

Globular proteins

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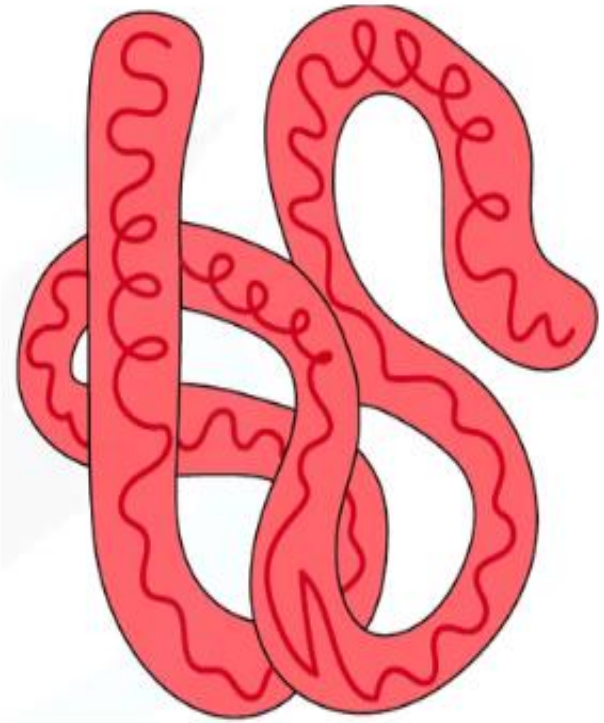
Globular proteins

- **Globular proteins or spheroproteins:** are compact, spherical proteins that are generally soluble in water, unlike fibrous proteins.
- **Examples of Globular Proteins**
- **Hemoglobin, Myoglobin**
- **Immunoglobulins**
- **Enzymes**
- **Insulin**

Globular Protein

Globular proteins are spherical and function in transport, enzymes, and regulation



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Fibrous Protein

Fibrous proteins are elongated and structural, providing support and strength to tissues.



Hemoproteins

- **Definition:** are conjugated protein formed of protein part (globin) and nonprotein prosthetic part (heme).
- **Hemoproteins Include many biologically active compounds as:**
- **Hemoglobin:** This carries oxygen.
- **Myoglobin:** This stores oxygen in muscles.
- **Respiratory enzymes:** These use oxygen.

Hemoglobin Structure

Hemoglobin: is a metalloprotein formed of heme and globin.

Location: in red blood cells (RBC)

Structure of heme:

✓ Four Pyrrol rings → protoporphyrin Ill.

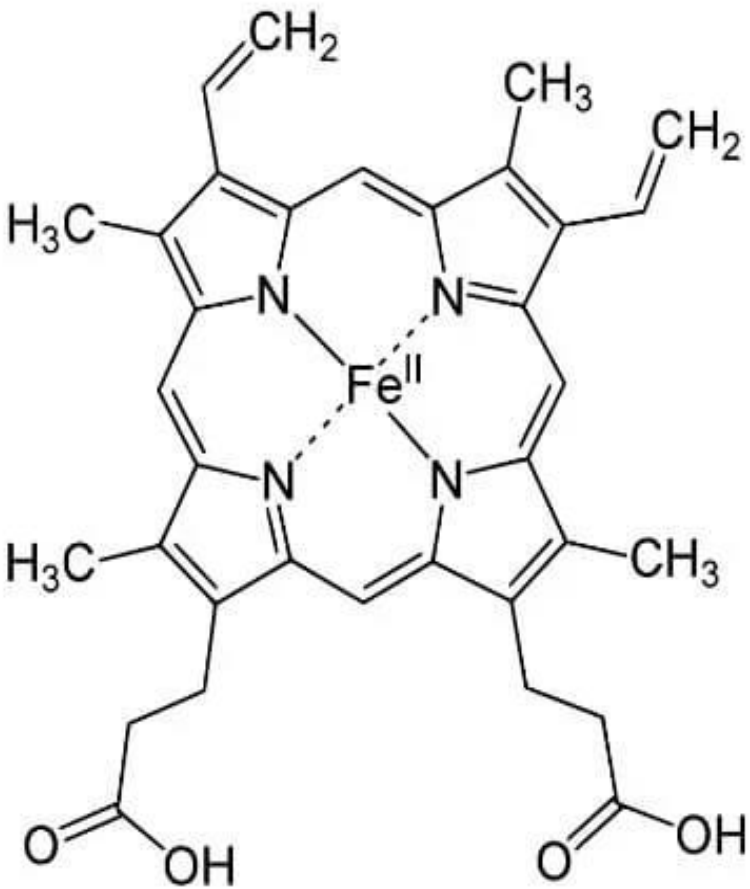
✓ Iron in (Fe^{+2}) is incorporated in nitrogens of protoporphyrin Ill to form heme.

