MEDICAL CHEMISTRY
GENERAL CHEMISTRY

University Of Fallujah
College Of Medicine

Lecture : Medical Chemistry (2) (Proteins)

Stage : 1st Stage

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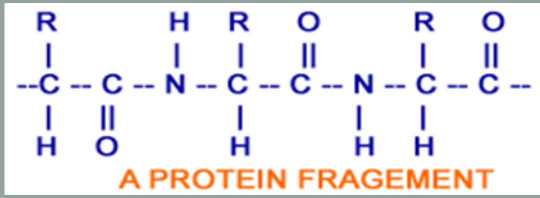
Learning Objective :

- Define Proteins and Their Composition.
- Understand the Hierarchical Structure of Proteins.
- Classify Proteins Based on Shape and Solubility.
- Describe the Functional Roles of Proteins.
- Classify Proteins Based on Composition.
- Recognize the Importance of Protein Folding.

Proteins

Proteins are polymers made of monomers called the amino acids.

There are 20 different kinds of amino acids that make up the proteins. However, they are present in different proportions in each of the proteins.



Proteins consist of one or more polypeptides arranged in a biologically functional way, often bound to ligands such :
as coenzymes and cofactors, or to another protein or other macromolecule such as DNA or RNA, or to complex macromolecular assemblies.

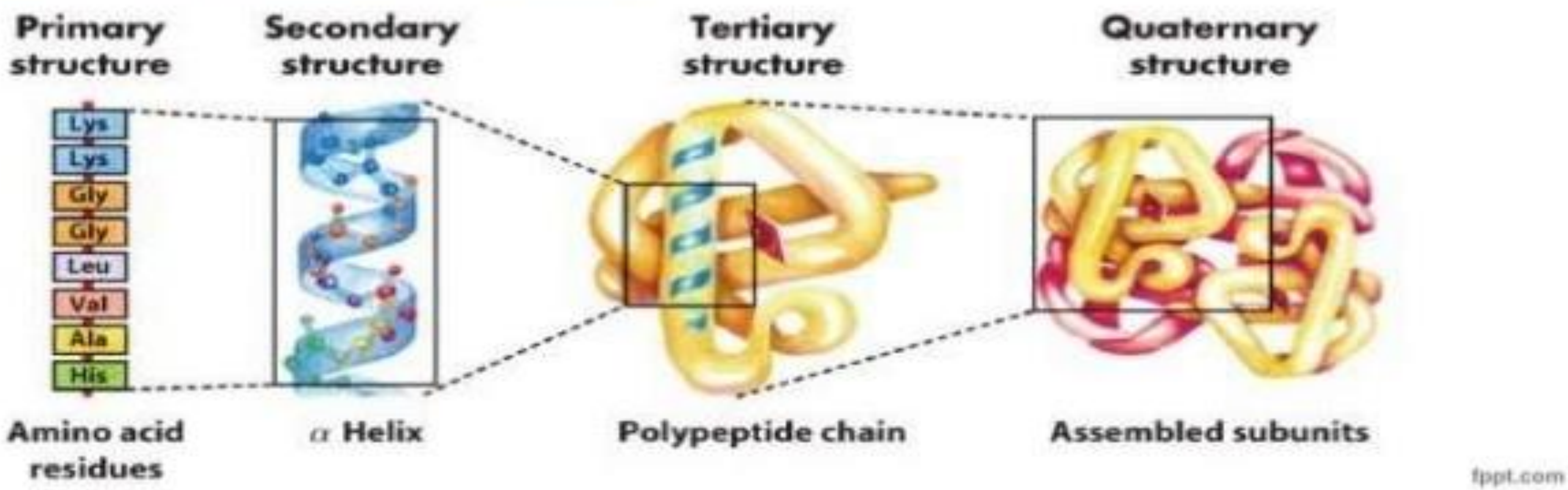
Different Levels of Protein Structure

Protein structure is organized hierarchically from so-called primary structure to quaternary structure.

