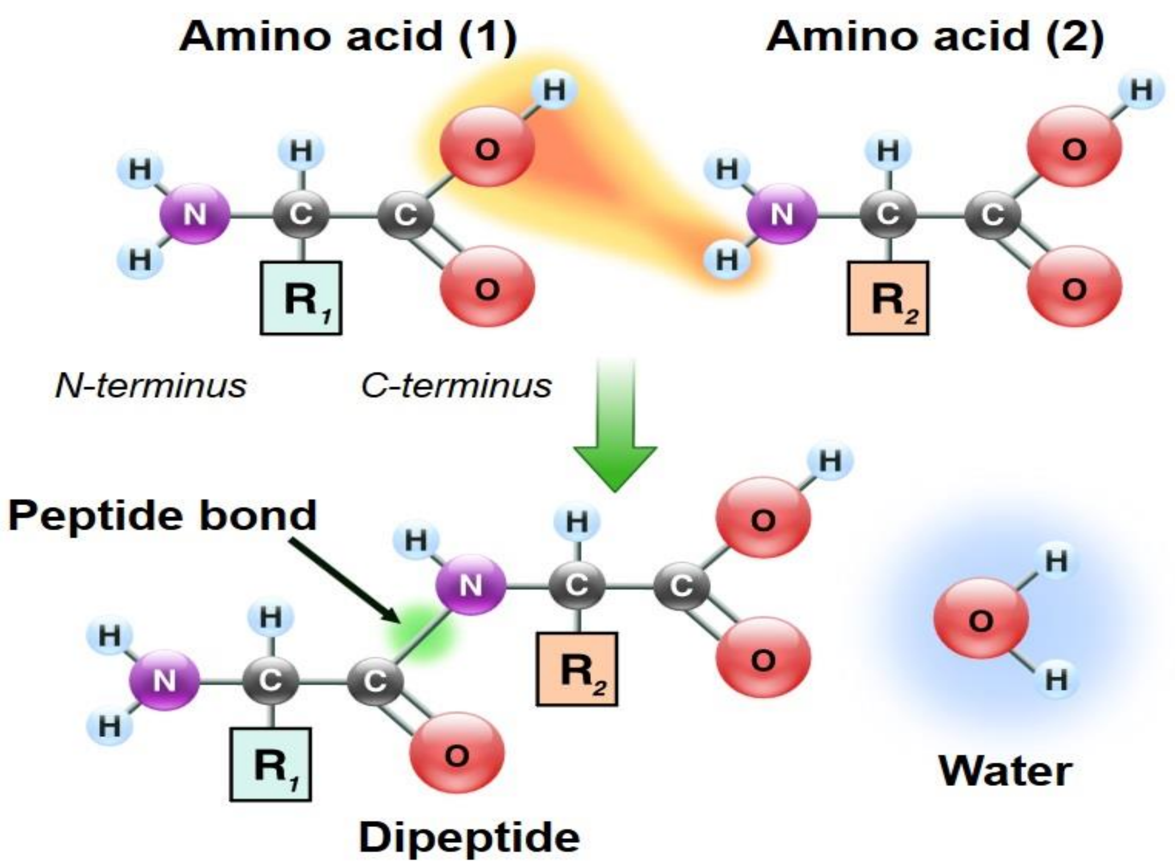

Figure 4.2: Peptide bond formation.

Classification of amino acids

The amino acids grouping into four main classes based on their polarity, or tendency to interact with water at biological pH (near pH 7.0). The polarity of the R groups varies, from nonpolar and hydrophobic (water-insoluble) to highly polar and hydrophilic (water-soluble).

1- Non polar amino acids: have equal number of amino and carboxyl groups (neutral). These amino acids are hydrophobic and have **no charge** on the 'R' group. The amino acids in this group are alanine, valine, leucine, isoleucine, phenyl alanine, glycine, tryptophan, methionine, and proline (Figure 4.3).

