COURSE CODE: SC202(CHEMISTRY)

COURSE INSTRUCTOR: DR. DEBARATI MITRA &

DR. SANGITA TALUKDAR

DEPT. OF SCIENCE AND MATHEMATICS

IIITG, GUWAHATI

LECTURE-BIOINORGANIC CHEMISTRY

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- What is Bioinorganic Chemistry?

- It is an interdisciplinary research field at the interface of the classical areas of Inorganic Chemistry and Biochemistry/Biology.
- Understanding the roles that the metallic and non-metallic ions play in biological systems is the goal of Bioinorganic Chemistry.

Chemical elements essential to life

- Bulk elements: C, H, N, O, P, S
- Macro minerals and ions: Na, K, Mg, Ca, Cl^-, SO_4^{2-}, PO_4^{3-}
- Trace elements: Fe, Zn, Cu
- Ultra-trace elements:

  a) Metals: Mn, Mo, Co, Cr, V, Ni, Cd, Sn, Pb, Li

  b) Non-metals: F, I, Se, Si, As, B

Roles of metal ions

Role of Na^+

- Plays crucial role in maintaining extracellular fluid volume
- Maintains osmotic balance/sodium pump
- Maintains acid-base balance
- Involved in muscle contraction and relaxation
- Binding leads to regulations of enzyme function, stability and cell signalling.

Role of K+

- ✓Acts as an enzyme activator
- ✓Involved in secretion of gastric acids thereby maintains the pH
- ✓Involved in closing and opening of plant stomata
- ✓Plays major role in the stabilization of messenger RNA and transfer RNAs, ribosomal RNAs and ribosomal protein
- ✓Leads to skeletal muscle contraction, hormone release and smooth muscle and heart contraction
- ✓Helps to maintain normal levels of fluid inside our cells.

Roles of Mg^{2+}

- Plays role as an enzyme activator
- Involved in active transport mechanism
- Acts as a Ca^{2+} agonist
- Helps to maintain normal nerve and muscle function
- Acts as a regulator of ion channels such as voltage-dependent Ca^{2+} channels
- Supports a healthy immune system.

Roles of Ca^{2+}

- Plays an important role in signal transduction pathway
- Involved in neurotransmitter release
- Helps in blood clotting
- Associated with the formation and metabolism of bone
- Stabilises extracellular proteins.

Roles of Fe

- Involved in Oxygen transport
- Involved in Electron transfer
- Helps in Nitrogen fixation
- Essential element for blood production.

Roles of Cu

Required for adequate growth, cardiovascular integrity, lung elasticity, neovascularization, neuroendocrine function and iron metabolism.

Roles of Zn

- Acts as structure promoters
- Plays a role in cell division, cell growth
- Acts as a Lewis acid
- Takes part in the catalytic function of many metalloenzymes
- Helps in immune system and metabolism function.

Heavy metal toxicity

- Heavy metal poisoning refers to the condition where excessive exposure to heavy metals disrupts the normal functions of body.
- Examples: Lead, Mercury, Arsenic, Cadmium.
- Heavy metals are dangerous because they tend to bio accumulate.
- They bind with oxygen, nitrogen thereby causing alternation to the enzymatic activity.

Arsenic

- As is the most common cause of heavy metal poisoning in adults.
- It is declared as Carcinogen by Environmental Protection Agency (EPA).
- It causes Hemoglobinurea, Diarrhoea, Jaundice, Encephalitis.

Lead

- It accounts for most of the cases of paediatric heavy metal poisoning.
- It causes anaemia, miscarriage, high blood pressure, memory loss, severe abdominal pain.

Mercury

- Hg poisoning leads to several diseases like Acrodynia, Hunter-Russel syndrome & Minamata disease.

Cadmium

- Cd causes flu like disease called Cadmium-blue.

Metalloproteins

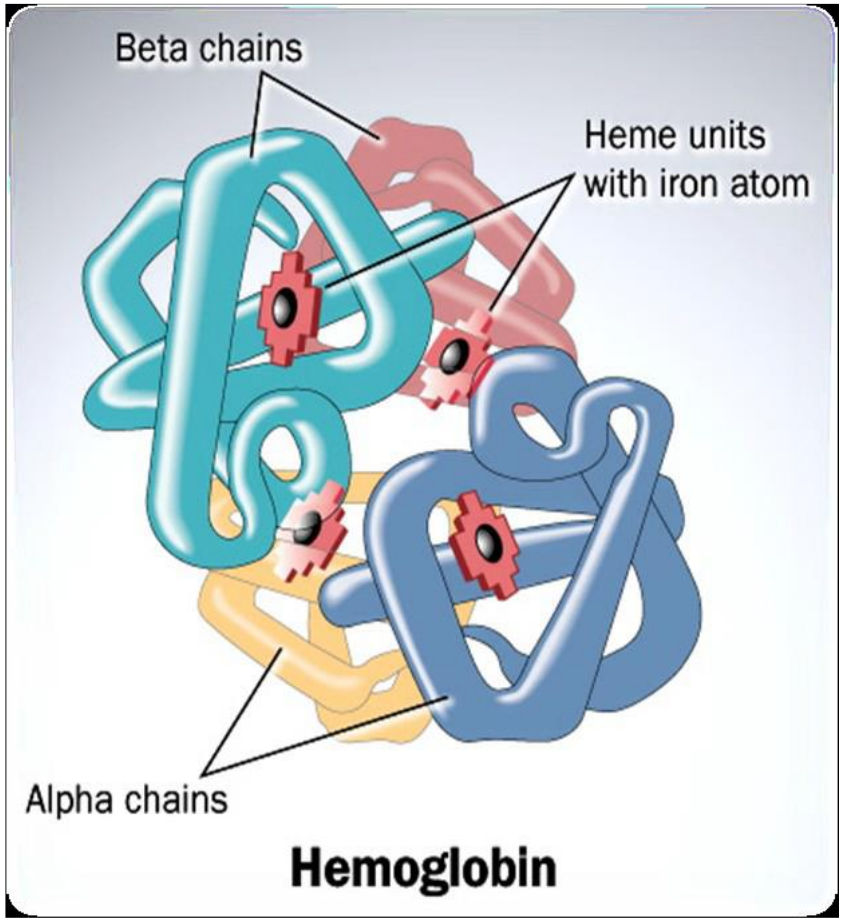
- A protein that contains a bound metal ion as part of its structure is known as metalloprotein.
- Metal ions are usually coordinated by four sites consisting of the protein's nitrogen, sulphur and/or oxygen atoms. In metalloenzymes, one of the coordination sites is labile.
- Major examples are haemoglobin and metallopeptidases, but many other metalloproteins are also known.