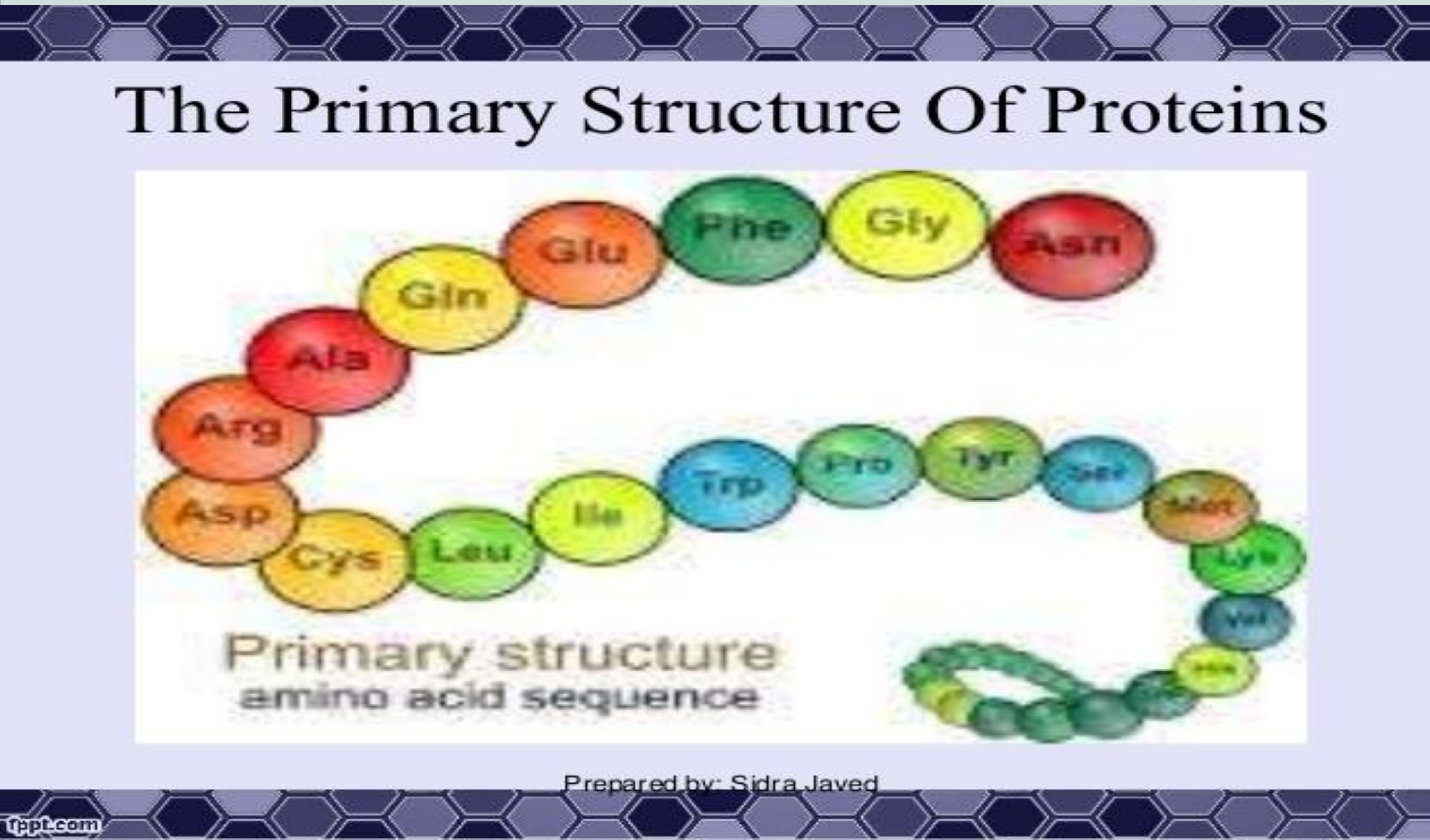
STRUCTURAL ORGANIZATION OF PROTEINS

The structural and functional features of proteins and protein complexes are addressed at four levels of hierarchal organization. These are:

1. Primary structure (1°-Structure)
2. Secondary structure (2°-Structure)
3. Tertiary structure (3°-Structure)
4. Quaternary structure (4°-Structure)



- **Primary structure**: The primary structure of a peptide or protein is the linear sequence of its amino acid structural units.