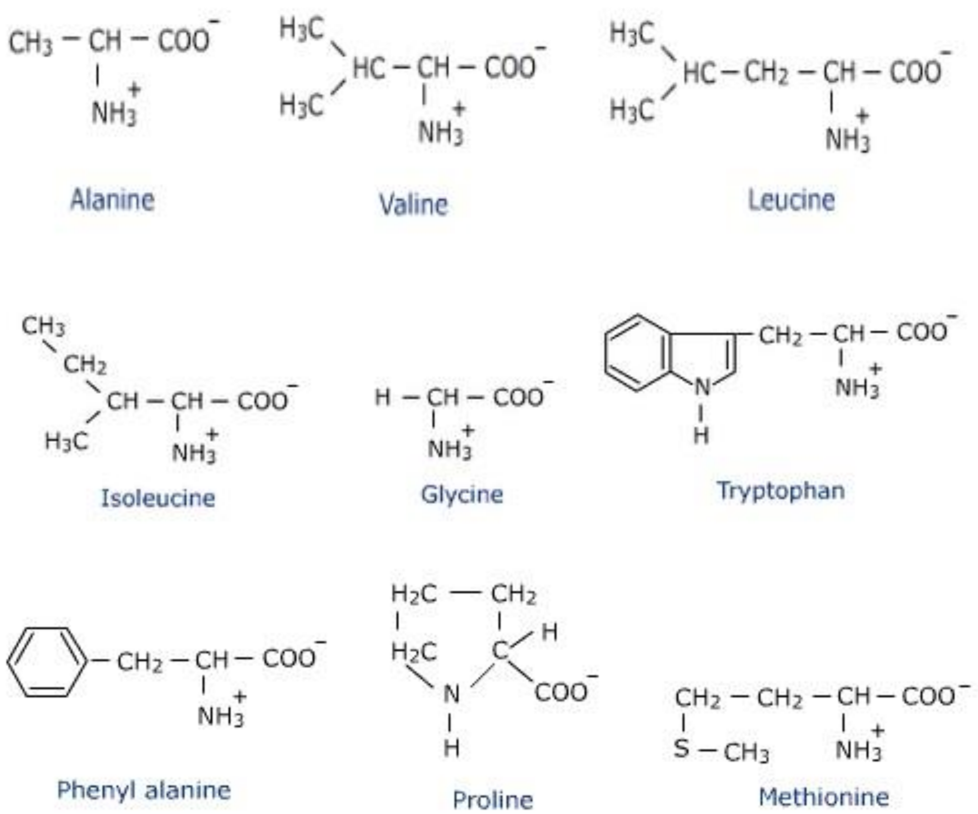

Figure 4.3: The structures of non-polar amino acids.

2- Polar amino acids with no charge: these amino acids do not have any charge on the 'R' group. The amino acids in this group are serine, threonine, tyrosine, cysteine, glutamine, and aspargine (Figure 4.4).

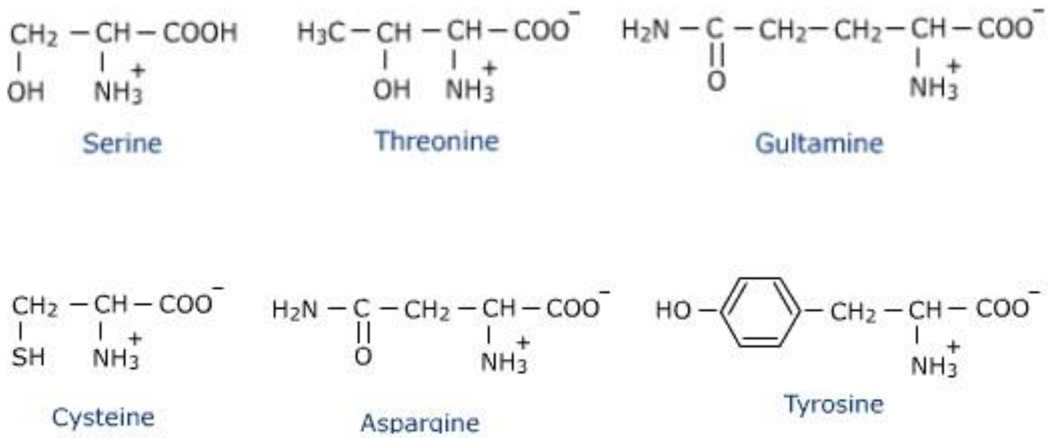

Figure 4.4: The structures of polar amino acids with no charge.

3- Polar amino acids with positive charge: have more amino groups as compared to carboxyl groups making it basic. The amino acids, which have positive charge on the 'R' group are placed in this category. They are lysine, arginine, and histidine (Figure 4.5).

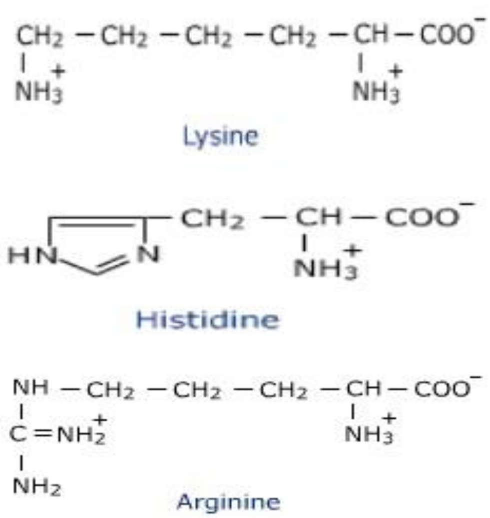

Figure 4.5: The structures of polar amino acids with positive charge.