Functions of metalloproteins

- Catalytic activities in hydrolysis and dehydration reactions by zinc enzyme: e.g., Carbonic anhydrase
- Catalytic activity in electron transfer reactions: e.g., Cytochromes, non- heme-iron enzymes
- Transportation activity: e.g., Hemoglobin, Hemocyanine, Hemerythrine
- Signal transduction activity: e.g., Calmodulin (Ca^{2+} binding protein)

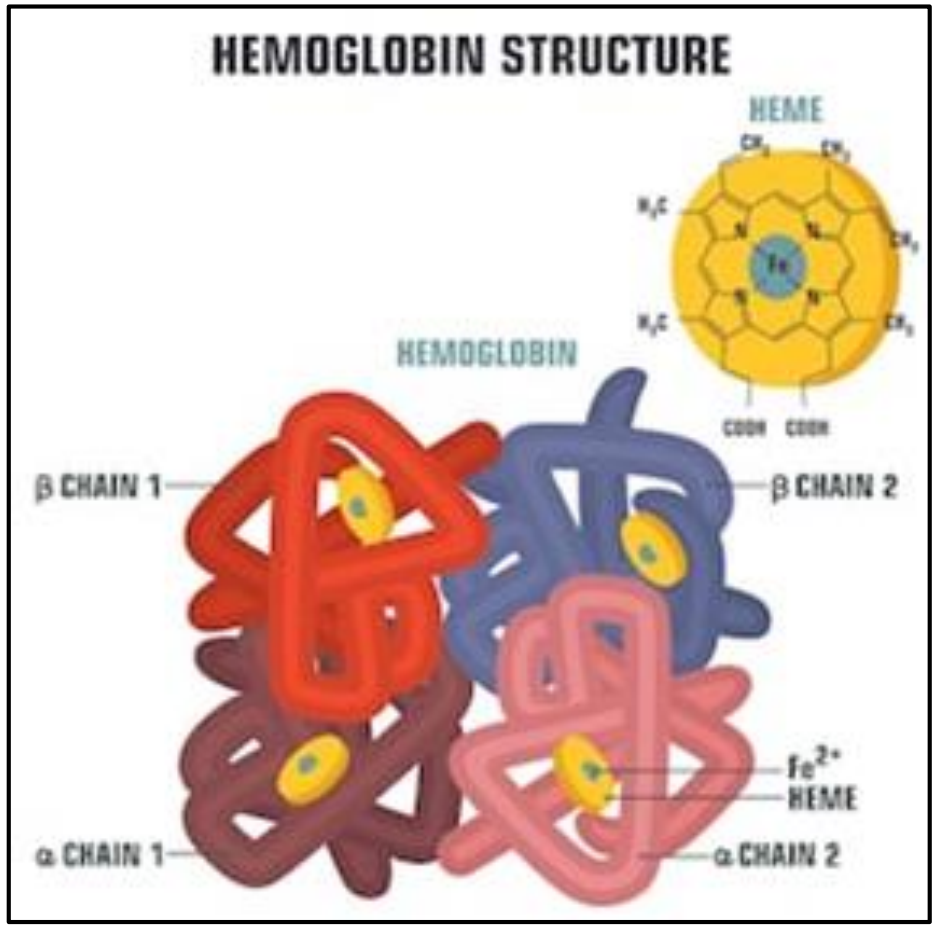
Hemoglobin

- It is a red pigment.
- It is found in RBC of blood.
- It is made up of iron and protein.
- It is a chromoprotein and conjugated protein in nature.
- Its molecular weight is 68000.
- It carries oxygen from lungs to tissues and return the carbon-di-oxide from tissues to lungs.