- **Secondary structure:** regularly repeating local structures stabilized by hydrogen bonds.There are two types of stable secondary structures: **Alpha helices** and **beta-sheets** (see Figure 1 and Figure 2). Alpha-helices and beta-sheets are preferably located at the core of the protein, where at loops prefer to reside in outer regions.

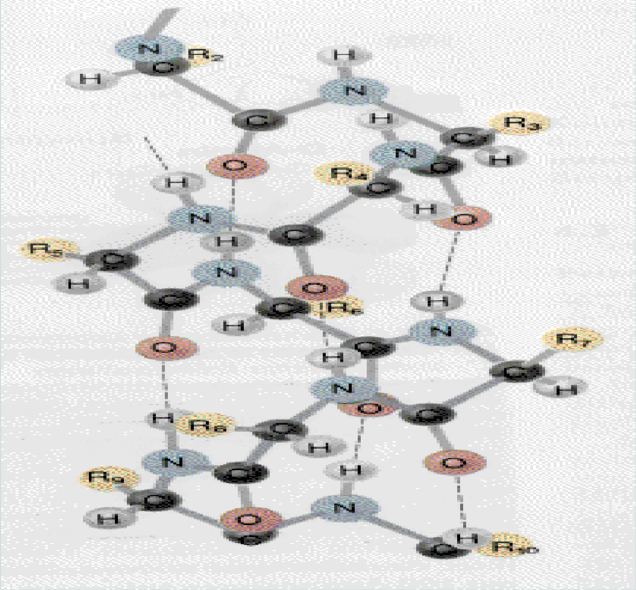


Figure 1: An alpha helix: The backbone is formed as a helix. There are hydrogen bonds between the carboxyl group of amino acid n and the amino group of another amino acid.