Hemoglobin Structure

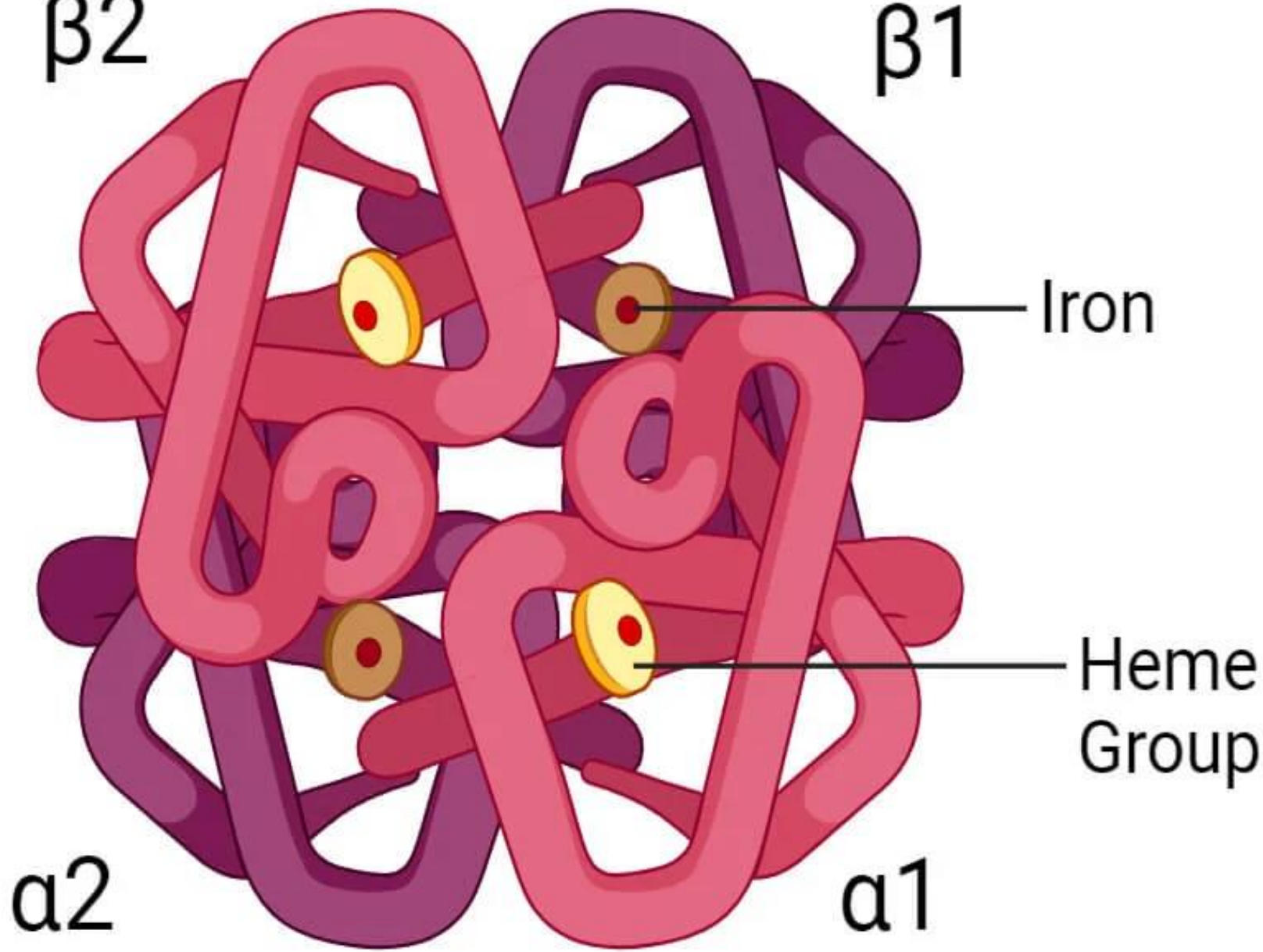
Structure of Globin:

Is a globular protein with quaternary structure, formed of **2α chains & 2 βchains**, rich in **histidine** amino acid, each chain non-covalently associated with a heme group (heme-binding pocket), with a (Fe^{2+}) iron at its center that reversibly binds with oxygen molecules.