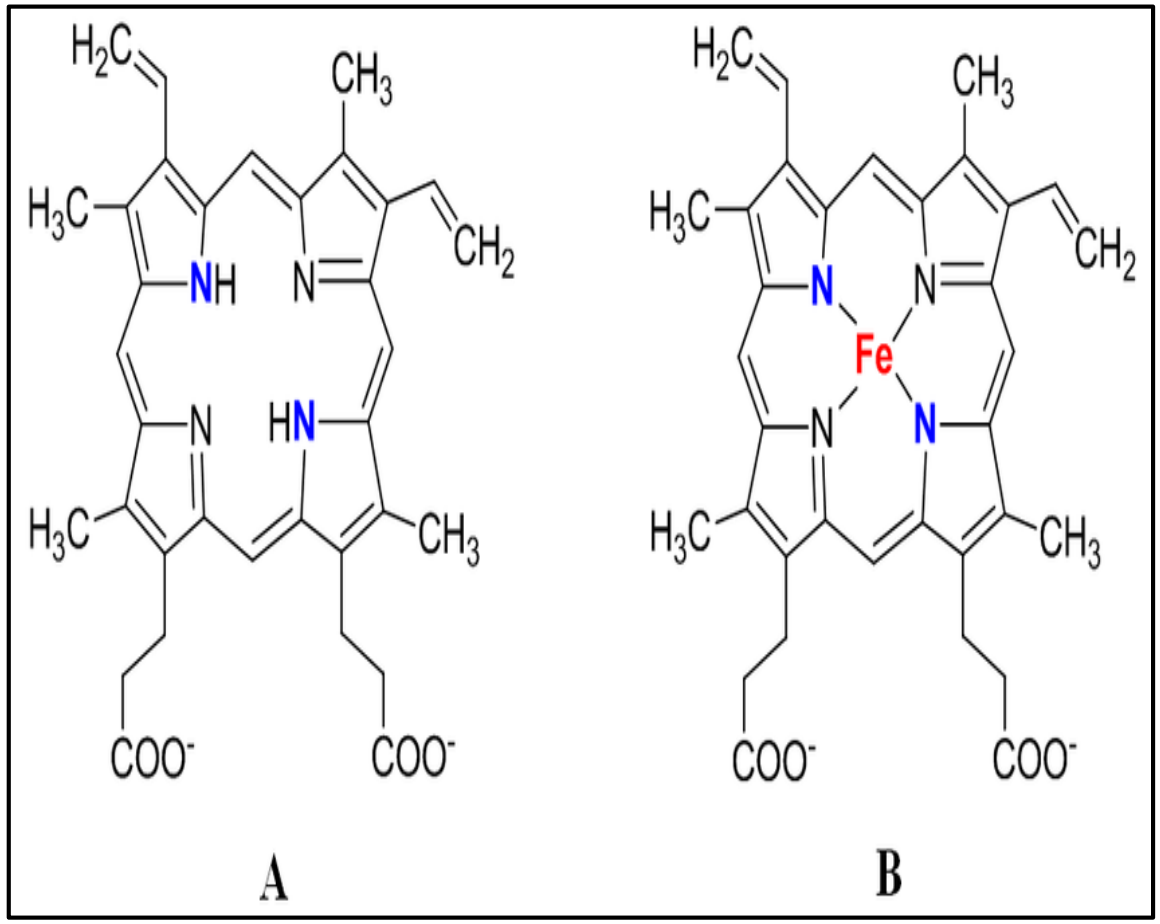
Structure of Hemoglobin

- Iron containing pigment Heme is attached with a protein-Globin.
- Heme is Iron-porphyrin complex called Iron-protoporphyrin IX.
- Heme consists of a porphyrin ring chealted to an Iron atom.
- There are 4 heme groups, each attached to one subunit of each globin protein.



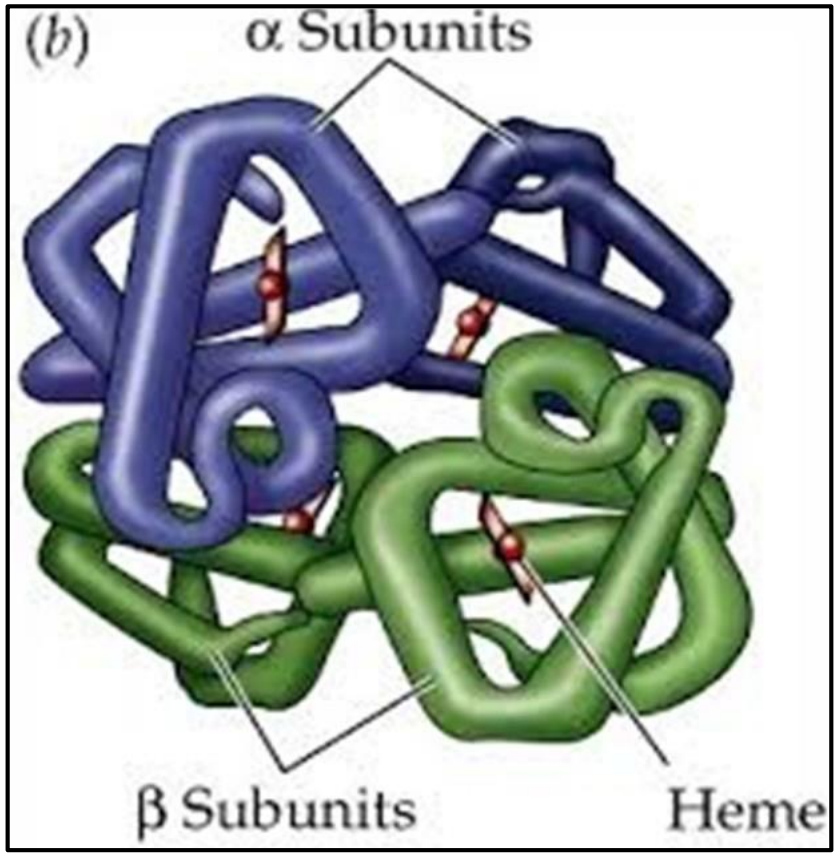
Structure of Iron-protoporphyrin IX

- One of the most important class of chelating agent in nature is porphyrin.
- Each porphyrin ring consists of 4 pyrole rings linked by methine (-CH) group.
- A porphyrin group can coordinate to a metal using four of its nitrogen atoms.
- The porphyrin in Heme, with its particular arrangement of 4 methyl, two propionate and two vinyl substituents, is known as protoporphyrin IX.