beta-sheets

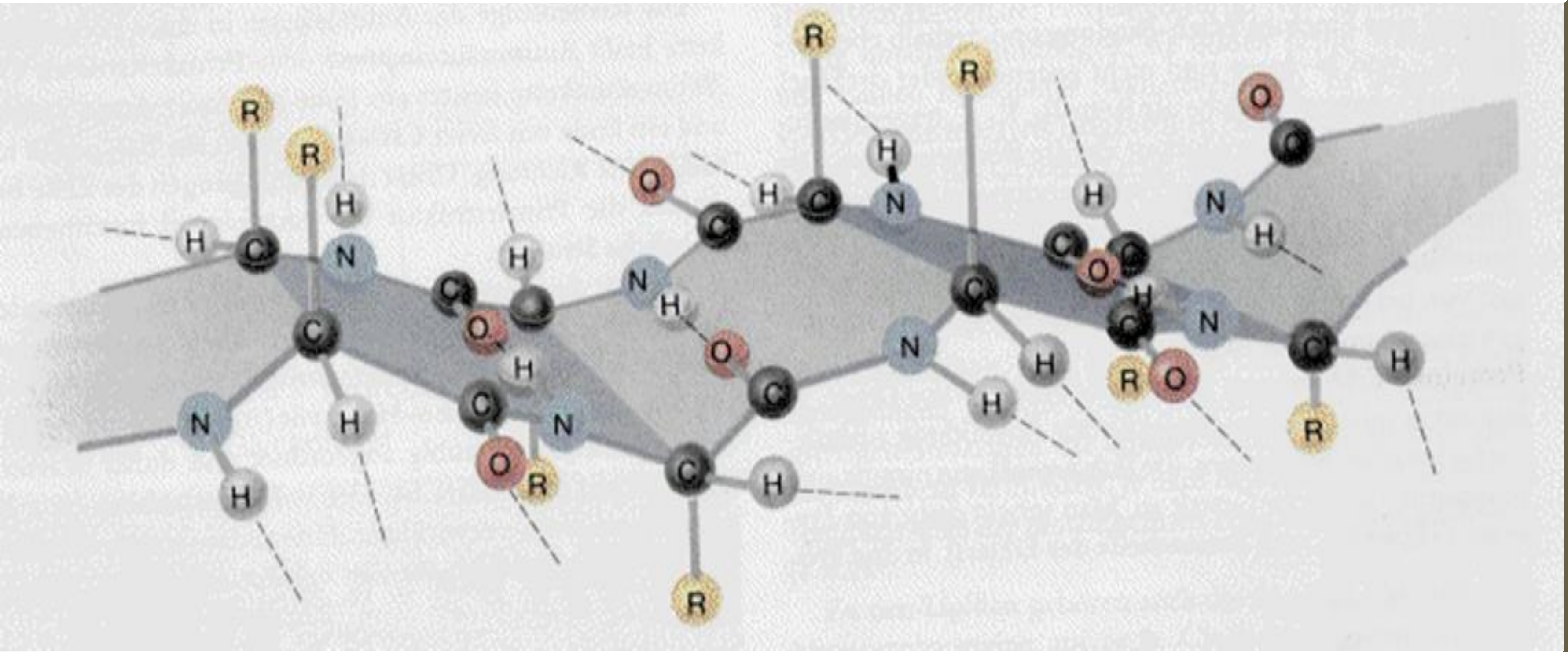


Figure 2: An antiparallel beta sheet. Beta sheets are created, when atoms of beta strands are hydrogen bound. Beta sheets may consist of parallel strands, antiparallel strands or out of a mixture of parallel and antiparallel strands.

- **Tertiary structure**: describes the packing of alpha-helices, beta-sheets and random coils with respect to each other on the level of one whole polypeptide chain. Figure 3 shows the tertiary structure of Chain B of Protein Kinase C Interacting Protein.

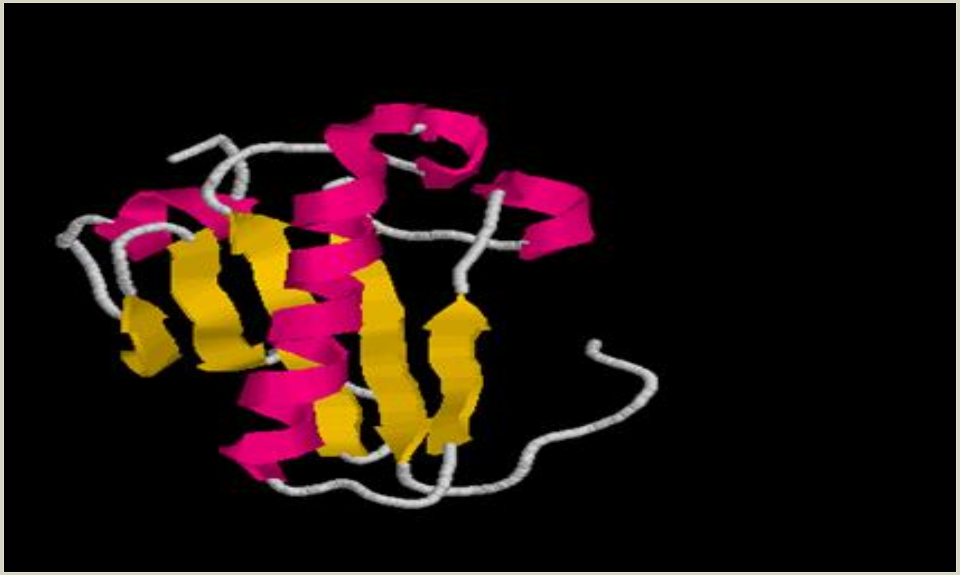


Figure 3: Chain B of Protein Kinase C Interacting Protein. Helices are visualized as ribbons and extended strands of beta sheets by broad arrows.

Tertiary structure is generally stabilized by nonlocal interactions, most commonly the formation of a hydrophobic core, but also through salt bridges, hydrogen bonds, disulfide bonds, and even post translational modifications. The term **"tertiary structure"** is often used as synonymous with the term **fold**.

The wide variety of 3-dimensional protein structures corresponds to the diversity of functions proteins fulfill.

Most proteins fold into unique 3-dimensional structures. The shape into which a protein naturally folds is known as its native conformation.

- **Quaternary structure**: the structure formed by several protein molecules (polypeptide chains), usually called protein subunits in this context, which function as a single protein complex.

only exists, if there is more than one polypeptide chain present in a complex protein. Then quaternary structure describes the spatial organization of the chains. Figure 4 shows both, Chain A and Chain B of Protein Kinase C Interacting Protein forming the quaternary structure.