4- Polar amino acids with negative charge: have more carboxyl groups than amino groups making them acidic. The amino acids, which have negative charge on the 'R' group are placed in this category. They are aspartic acid and glutamic acid (Figure 4.6).

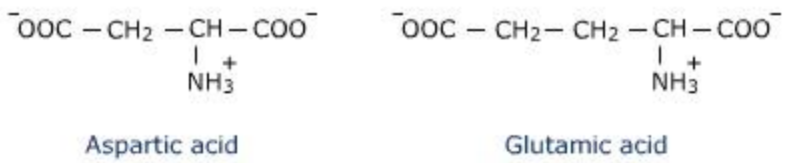

Figure 4.6: The structures of polar amino acids with negative charge.

Zwitterions

The carboxylic acid group (−COOH) of amino acids is release hydrogen to become negative carboxylates ($-COO^-$) at moderate pH values. The amino groups (NH_2-) accept hydrogen to become positive ammonium groups ($^+NH_3-$). Because all amino acids contain amine and carboxylic acid functional groups, they share amphiprotic (accept and donate H^+) properties. At pH between 2.2 and 9.4, an amino acid usually contains both a negative carboxylate and a positive ammonium group (Figure 4.7), so has net zero charge. This molecular state is known as a **zwitterion.** The pH at which an amino acid carries no net electrical charge (**zwitterion)** is called **Isoelectric point (PI).**

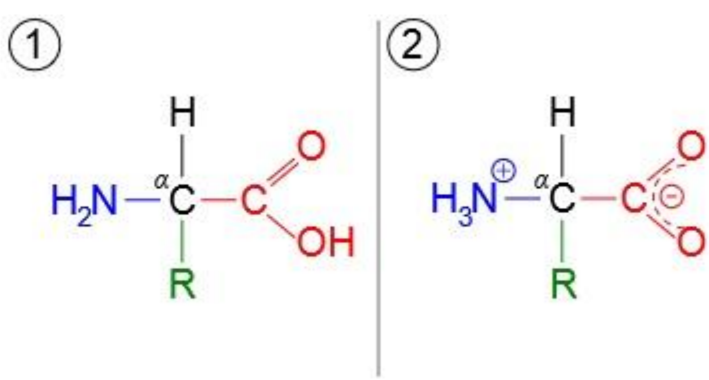

Figure 4.7: An amino acid in its (1) un-ionized and (2) zwitterionic forms.

Levels of protein structure (Figure 4.8)

There are four distinct levels of protein structure:-

1- Primary structure: refers to the sequence of amino acids in the polypeptide chain. The primary structure is held together by peptide bonds that are made during the process of protein biosynthesis. The two ends of the polypeptide chain are referred to as the carboxyl terminus (C-terminus) and the amino terminus (N-terminus). The primary structure of a protein is determined by the gene corresponding to the protein. A specific sequence of nucleotides in DNA is transcribed into mRNA, which is read by the ribosome in a process called translation. The sequence of a protein is unique to that protein, and defines the structure and function of the protein.

2- Secondary structure: there are two main types of secondary structure, the α-helix and the β-strand or β-sheets, these secondary structures are defined by patterns of hydrogen bonds between the main-chain peptide groups.

3- Tertiary structure: the α-helixes and β-pleated-sheets are folded into a compact globular structure; the folding is driven by the non-specific hydrophobic interactions, hydrogen bonds, and disulfide bonds.

4- Quaternary structure: consisting of the aggregation of two or more individual polypeptide chains (subunits) that operate as a single functional unit, the quaternary structure is stabilized by the same non-covalent interactions and disulfide bonds as the tertiary structure.