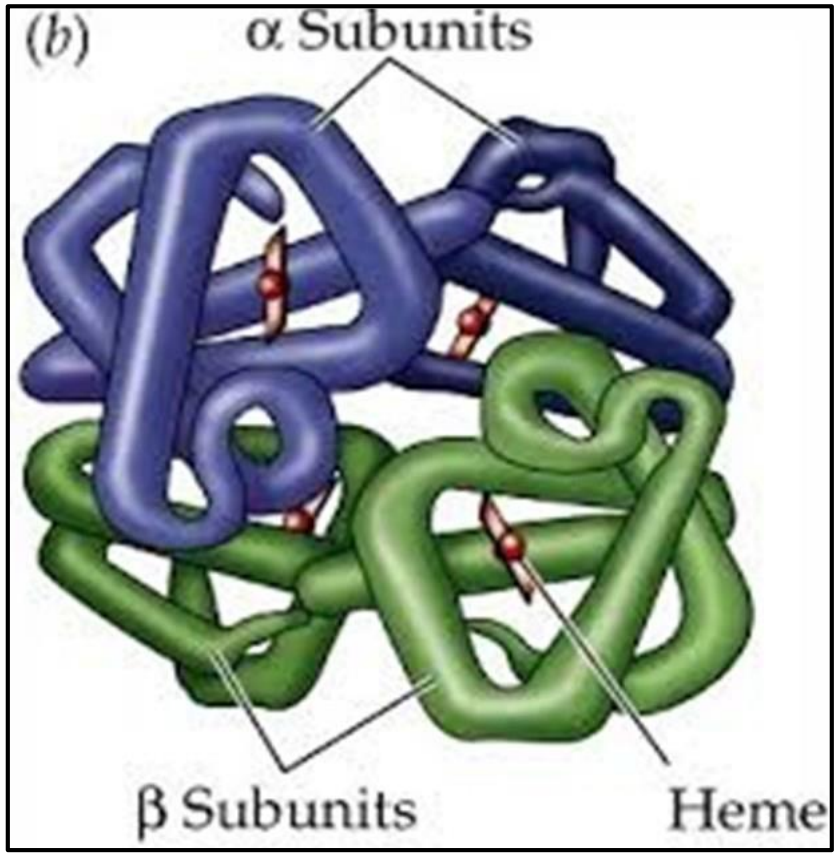
Structure of Globin

- Made up of 4 polypeptide chains
- Contains two α chains having 141 aa and two β chains having 146 units.



Attachment of heme to Globin

- Four units of heme are present altogether in a Globin protein (each heme linked to one subunit of Globin).
- So, one haemoglobin molecule contains four Iron atoms which carry four molecules of oxygen.

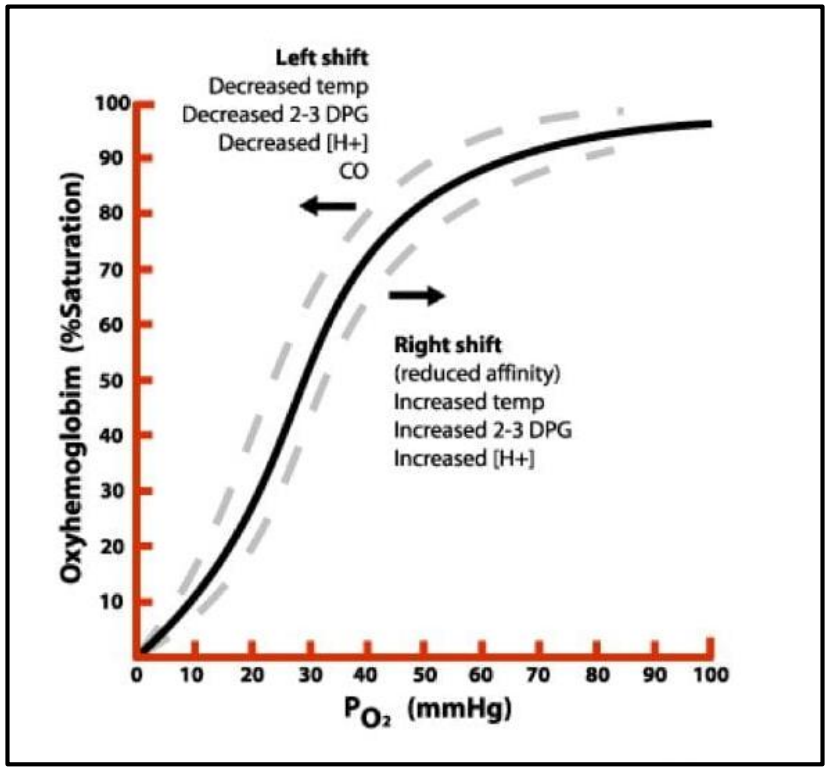


Functions of Hemoglobin

- Transport oxygen to tissues
- Transport carbon-di-oxide to lungs
- Maintains acid-base balance as buffer
- Takes part in oxidative phosphorylation

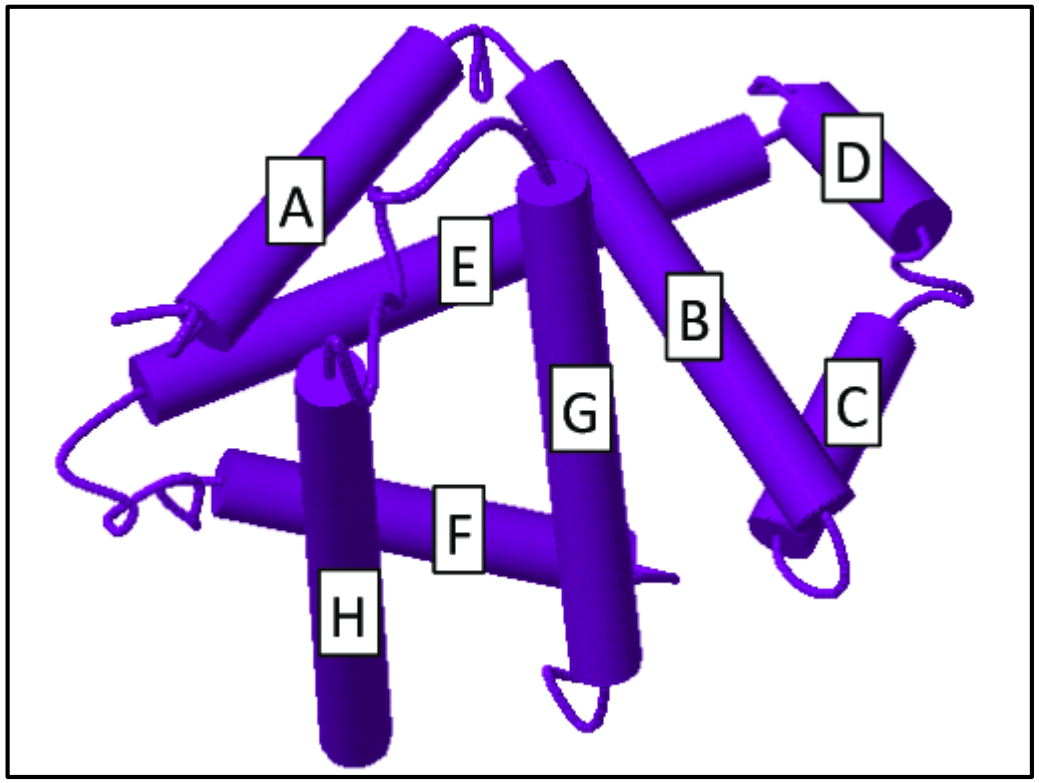
Oxygen Dissociation Curve (ODC)

