بسم الله الرحمن الرحيم

Basic Principles and Perspectives in Medical Chemistry and Biochemistry

Amino Acids & Proteins

Part 3

3rd Medical and Biochemistry (BIQC-101) Lecture

Second Semester

by

Prof. Dr. Salih Mahdi Salman

Classification of Protein

Learning Objectives

1. Classify proteins according to different parameters including chemical composition, shape, biological function, solubility in water.
2. Describe, using examples, the relationship between protein structure and function
3. Explain of biological activity of some important proteins

Protein classification

Different methods of protein classification have been proposed. Below, some examples based on chemical composition, shape, functions, and solubility in different solvents.

Protein classification based on chemical composition

On the basis of chemical composition, proteins may be divided into two classes: **simple** and **complex**.

1. Simple proteins

Also known as homoproteins, they are made up of only amino acids. Examples are plasma albumin, collagen, and keratin.

2. Complex (conjugated) proteins

Sometimes also called heteroproteins, they contain in their structure a non-protein portion. They are three classes:-

1) Glycoproteins

Proteins covalently bind to one or more carbohydrate units to the polypeptide backbone. Typically, about 15-20 carbohydrate units such as arabinose, fucose (6-deoxygalactose), galactose, glucose, mannose, N-acetylglucosamine (GlcNAc, or NAG), and N-acetylneuraminic acid (Neu5Ac or NANA).

Examples of glycoproteins are:

1. Glycophorin, the best known among erythrocyte membrane glycoproteins;
2. Fibronectin, that anchors cells to the extracellular matrix through interactions on one side with collagen or other fibrous proteins, while on the other side with cell membranes;
3. All blood plasma proteins, except albumin;
4. Immunoglobulins or antibodies.

2) Chromoproteins

They are proteins that contain colored prosthetic groups. Typical examples are:

Hemoglobin and myoglobin, which bind, respectively, four and one heme groups

Chlorophylls, which bind a porphyrin ring with a magnesium atom at its center.

3) Phosphoproteins

They are proteins that bind phosphoric acid to serine and threonine residues. Generally, they have a structural function, such as tooth dentin.

Protein classification based on shape

On the basis of their shape, proteins may be divided into two classes: fibrous and globular.

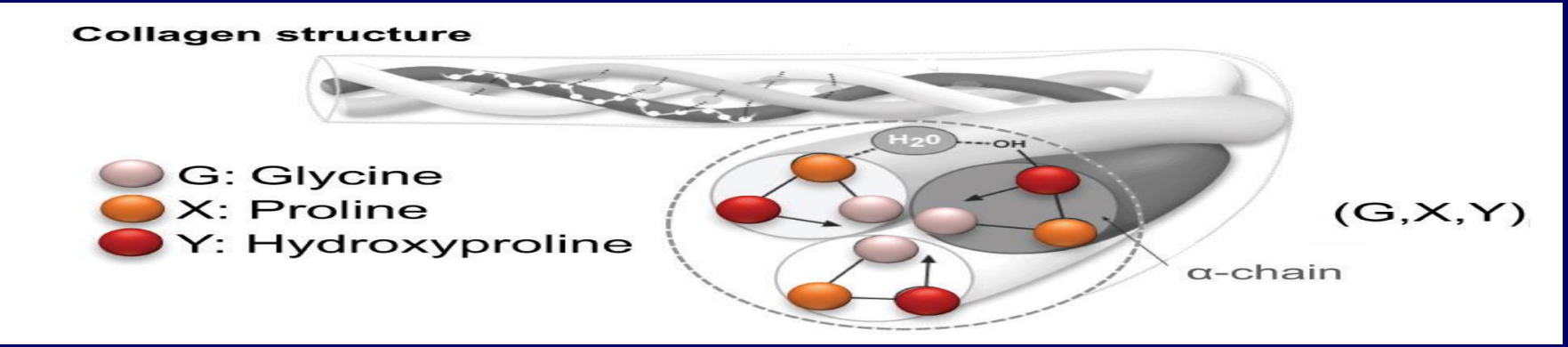
1. Fibrous proteins

- Have primarily mechanical and structural functions, providing support to the cells as well as the whole organism.
- Insoluble in water as they contain, both internally and on their surface, many hydrophobic amino acids.
- The presence on their surface of hydrophobic amino acids facilitates their packaging into very complex supramolecular structures.
- So, their polypeptide chains form long filaments or sheets, where in most cases only one type of secondary structure, that repeats itself, is found.
- Examples. (Collagen , α-Keratins & Elastin)

Collagen

- Collagen indicates not a single protein but a family of structurally related proteins (at least 29 different types), which constitute the main protein component of connective tissue,
- They are found in different tissues and organs, such as tendons and the organic matrix of bone, where they are present in very high percentages, but also in cartilage and in the cornea of the eye.
- In the different tissues, they form different structures, each capable of satisfying a particular need. For example, in the cornea, the molecules are arranged in an almost crystalline form, so that they are virtually transparent, while in the skin they form fibers not very intertwined and directed in all directions, which ensure the tensile strength of the skin itself.
- Note: the different types of collagen have low nutritional value as deficient in several amino acids (in fact, they contain no tryptophan and low amount of the other essential amino acids).