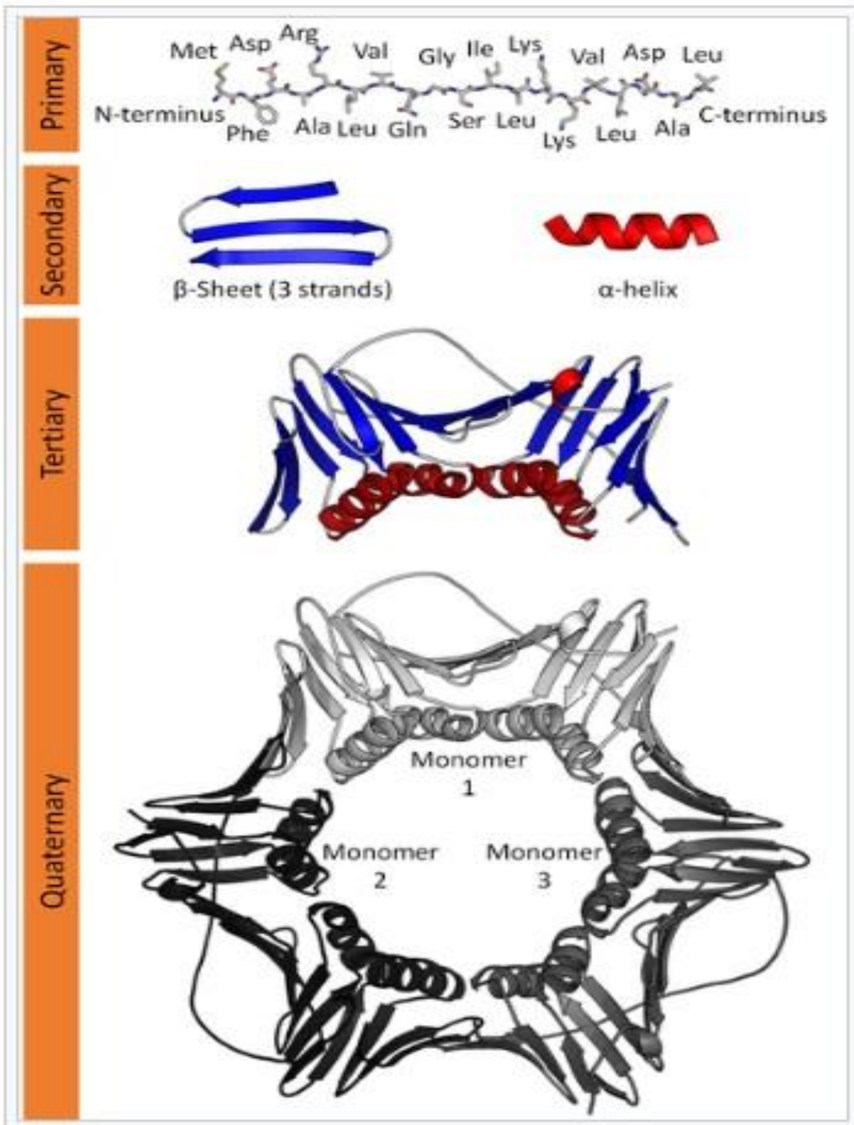

Figure 4.8: Levels of protein structure.

Cellular functions of proteins

1- Enzymes: The best-known role of proteins in the cell is as enzymes, which catalyze chemical reactions.

2- Cell signaling and ligand binding: Many proteins are involved in the process of cell signaling and signal transduction, such as insulin. Haemoglobin is a ligand-binding protein, which transports oxygen from the lungs to other organs and tissues. Receptors and hormones are highly specific binding proteins.

3- Structural proteins: Collagen and elastin are components of cartilage. Keratin is found in hair and nails. Actin and tubulin are stiff fibers that make up the cytoskeleton, which allows the cell to maintain its shape and size.

Biosynthesis of amino acids

Amino acid synthesis is the set of biochemical processes (metabolic pathways) by which the various amino acids are produced from other compounds. Not all organisms are able to synthesize all amino acids. Humans are an excellent example of this, since humans can only synthesize 11 of the 20 standard amino acids. Certain microorganisms capable of reducing the inert N≡N molecule (nitrogen gas) to ammonia (NH3). Ammonia is the source of nitrogen for all the amino acids. The carbon backbones come from the glycolytic pathway, the pentose phosphate pathway, or the citric acid cycle.

In plants, nitrogen is first assimilated into organic compounds in the form of glutamate, formed from alpha-ketoglutarate and ammonia in the mitochondrion. In order to form other amino acids, the plant uses transaminases.

Catabolism of proteins

Protein catabolism is the breakdown of proteins into amino acids and simple derivative compounds, for transport into the cell through the plasma membrane and for the polymerization into new proteins.

The amino acids produced by catabolism may be directly recycled to form new proteins, converted into different amino acids, or can undergo amino acid catabolism to be converted to other compounds via the Krebs cycle.

Medical and biological importance of proteins

1- Proteins are involved in the transport of substances in the body. Example, haemoglobin transport oxygen.

2- Enzymes which catalyze chemical reactions in the body are proteins.

3- Proteins are involved in defence function. They act against bacterial or viral infection. Example, immunoglobulins.

4- Hormones are proteins. They control many biochemical events. Example, insulin.

5- Some proteins have role in contraction of muscle. Example, muscle proteins.

6- Proteins are involved in gene expression. Example, histones.

7- Proteins serve as nutrients. Example, casein of milk.

8- Proteins act as buffers. Example, plasma proteins.

9- Proteins are infective agents. Example, prions which cause mad cow disease are proteins.

10- Some toxins are proteins. Example, enterotoxin of cholera microorganism.

11- Some proteins provide structural strength and elasticity to the organs and vascular system. Example, collagen and elastin of bone matrix and ligaments.

12- Some proteins are components of structures of tissues. Example, α-keratin is present in hair and epidermis.