- The oxygen–hemoglobin dissociation curve, also called the oxyhemoglobin dissociation curve or oxygen dissociation curve (ODC), is a **curve that plots the proportion of hemoglobin in its saturated (oxygen-laden) form on the vertical axis against the prevailing oxygen pressure on the horizontal axis**.
- It is a sigmoid curve.
- As affinity of Hb falls for O_2, graph shifts to right (hemoglobin holds less tightly onto oxygen and delivers more oxygen to the tissues at a given arterial oxygen pressure).
- If affinity of Hb rises for O_2, graph shifts to left (hemoglobin holds more tightly onto oxygen and delivers less oxygen to the tissues at a given arterial oxygen pressure).
- pH, temperature, P_{CO_2} affects the shift.



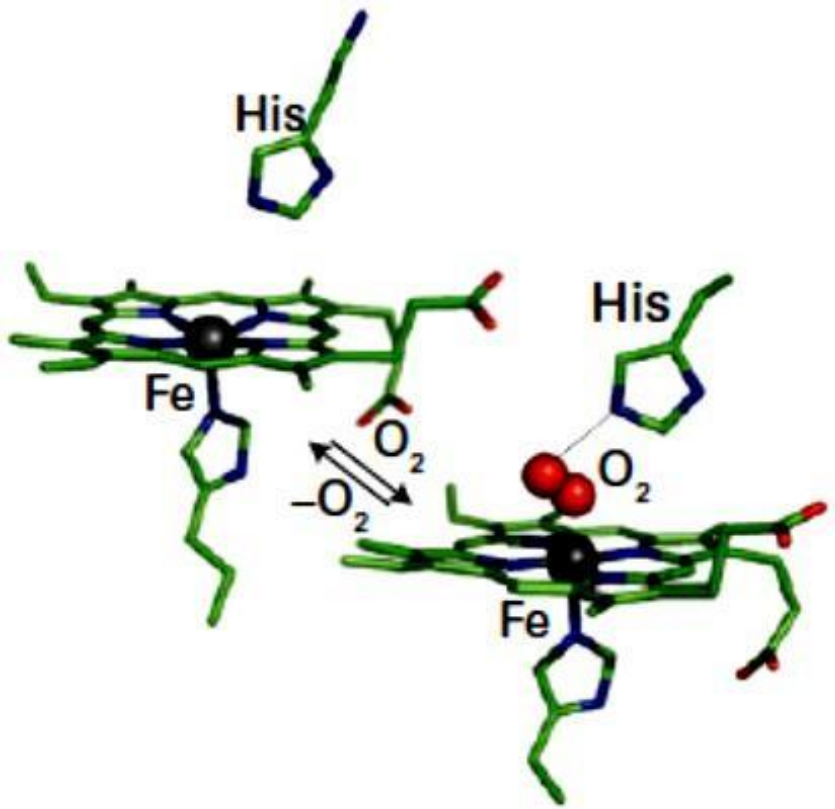
Myoglobin

- Myoglobin was the first protein whose structure was determined by X-ray crystallography.
- It contains 153 aa.
- 121 residues are in an a helix. Helices are named A, B, C, …H. The heme pocket is surrounded by E and F but not B, C, G; also H is near the heme.
- Amino acids are identified by the helix and position in the helix, or by the absolute numbering of the residue.
- It is mainly a storage protein.