- A special quaternary structure called a triple helix forms the fibrous structure of collagen.
- Each polypeptide chain of a triple helix is a left-handed helix.
- Collagen primarily contains the amino acids glycine, proline, alanine, and hydroxyproline.



- Hydrogen bonds between the polypeptide chains in collagen are formed through the hydroxyl group on hydroxyproline.
- Proline is converted to hydroxyproline with the aid of Vitamin C.
- A deficiency of Vitamin C causes scurvy, which is a collagen malformation disease. Scurvy can be reversed with a vitamin C diet.

α-Keratins

- They constitute almost the entire dry weight of nails, hair, and a large part of the outer layer of the skin.
- The different stiffness and flexibility of these structures is a consequence of the number of disulfide bonds that contribute, together with other binding forces, to stabilize the protein structure.
- And this is the reason why wool keratins, which have a low number of disulfide bonds, are flexible, soft and extensible, unlike nails keratin that are rich in disulfide bonds.

Elastin

Provides elasticity to the skin and blood vessels, a consequence of its random coiled structure, that differs from the structures of the α-keratins and collagens.

2. Globular proteins

- Most of the proteins belong to this class.
- They have a compact and spherical structure, more complex than fibrous proteins.
- In this regard, tertiary and quaternary structures are found, in addition to the secondary structures.
- They are generally soluble in water but can also be found inserted into biological membranes (transmembrane proteins), thus in a hydrophobic environment.

- ✓ They act as:

1. Enzymes.
2. Hormones.
3. Membrane transporters and receptors.
4. Transporters of triglycerides, fatty acids and oxygen in the blood.
5. Immunoglobulins or antibodies.
6. Grain and legume storage proteins.

- ✓ Examples of globular proteins are myoglobin, hemoglobin, and cytochrome.
- ✓ At the intestinal level, most of the globular proteins of animal origin are hydrolyzed almost entirely to amino acids.

Protein classification based on biological functions

The multitude of functions that proteins perform is the consequence of both the folding of the polypeptide chain, therefore of their three-dimensional structure, and the presence of many different functional groups in the amino acid side chains, such as thiols, alcohols, thioethers, carboxamides, carboxylic acids and different basic groups.

From the functional point of view, they may be divided into several groups.

1. Biochemical catalysts

Almost all known enzymes, and in the human body they are thousand, are proteins (except some catalytic RNA molecules called ribozymes, that is, ribonucleic acid enzymes).

2. Transport proteins

- Many small molecules, organic and inorganic, are transported in the bloodstream and extracellular fluids, across the cell membranes, and inside the cells from one compartment to another, by specific proteins.
- Examples are:

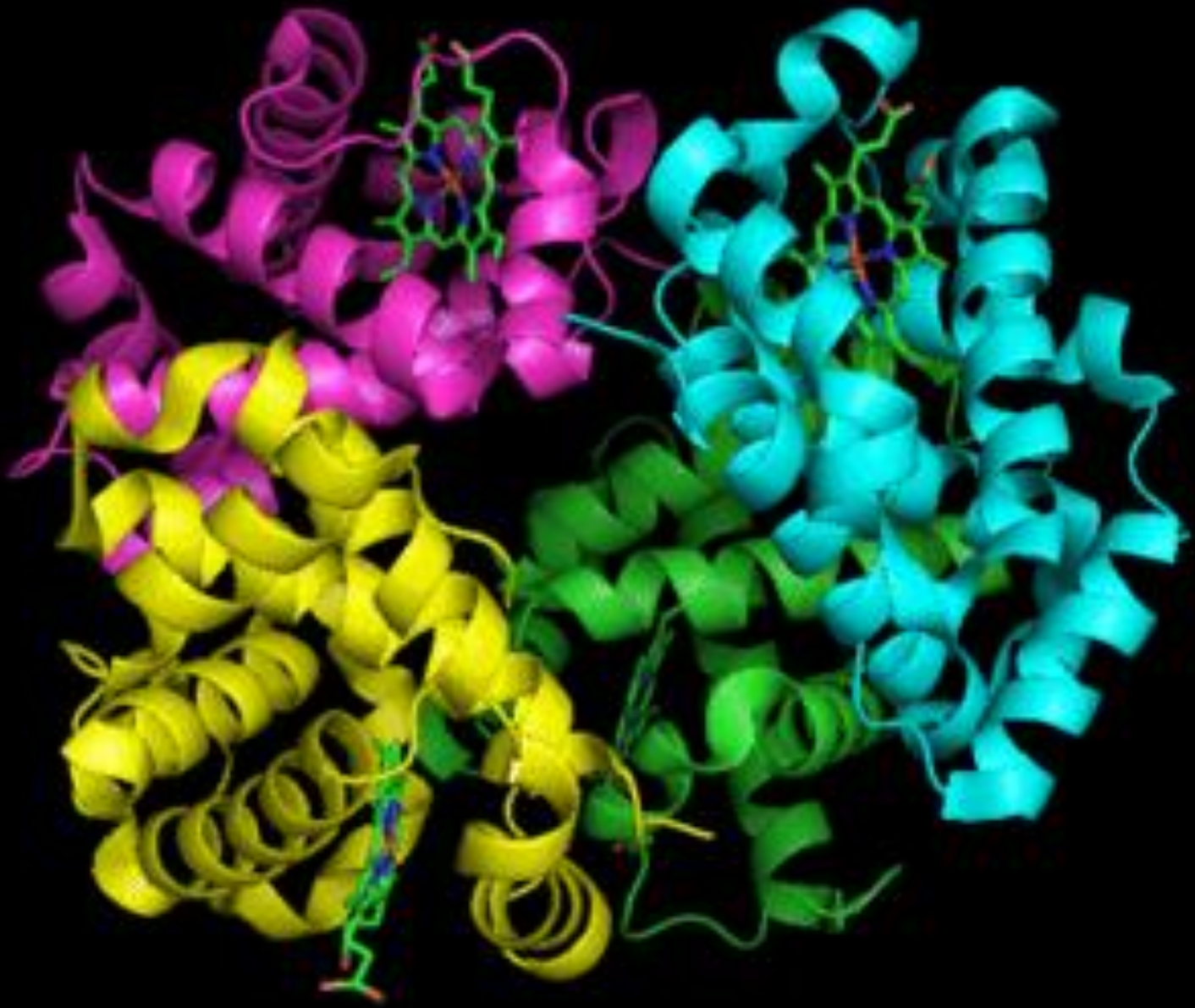
1. Hemoglobin, that carries oxygen from the alveolar blood vessels to tissue capillaries.
2. Transferrin, which carries iron in the blood.
3. Fatty acid binding proteins (FABP), that is, the proteins involved in the intracellular transport of fatty acids.

4. Proteins of plasma lipoproteins, macromolecular complexes of proteins and lipids responsible for the transport of triglycerides, which are otherwise insoluble in water;
5. Albumin, that carries free fatty acids, bilirubin, thyroid hormones, and certain medications such as aspirin and penicillin, in the blood.

Many of these proteins also play a protective role, since the bound molecules, such as fatty acids, may be harmful for the organism when present in free form.

Hemoglobin

- **Hemoglobin** transports oxygen in blood.
- It is composed of two alpha subunits and two beta subunits held together by hydrogen bonds, london forces, and salt bridges.
- Each subunit contains a nonprotein part called a **prosthetic group**, which is called a **heme**.
- Each heme group binds an Fe2+, which binds O2, so a molecule of hemoglobin can bind up to four molecules of O2.
- When O2 binds to the Fe2+ of hemoglobin, the shape of hemoglobin changes, which allows the hemoglobin to hold on to the oxygen until it is delivered to tissues. This change in shape is known as a conformational change.
- After the oxygen is delivered to the tissues, the shape of the hemoglobin changes back to its pre-oxygenated form.



3. Storage proteins

Examples are:

Ferritin, that stores iron intracellularly in a non-toxic form.

Egg yolk phosvitin, that contains high amounts of phosphorus.

prolamins and glutelins, the storage proteins of cereals.

4. Mechanical support

Proteins have a pivotal role in the stabilization of many structures. Examples are α-keratins, collagen and elastin. The same cytoskeletal system, the scaffold of the cell, is made of proteins.

4. Nerve transmission

An example is the receptor for acetylcholine at synapses.

5. Control development and differentiation

Some proteins are involved in the regulation of gene expression. An example is the nerve growth factor (NGF), that plays a leading role in the formation of neural networks.