Hemoglobin



heme *b*



Functions of hemoglobin

- **Carries O_2 to tissues and removes CO_2 from them to the lungs.**
- **Acts as blood buffer.**
- **Red Color of the blood: (heme group + iron atom)**

Hemoglobin Buffering system in tissues

1. **CO_2 Production:** Tissues produce CO2 from cellular respiration.

2. **Carbonic Acid Formation: in RBCs**

$CO_2 + H_2O \xrightleftharpoons{\textbf{carbonic anhydrase}} H_2CO_3$.

3. **H^+ Generation:** Carbonic acid $\rightleftharpoons$ $HCO_3^- + H^+$.

4. **H^+ Buffering:** Hemoglobin accepts the liberated H^+ and releasing its bound oxygen to the tissues (Bohr effect)

✓ **This process prevents a large buildup of H+ and maintain blood PH.**

Hemoglobin Buffering system in lungs

1. **Oxygen Binding:** ↑ pressure of oxygen promotes its binding to hemoglobin.
2. **H^+ Release: due to** binding of oxygen; hemoglobin release the H^+ that it was holding.
3. **CO_2 Formation:** H^+ + bicarbonate $\rightleftharpoons$ H_2CO_3

H_2CO_3 **Carbonic anhydrase** CO_2 + H_2O.

4. **CO_2 Exhalation:** Through alveoli.

Normal types of Hemoglobin

1. **Hemoglobin A: the major hemoglobin in adults.**
2. **Fetal hemoglobin**

- HbF consisting of two α chains & **two γ chains**
- **Synthesized by the embryonic yolk sac**, in the fifth week of gestation, the site of globin synthesis shifts, first to the liver and then to the bone marrow.

Functions of Fetal hemoglobin

- **HbF has a higher affinity for oxygen than HbA**
- The higher oxygen affinity of HbF **facilitates the transfer of oxygen from the maternal circulation across the placenta to the RBC of the fetus (even at low oxygen levels) .**

Normal types of Hemoglobin
3. Hemoglobin A2

- HbA2 is a minor component of normal adult hemoglobin, first **appearing shortly before birth** and constituting about 2-3% of the total adult hemoglobin.
- It is composed of two α-globin chains and **two δ-globin chains** (α2δ2)
- **Functions: Transport oxygen from lungs to tissues**
- **HbA2 levels** are important in **diagnosis** of thalassemia & iron deficiency anemia