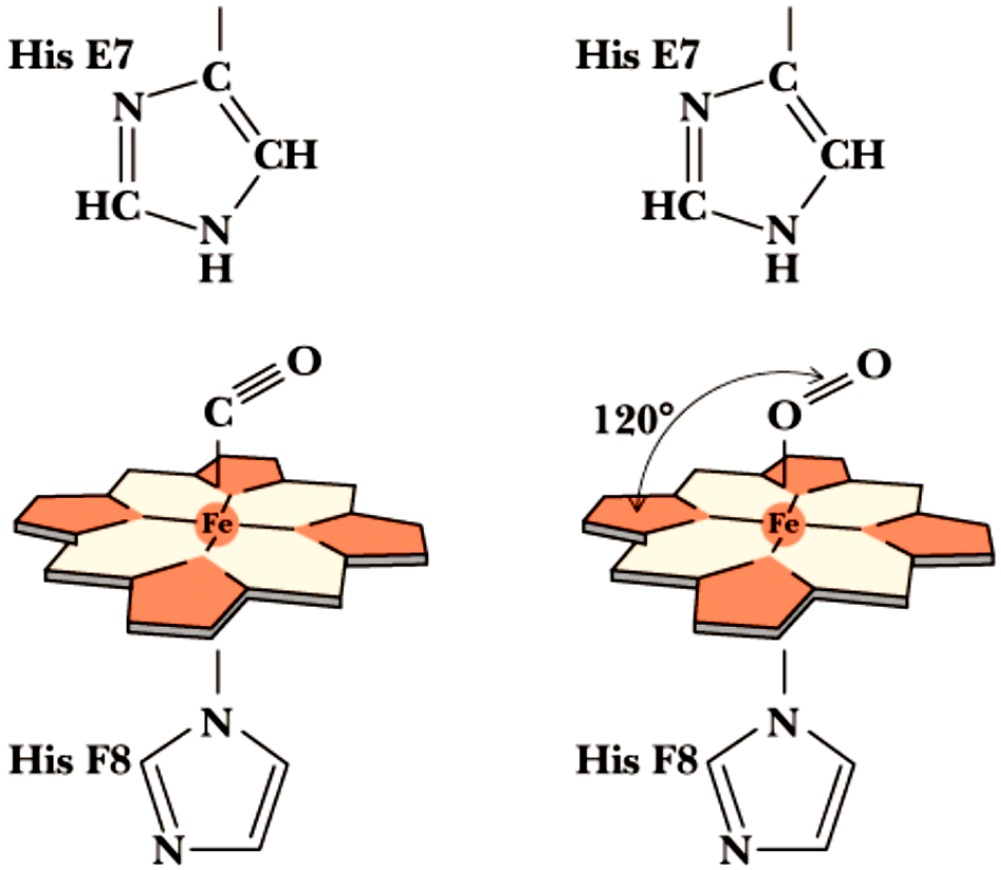


- Oxygen binding changes the Mb conformation.
- Without oxygen bound, Fe is out of heme plane.
- Oxygen binding pulls the Fe into the heme plane.
- Fe pulls its His-F8 ligand along with it.
- The F helix moves when oxygen binds.
- Total movement of Fe is 0.029 nm - 0.29 A.

- Myoglobin, an iron containing protein in muscles, receives oxygen from RBC and transports it to the mitochondria of muscle cells, where oxygen is used in cellular respiration to produce energy.
- Oxymyoglobin is used in oxygen supply and act as scavenger of NO [MYOCYTES].
- Oxymyoglobin +NO= Harmless nitrates with ferric myoglobin, which is recycled by metmyoglobin reductase.



(a) Reversible binding of O_2 to myoglobin: coordination by O_2 causes the Fe to become low spin and move into the plane of the porphyrin ring