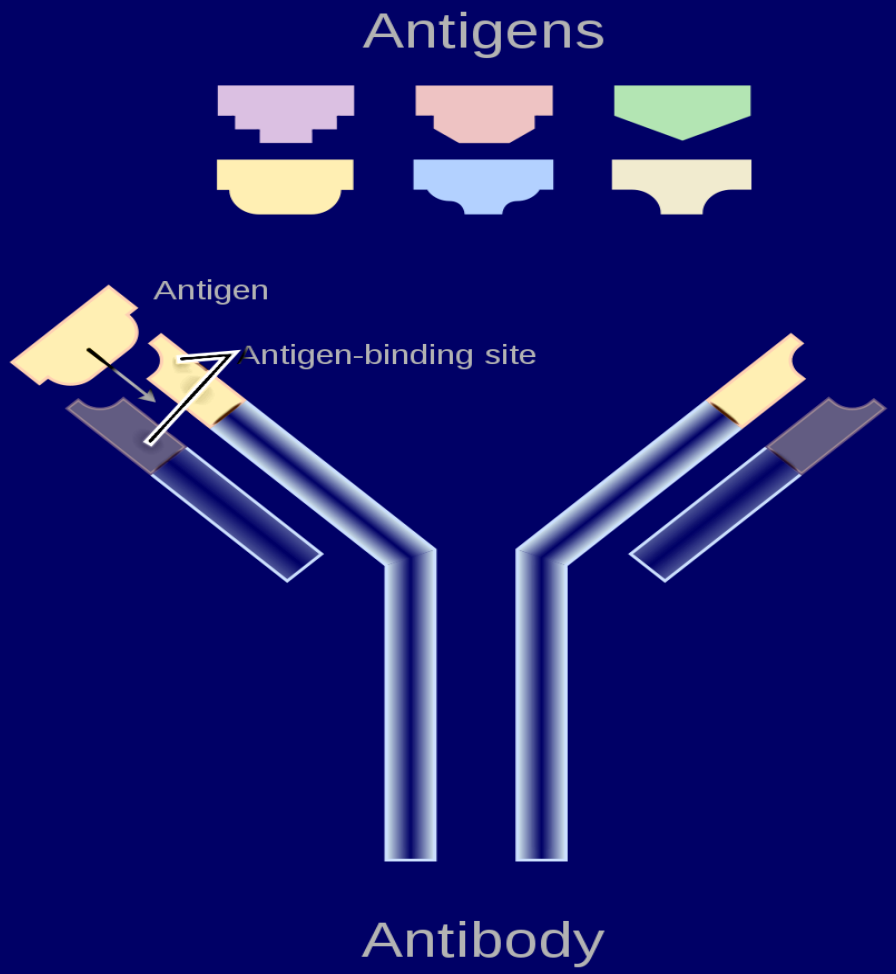
6. Hormones

- Many hormones are proteins.
- They are regulatory molecules involved in the control of many cellular functions, from metabolism to reproduction. Examples are insulin, glucagon, and thyroid-stimulating hormone (TSH).

7. Protection against harmful agents.

- The antibodies or immunoglobulins are glycoproteins that recognize antigens expressed on the surface of viruses, bacteria and other infectious agents.
- Interferon, fibrinogen, and factors of blood coagulation are other members of this group.
- The foreign agent recognized by antibodies is known as an antigen.
- Antibodies consists of four polypeptide chains held together by disulfide bonds and intermolecular forces.
- Antibodies are “Y” shaped. Antigens bind at the top of each arm of the Y.

The top of each Y has a unique primary structure for a particular antigen and binds only one antigen, which is then destroyed by the immune system.



8. Storage of energy.

Proteins, and in particular the amino acids that constitute them, act as energy storage, come in the second order after the adipose tissue, that in particular conditions, such as prolonged fasting, may become essential for survival. However, their reduction of more than 30% leads to a decrease of the contraction capacity of respiratory muscle, immune function, and organ function, that are not compatible with life. Therefore, proteins are an extremely valuable fuel.

Insoluble in water -Fibrous proteins (Collagen, α-Keratins, Elastin)
Soluble in water- Globular proteins (Transmembrane proteins)

Fibrous proteins
Collagen
α-Keratins
Elastin

Globular proteins
Myoglobin
Hemoglobin
Cytochrome

Protein Classification Base

Solubility

Shape

Chemical Composition

Biological functions

Simple proteins (Homoproteins) plasma albumin collagen, keratin

Complex (conjugated) (Heteroproteins)

Glycoproteins Immunoglobulins, Glycophorin, Fibronectin,

Chromoproteins Hemoglobin , myoglobin

Phosphoproteins Milk caseins, Egg yolk

Biochemical catalysts (**E**nzymes)

Transport proteins (Hemoglobin, Transferrin, Membrane carriers, Fatty acid binding proteins)

Storage proteins (α-keratins, collagen ,elastin)

Mechanical support (Ferritin)

Nerve transmission (**A**cetylcholine)

Control development and differentiation (**N**erve growth factor)

Hormones (**I**nsulin, glucagon, thyroid-stimulating hormone)

Protection against harmful agents (**I**nterferon, fibrinogen


Thank you for your attention