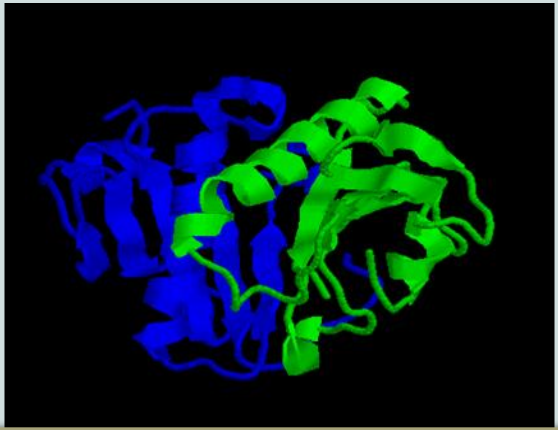


Figure 4: Quaternary structure of Protein Kinase C Interacting Protein.

TYPES OF PROTEINS

According to their "environmental conditions" and general structure, proteins can be roughly divided into three classes:

1) FIBROUS PROTEIN: It is usually water-deficient aggregates; their structure is usually highly hydrogen bonded; highly regular and maintained mainly by interactions between various chains.

2) MEMBRANE PROTEINS: It reside in a water-deficient membrane environment (although they partly project into water). The intra-membrane portions are highly regular and highly hydrogen-bonded; but restricted in size by the membrane thickness.

3) GLOBULAR PROTEINS: They are less regular and their structure is maintained by interactions of chain with itself and sometimes by chain interactions with cofactors.

Classification of Proteins According to Shape and Solubility:

Proteins can be informally divided into three main classes, which correlate with typical tertiary structures:

- **Fibrous proteins**
- **Globular proteins, and**
- **Membrane proteins.**

Proteins can be broadly classified into three groups:

Fibrous proteins: these proteins have a rod like structure. They are not soluble in water.

Fibrous proteins are often structural, such as **collagen**, the major component of connective tissue, or **keratin**, the protein component of hair and nails, and **Elastin**, present in connective tissues .

Globular proteins: These proteins more or less spherical in nature. Due to their distribution of amino acids (hydrophobic inside, hydrophillic outside) they are very soluble in aqueous solution. Almost all globular proteins are soluble and many are enzymes. Myoglobin, hemoglobin, albumin are also an examples of a globular protein.

Membrane proteins: These are protein which are in association with lipid membranes. Those membrane proteins that are embedded in the lipid bilayer have extensive hydrophobic amino acids that interact with the non-polar environment of the bilayer interior.

Membrane proteins are not soluble in aqueous solution.

Rhodopsin is an example of a membrane protein. Note that rhodopsin is an integral membrane protein and is embedded in the bilayer. Membrane proteins often serve as receptors or provide channels for polar or charged molecules to pass through the cell membrane. Microsomal enzymes are also membrane proteins

Classification and Function of Proteins:

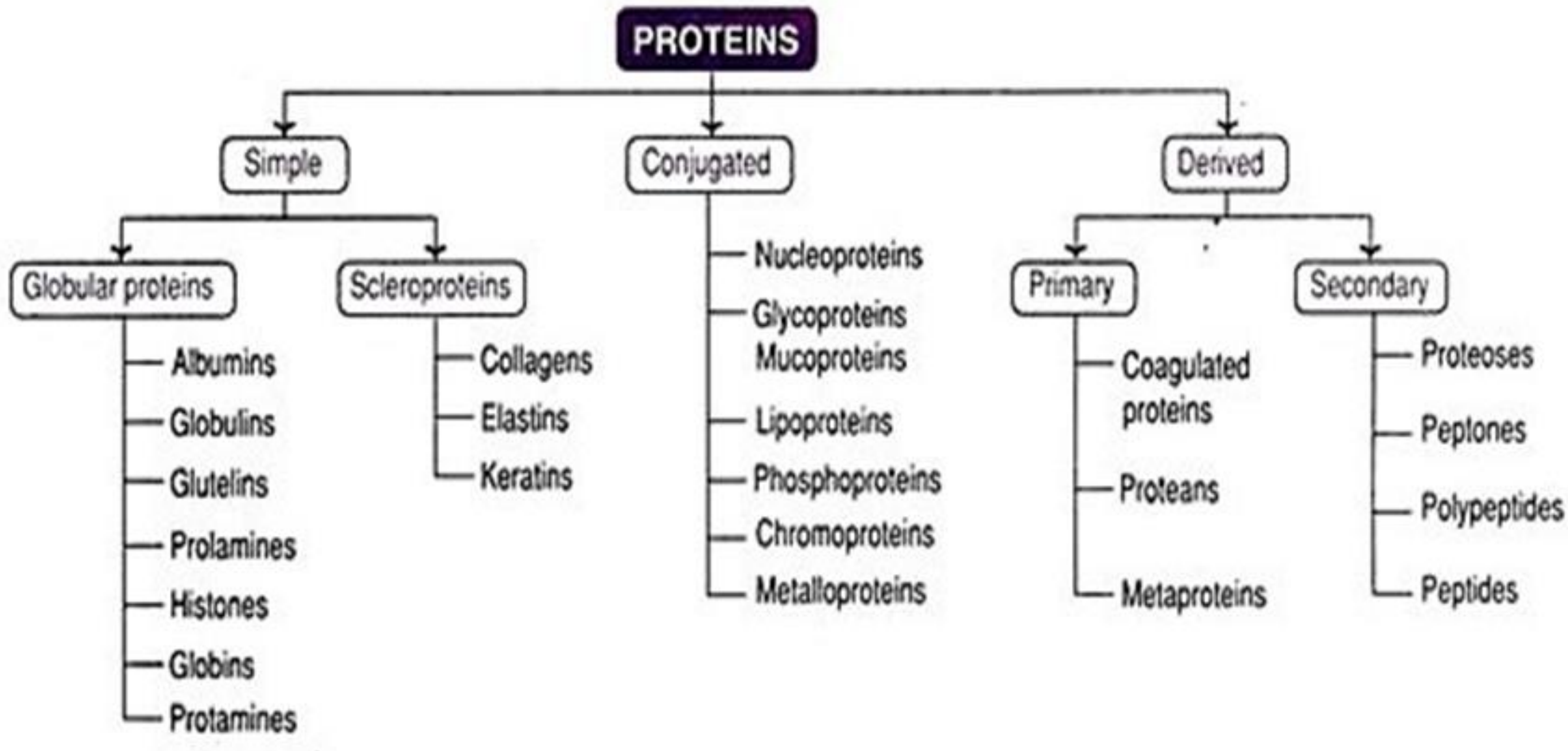
Proteins are the chief body builders of the body. They are complex molecules made up of carbon, hydrogen, oxygen and nitrogen (sometimes sulphur and phosphorus).

Examples of Body Proteins are: **enzymes** (e.g., **pepsin, trypsin**), **hormones** (e.g., **insulin, prolactin**), **carrier proteins** (e.g., **Haemoglobin**), **contractile proteins** (e.g., **myosin, actin**), **structural proteins** (e.g., **collagen**) and **protective proteins** (**antibodies**). They also form skin pigments like **melanin** and **nucleic acids** of the genetic material, **DNA and RNA** - purines and pyrimidines.

Classification based on composition:

Proteins are divided into three main classes :

1. **Simple proteins**
2. **Conjugated proteins**
3. **Derived proteins**



1. Simple proteins:

These are of globular type except for scleroproteins which are fibrous in nature. This group includes proteins containing only amino acids, as structural components.

The simple proteins are those which are made of amino acid units only, joined by peptide bond. Upon hydrolysis they yield mixture of amino acids and nothing else.

Examples: **Blood proteins** (**albumins, Globulins**..), **proteins connected with DNA** (**Histones**..), **structural proteins** (**collagens, Keratins**..).

Many proteins contain only amino acids and no other chemical groups, and they are called **simple proteins**.

However, other kind of proteins yield, on hydrolysis, some other chemical component in addition to amino acids and they are called conjugated proteins. The non-amino part of a conjugated protein is usually called its prosthetic group.

2. Conjugated or Complex Proteins:

These are also of globular type. These are the simple proteins linked with a separable non protein portion called prosthetic group. The prosthetic group or cofactor (in enzymes called coenzyme), may be either a metal or a compound.