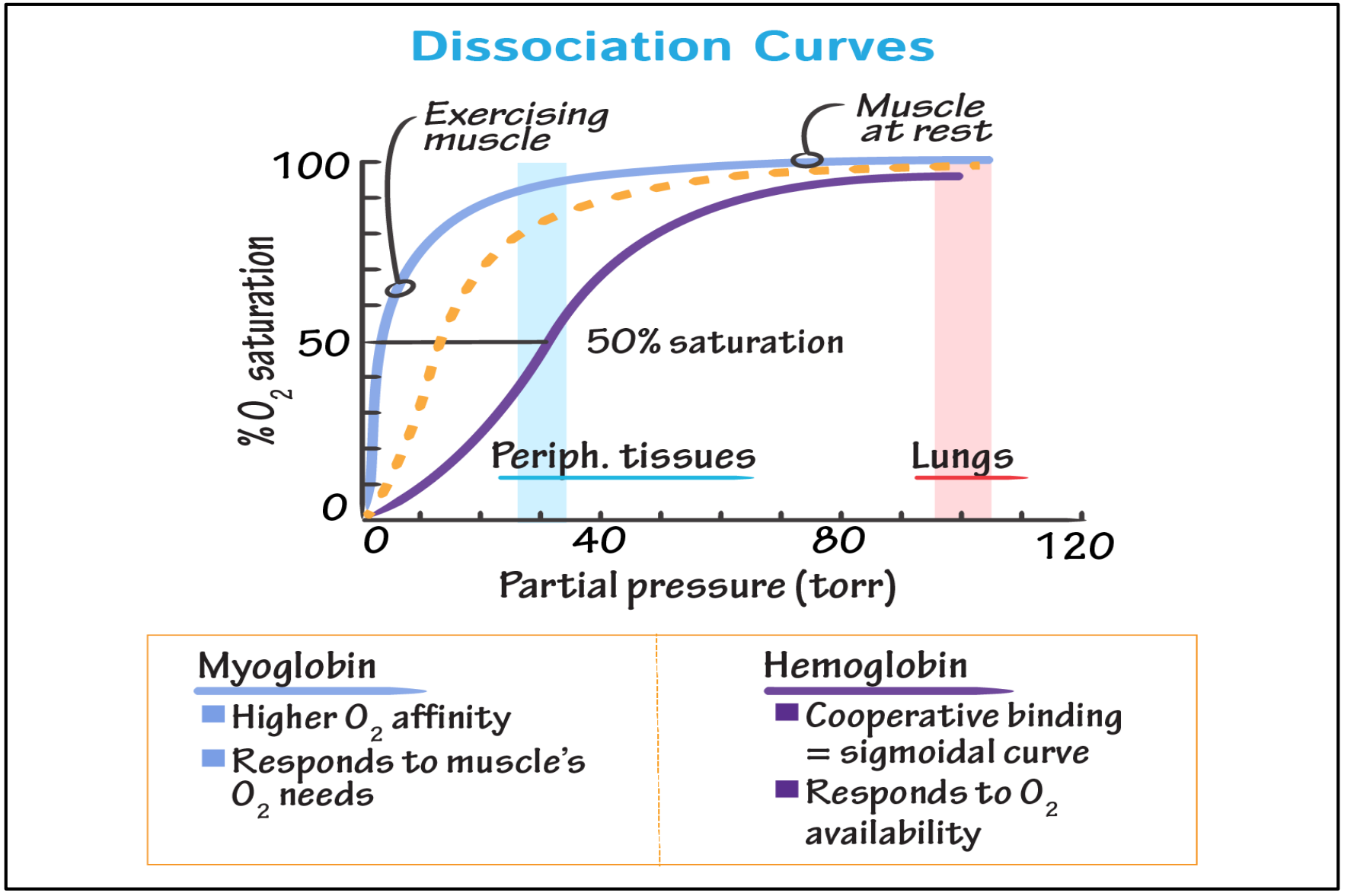
(b) Mb:CO complex

(c) Oxymyoglobin

Functions of Myoglobin

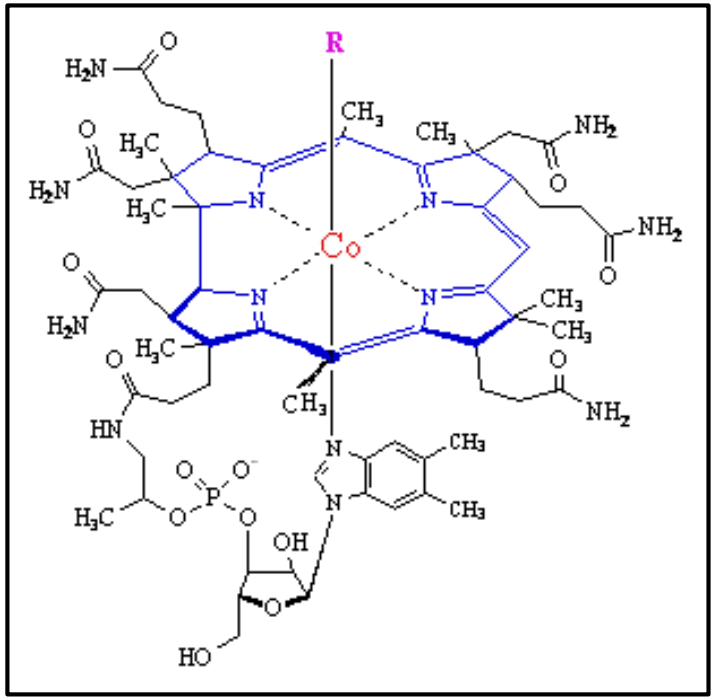
- The rate of O_2 diffusion from capillaries to tissue is slow because of the solubility of oxygen. Myoglobin increases the solubility of oxygen.
- Myoglobin facilitates oxygen diffusion.
- Oxygen storage is also a function because Myoglobin concentrations are 10-fold greater in whales and seals than in land mammals.

Oxygen Dissociation Curve



Vitamin B12

- Vitamin B12, vitamin B_{12} or vitamin B-12, also called cobalamin, is a water-soluble vitamin with a key role in the normal functioning of the brain and nervous system, and for the formation of blood. It is one of the eight B vitamins.



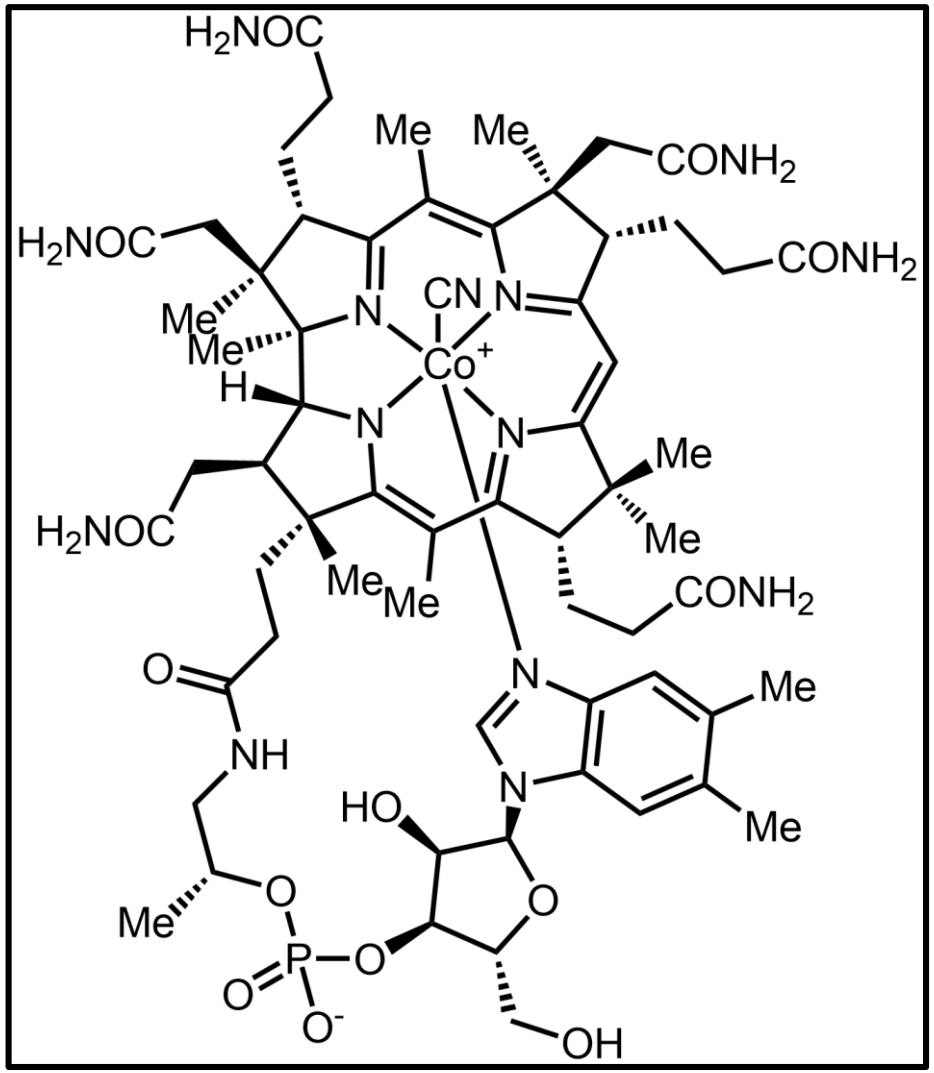
Structure of Vitamin B12

Physical properties

- Vitamin B12 is very stable at high temperatures just if pH is ranged from 4.5 to 5.0, while the strong acidic and highly alkaline environment loses its vitamin activity.
- This vitamin is rapidly degraded in the light, and therefore it is necessary to keep it in the dark. Vitamin B12 is negatively affected by alcohol, sleeping pills, estrogen, etc.
- Vitamin B12 is well soluble in water, ethanol and methanol.
- These are red coloured crystals.

