IRON and its application in biosystem

Iron:
- Highly abundant
- two stable O.S. (II & III)
  - → H.S oct/td quite labile
  - → L.S, axially ligated are quite inert
- → Redox pot. for Fe(III) & Fe(II) couple (0.77V to −0.5V).

Because of these properties it is used in
1) Oxygen transport and storage system (ie hemoglobin and myoglobin)
2) Electron transport System (cytochromes & ferredoxins)
3) Redox metalloenzymes (e.g oxidases, hydrogenases, reductase etc)
4) (Biological reactions).

All plants and animals and microorganism use iron abundantly in life processes except LACTOBACILLUS which has high conc. of Mn instead of Fe.

The iron turnover process in an adult requires about 30 mg of iron per day. 70% of which is required in the biosynthesis of RBC and this amount is not absorbed from our

daily diet. Destruction of RBC gives 20 mg Fe which is mostly recycled and carried by serum transferrin to bone marrow. The rest amount comes from the iron storage site.

To carry out the above mentioned metabolic cycle of iron.

Transferrin acts as carrier to transport Fe from one site to other
Ferritin & Hemosiderin serve to store Fe.

II. Structural features of different Fe proteins :-

a) Heme proteins (Fe - porphyrin Protein) : Fe chelated by a porphyrin ring (e.g hemoglobin, myoglobin, cytochrome P-450, cytochrome c oxidase, cytochromes, catalase, peroxidase)

b) Non - Heme Fe - proteins Ferritin, Transferrin & hemosiderin required for iron storage & transport.

c) Non - heme oxo-bridged dinuclear or polynuclear Fe-containing proteins :- hemerythrin, ribonucleotide reductase,

purple acid phosphatase, methane monooxygenase, etc that contain the $Fe_2(\mu-O)(\mu-O_2CR)_x$ ($x = 1$ or 2) core. The number of bridging carboxylate groups may differ. Ferritin and hemosiderin contain poly Fe O(OH) aggregates.

d) Non heme Fe-S proteins (ferredoxins)
Fe is coordinated by cysteine S and acid labile S.

III. Fe proteins Involved in Transport and storage of Fe in higher animals

A:- Ferritin:- The excess of iron is stored in nontoxic forms in ferritin which is distributed in various organs like Liver, spleen and bone marrow.

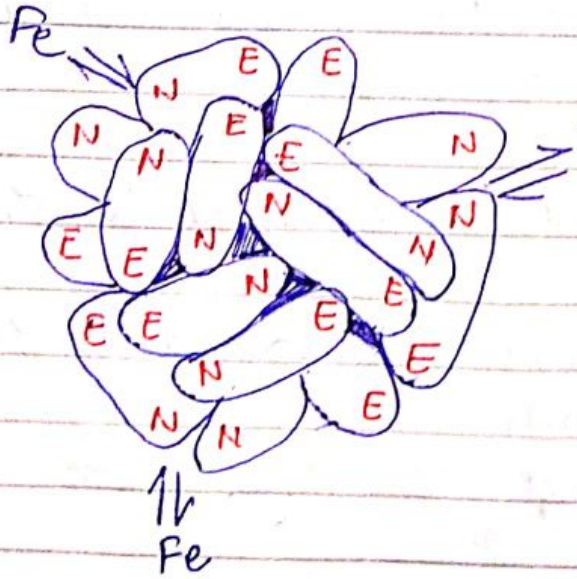
It contains 12-20% Iron (i.e 2000 - 4000 Fe atoms per molecule)

The structure of Ferritin can be considered to consist of three units
1) The protein coat or sheath
2) the iron protein interface
3) the iron core.

The protein sheath called apoferritin, consists of 24 subunits of coiled polypeptide chain. Each chain looks cylindrical The subunits are arranged in the outer surface and the ferritin micelle looks spherical. Thus the thickness of organic surface of this micelle is 3×10^3 pm. The subunit, cylindrical, the two ends are different. one end designated 'N' (polar) and other end 'E' (Non polar)

The 24 subunits of apoferritin in such a fashion that at 8 places, three subunits with their N-ends to form a polar channel through which iron can be transfered in or out.

At 6 non-polar channels produced by the meeting of four subunits with their E-ends.



Arrangement of 24 ellipsoidal protein subunits

The lipophilic sheath makes Fe (III) complex soluble in biological fluid. During ferritin formation Fe(II) is oxidised by O_2 and apoferritin probably catalyse this oxidation reaction.

The core :-

It primarily consists of a sheet structure of Fe(III) oxide in which all iron centres are octahedrally surrounded by oxygen.

It provides a close-packed matrix of O^{2-} ions and Fe^{+3} ions randomly distributed in the octahedral holes.

The hydroxide and phosphate groups present in the core help to balance the charge and binding at the protein surface. Iron is deposited as $Fe_2O_3(H_2O)_x$ (comparable to rust) with various amount of phosphate. These phosphate groups acts as terminators and linking groups to the protein shell. This core of ferric hydroxyphosphate can be compared to a mineral.