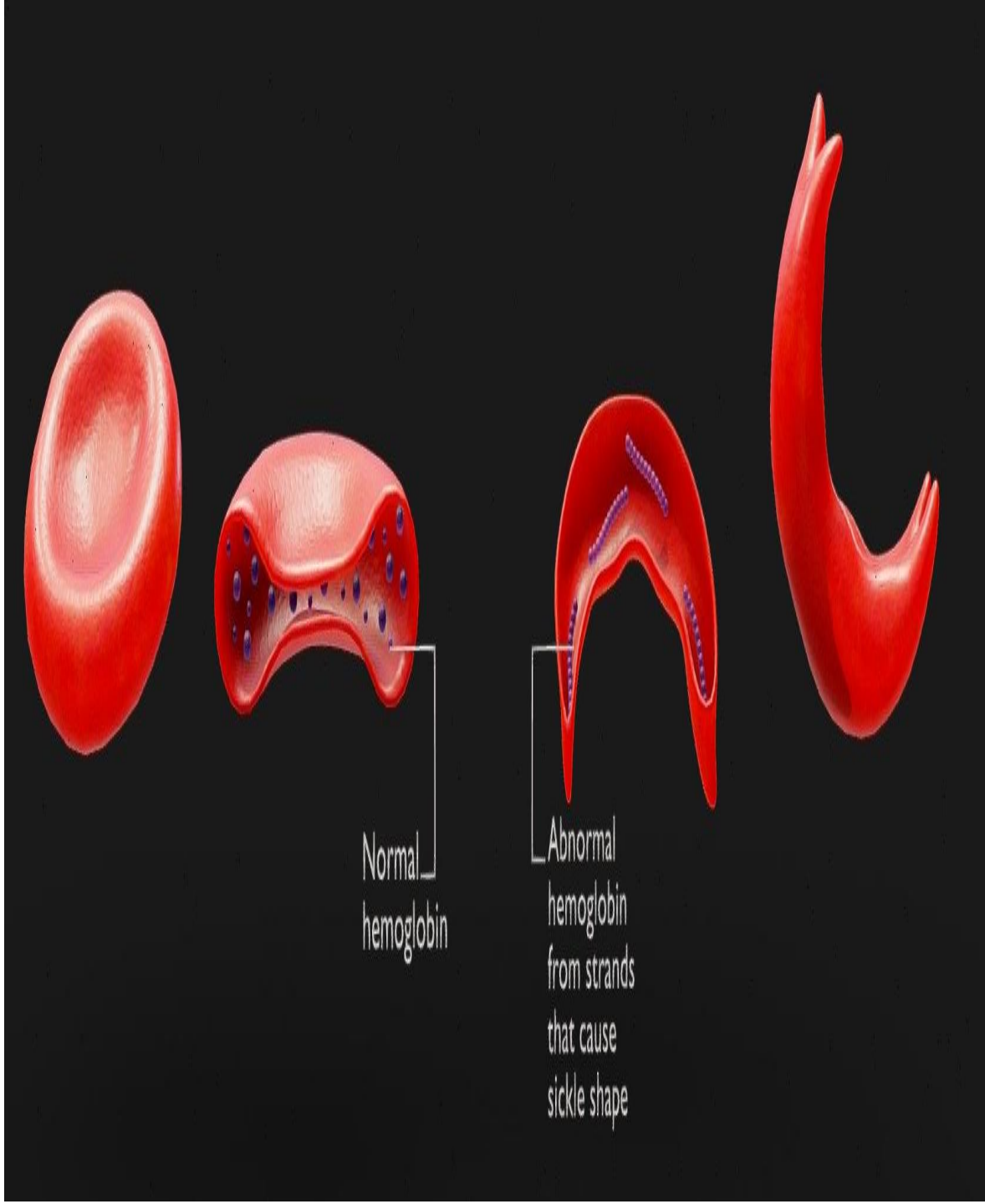
Normal types of Hemoglobin
4. Hemoglobin A1c

- HbA is slowly **glycated** (depending on plasma concentration of hexose).
- Glucose residues attached to the NH2 groups of valines of the β-globin chains.
- **Function:** **Diagnosis & monitoring diabetes.**
- ↑ **HbA1**c are found in RBCs of patients with **diabetes mellitus.**

Hemoglobin Diseases

1. Sickle cell anemia

- The red cells contain abnormal hemoglobin called **hemoglobin S (HbS).**
- HbS contains 2 normal α-chains and **2 mutant β-chains**
- **Glutamate is replaced by valine.**
- **Sickle shape RBCs → breakdown or blockages in blood vessels.**



Hemoglobin Diseases

2. Thalassemia

- **Is an anemia characterized by reduced synthesis of either alpha chain (α -thalassemia) or beta chain (β-thalassemia) of hemoglobin**

3. Hb C

- Is a hemoglobin with a single amino acid substitution (**Lysine is substituted by glutamate)** in the β-globin chain, associated with **hemolytic anemia**.

Hemoglobin SC disease

4. Hb SC disease: some β-globin chains have the **sickle cell mutation**, whereas other β-globin chains carry the **mutation found in HbC** disease.

Abnormal (chemically modified) derivatives of haemoglobin

1. Met-hemoglobin (Met-Hb)

- It is oxidized hemoglobin (Fe^{+2} **oxidized** Fe^{+3})
- **Met-Hb binds oxygen irreversibly and is unable to act as an oxygen carrier.**
- **Causes of Met-Hb:** Some drugs, H_2O_2 , free radicals.

Abnormal derivatives of haemoglobin

2. Carboxy-hemoglobin (CO-Hb)

- It is haemoglobin combining with carbon monoxide (CO) .
- **Carbon monoxide combines at the same position in the Hb molecule as O_2 with affinity about 200 times greater than O_2 .**
- Concentration of CO-Hb above 40% usually results in unconsciousness, and may be fatal.