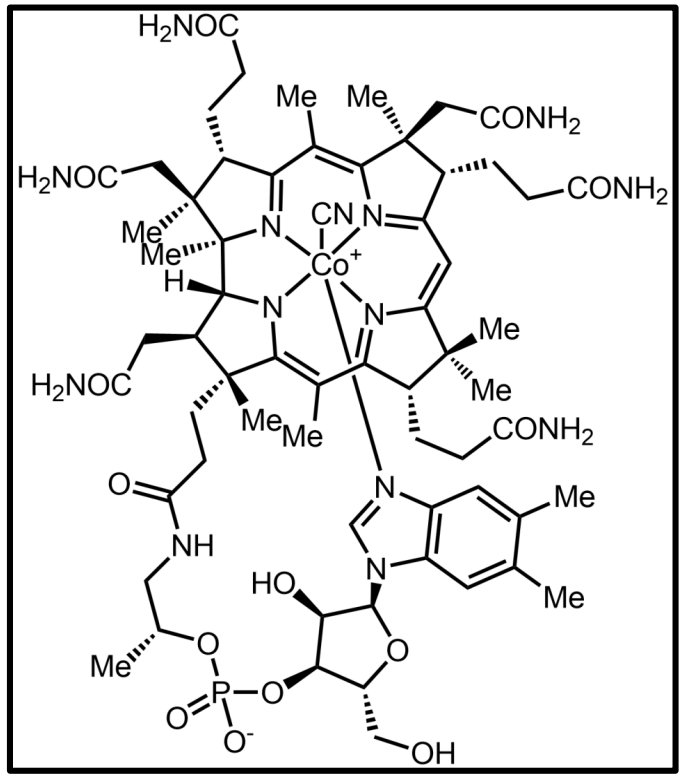
Chemical properties

- Under the term vitamin B12, several compounds that are similar in chemical structures are included. They are classified as: cyanocobalamin, oxycobalamin, nitrocobalamin, aquacobalamin, etc.
- In the structure of the vitamin B12, element cobalt is included. In the isolation of vitamin B12, we can get its cyanocobalamin derivative in which, structure includes cyanide group, linked to an atom of cobalt.

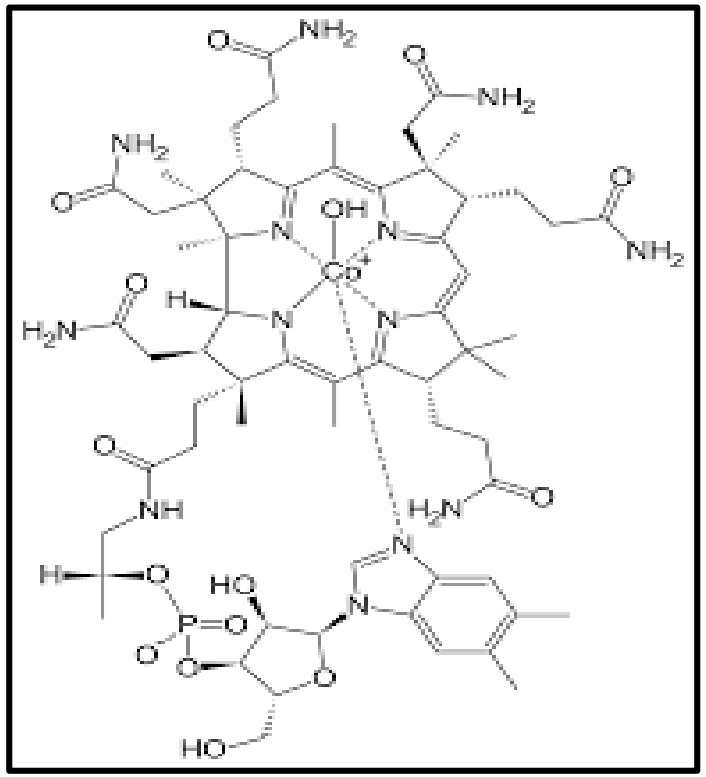


Cyanocobalamin

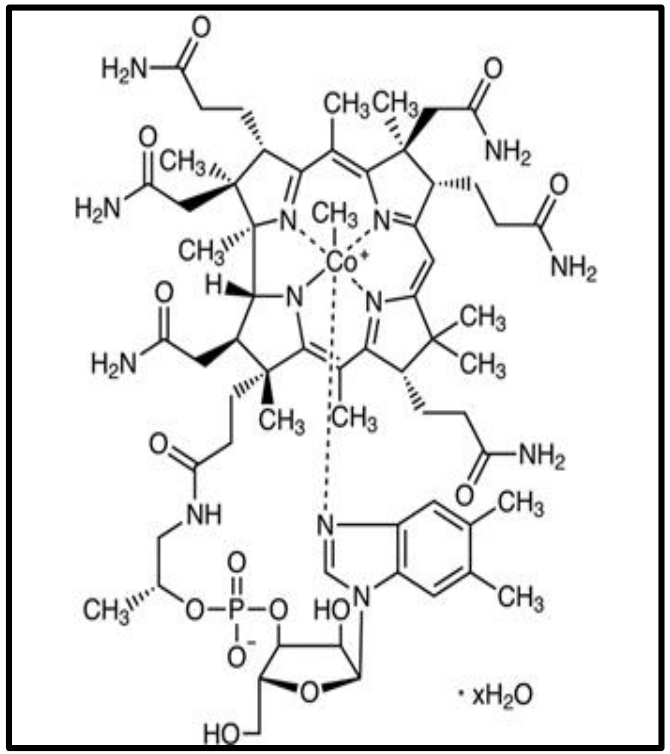
Types of Vitamin B12



Cyanocobalamin
Used in the treatment of pernicious anemia



Hydroxycobalamin
Used as an antidote to cyanide poisoning



Methylcobalamin
Used in the treatment of perpheral neuropathy

Applications

- Act as an antidote for Cyanide poisoning
- Regulates the over-production of the allergen antibody IgE in allergic individuals
- Responsible for reducing depression via the production of serotonin
- Used in the treatment of anaemia
- Helps in healthy regulation of the Homocysteine (risk factor for heart disease) control
- Helps in cell reproduction and constant renewal of the skin.

Acknowledgement

- Slideshare
- Google