The Fe core can be formed only from aq. Fe(II) ions so that oxidation of Fe (II) gives Fe(III) as shown :-

$$2Fe^{+2} + O_2 + 4H_2O \longrightarrow 2FeO(OH) + H_2O_2 + 4H^+$$

$$4Fe^{+2} + O_2 + 6H_2O \longrightarrow 4FeO(OH) + 8H^+$$

→ So Fe(III) is in High spin
→ full Iron core has 4500 Fe(II) that produces 4500 e^- & 11250 prot

B:- Transferrin:- a carrier of Iron. It is a protein that binds Fe(III) very strongly [not Fe(II)] and transport it from stomach to blood stream.

Apotransferrin has two binding ~~sites~~ sites which are similar but not identical.

Transferrin, Fe(III) is octahedrally coordinated in which CO_3^{2-} or HCO_3^- remains coordinated as a synergistic anion ligand. This anion bridges b/w Fe(III) and the cationic sites of encircling protein. So this anion minimises the electrostatic repulsion b/w the metal centre and the cationic site of of protein chain. Also it is believed that this CO_3^{2-} ion may participate in H-bonding interaction with amino acid residues of protein chain. This H-bonding interaction folds the protein chain to facilitate the interaction b/w the Fe(III) centre and coordinating sites coming from protein chain.

→ The stability of the chelate is highly pH dependent.
At pH = 7 highly stable
pH = 5 Iron readily dissociates

The binding sites in apotransferrin are hard bases and they prefer Fe(III) to Fe(II). That is why reduction of Fe(III) to Fe(II) may facilitate the release of iron from transferrin.

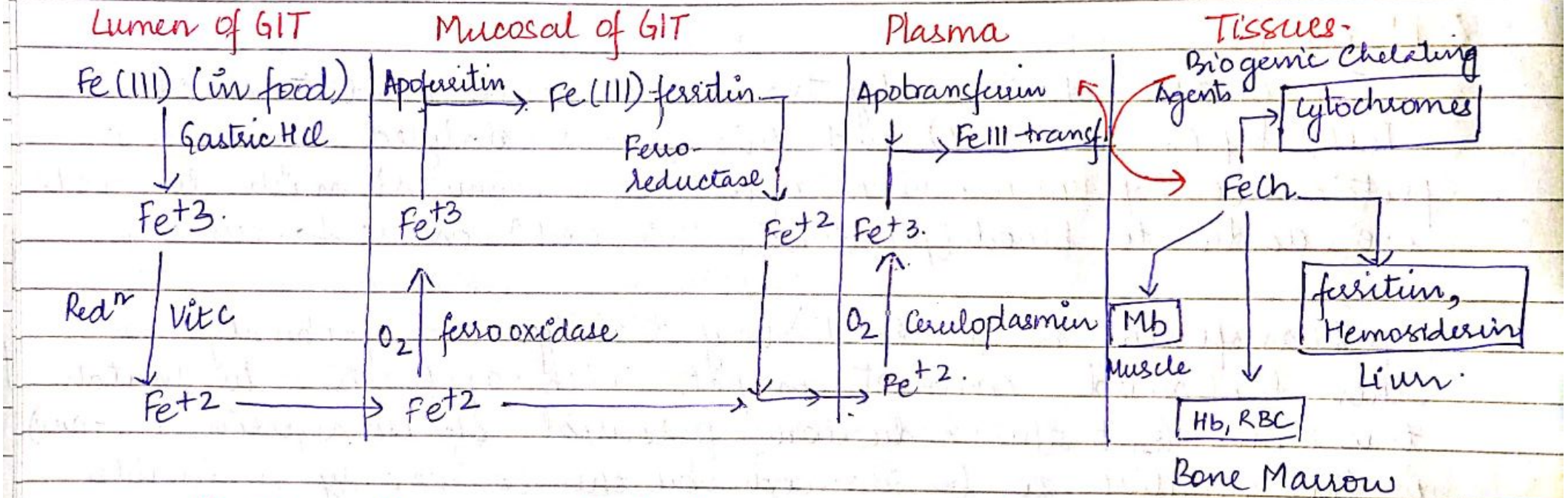
Explanation

The uptake of Iron by transferrin needs oxidation of Fe(II) by O_2 to Fe(III) and this process catalysed by a copper protein Ceruloplasmin. When iron passes from stomach to blood i.e acidic to blood (pH = 7.4), this oxdⁿ occurs favourably.

Apotransferrin binds Fe(III) very tightly and probably no other biligand cannot compete with apoferritin to snatch the iron. But the reduction potential of transferrin ($E_0 = -0.5$V is too negative to be reduced by the commonly available biological reducing agent. Also it is known that CO_3^{2-} or HCO_3^- bound in transferrin plays an imp. role in stabilisi apotransferrin-Fe(III) interaction.

A matter of fact is CO_3^{2-} or HCO_3^- removal is highly

acid catalysed and a slight fall in pH can drastically deminish the binding interaction of Fe(III). Therefore it is quite reasonable that the removal of CO_3^{2-} and HCO_3^- is the key step for release of Fe- from transferin. The transferin releases iron by binding to the cell surface and forming a vesicle inside the cell (where pH is low). After releasing iron, it again comes back to plasma to capture iron.



$Fe\text{-}Tr + Ch \rightleftharpoons Ch\text{-}Fe\text{-}Tr \rightleftharpoons Ch\text{-}Fe\text{-}Tr$.

→ Both Cu- Protein.

{ Ceruloplasmin → ferrioxidase.
ascorbic acid oxidase → ferrireductase.

Ch :- Biogenic chelating agent.
Tr :- Transferin