Abnormal derivatives of haemoglobin

3. Sulf-hemoglobin (S-Hb)

- Is haemoglobin combining with sulfur.
- Results from exposure of haemoglobin to the toxic effects of certain drugs as sulfonamides.
- **S-Hb produces anoxia and cyanosis because it can not act as oxygen carrier.**

Abnormal derivatives of haemoglobin

4. Hematin

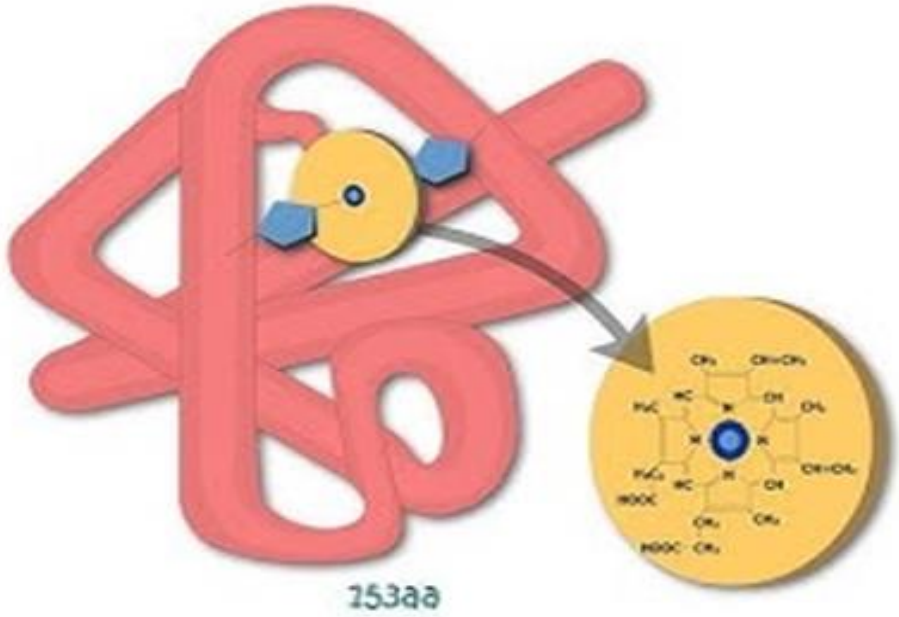
- It is haemoglobin without iron (protoporphyrin combining with globin).
- It may be formed following intravascular haemolysis.

Myoglobin Structure

- **Location:** It is found only in the red **skeletal muscles and cardiac muscle**, gives them characteristic red color.
- It is formed of **one heme** molecule attached to **one polypeptide chain** called globin.

Myoglobin Structure

Myoglobin



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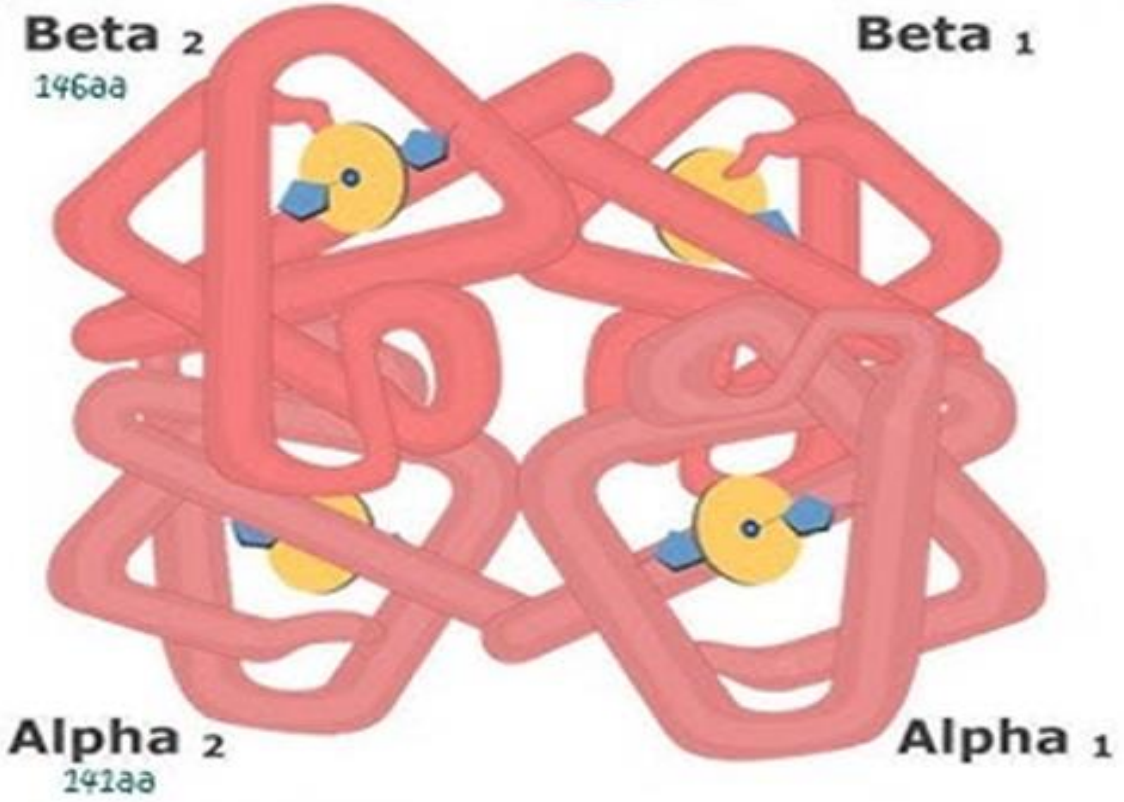
It is a single subunit protein