Their further classification is based on the nature of the prosthetic group present.

The various divisions are:

1. Metalloproteins:

Metalloproteins: are proteins bound by at least one metal ion cofactor. A large proportion of all proteins are part of this category. For instance, at least 1000 human proteins (out of ~20,000) contain zinc-binding protein domains although there may be up to 3000 human zinc metalloproteins.

2. Chromoproteins:

A chromoprotein is a conjugated protein that contains a pigmented prosthetic group (or cofactor). A common example is **haemoglobin**, which contains a heme cofactor, which is the iron-containing molecule that makes oxygenated blood appear red.

3. Glycoproteins:

Glycoproteins are proteins which contain oligosaccharide chains covalently attached to amino acid side-chains. **Glycoproteins** are generally the largest and most abundant group of conjugated proteins. Examples: Most enzymes, glycoprotein hormones….

4. Phosphoproteins:

Phosphoproteins are proteins that are phosphorylated, usually by kinases (Kinases are enzymes of phosphorylation of compounds). They may be part of signal transduction cascades in which one kinase phosphorylates one kinase (making it a phosphoprotein).

5. Lipoproteins: **Chylomicrons, VLDL, LDL,HDL.**

6. Nucleoproteins:

Nucleoproteins are any proteins that are structurally associated with nucleic acids, either DNA or RNA. Typical nucleoproteins include ribosomes, Histones are a family of basic proteins that associate with DNA in the nucleus and help condense it into chromatin.

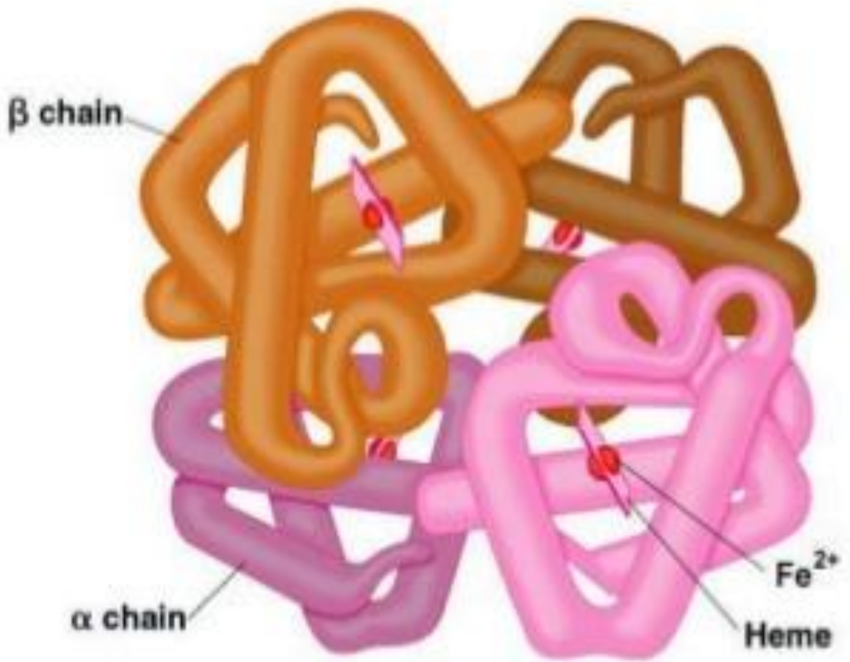
DERIVED PROTEINS

These are not naturally occurring proteins and are obtained from simple proteins by the action of enzymes and chemical agents.

Examples: Gelatin, peptones, peptides , proteoses etc.

HEMOGLOBIN

- Hemoglobin is a tetramer composed of two each of two types of closely related subunits, alpha and beta.
- Hemoglobin transport O_2 from lungs to tissues.
- Hemoglobin is hydrophilic.



MYOGLOBIN

- Myoglobin is a monomer (so it doesn't have a quaternary structure at all).
- Myoglobin binds oxygen more tightly than does hemoglobin. This difference in binding energy reflects the movement of oxygen from the bloodstream to the cells, from hemoglobin to myoglobin.
- Myoglobin is hydrophilic in outside and hydrophobic in inside.