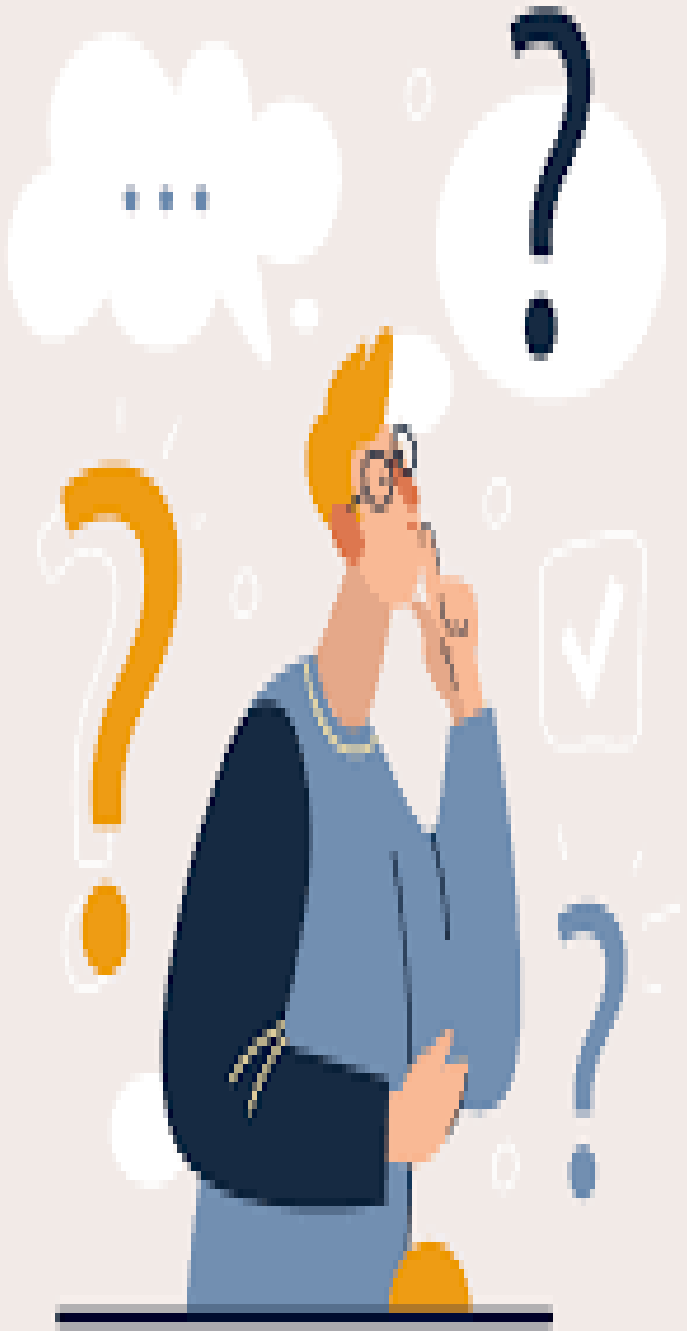
Hemoglobin



It has 4 subunits

Functions of Myoglobin

- Act as **oxygen reservoir** and **transporter** that increases the rate of transport of oxygen within the muscle cell.
- Myoglobin has much higher affinity for oxygen than hemoglobin.
- **It is unable to release oxygen except under very low oxygen tension (intense exercise).**



How can you describe the binding and releasing of oxygen to myoglobin and hemoglobin?

Clinical aspects of Myoglobin

Myoglobinuria: It is the release of myoglobin from muscles after massive crush injury.

- Myoglobin is excreted in urine → dark colour
- **Plasma myoglobin** is **increased** following **Myocardial Infarction**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