Iron Storage Proteins and Transfer: Ferritin and Transferrin

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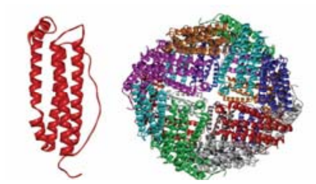
Fe storage and transport

Metal	Mass / mg	Biological roles
V	0.11	Enzymes (nitrogenases, haloperoxidases)
Cr	14	Claimed (not yet proven) to be essential in glucose metabolism in higher mammals
Mn	12	Enzymes (phosphatase, mitochondrial superoxide dismutase, glycosyl transferase); photoredox activity in Photosystem II (see eq. 21.54 and discussion)
Fe	4200	Electron-transfer systems (Fe–S proteins, cytochromes); O_2 storage and transport (haemoglobin, myoglobin, haemerythrin); Fe storage (ferritin, transferritin); Fe transport proteins (siderophores); in enzymes (e.g. nitrogenases, hydrogenases, oxidases, reductases)
Co	3	Vitamin B_{12} coenzyme
Ni	15	Enzymes (urease, some hydrogenases)
Cu	72	Electron transfer systems (blue copper proteins); O_2 storage and transport (haemocyanin); Cu transport proteins (ceruloplasmin)
Zn	2300	Acts as a Lewis acid (e.g. in hydrolysis processes involving carboxypeptidase, carbonic anhydrase, alcohol dehydrogenase); structural roles
Mo	5	Enzymes (nitrogenases, reductases, hydroxylases)

Iron is the most essential element of nature and plays a fundamental role in many natural processes, but it may have deleterious and toxic effect if not treated appropriately. Because iron usually is found in its oxidized form, iron (III) which is insoluble, and iron (II) which is pathophysiological toxic, storage and transport iron in people's body must meet the requirement that in a soluble and innoxious form. The table above gives the average mass of Fe present in a 70 kg human.[2]

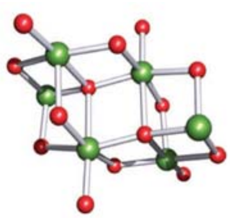
Essential Features of Ferritin[2]

- In mammals, Iron is stored mainly in the liver (typically 250-1400 ppm of Fe is present), bone marrow and spleen in the form of ferritin, a water-soluble metalloprotein.
- Ferritin consists a X-ray diffraction of 24 equiva-lent units and each units consists of a four-helix bundle which is > 5 nm in length (a). These units are arranged so as to form a hollow shell (b).
- In ferritin, it contains up to 4500 high-spin Fe^{3+} centers in the form of $(FeO\cdot OH)_8(FeO\cdot H_2PO_4)$. Adjacent [OFeO]- triple layer blocks are weakly associated with each other. The phosphate groups in the iron-containing core appear to function as terminators and linking groups to the protein shell.



a b

(a) one of the 24 equivalent units (a four-helix bundle) that are present in the protein shell of ferritin.
(b) The structure of the protein shell in ferritin which shows the polypeptide chains. It has a diameter of ≈ 8000 pm.



A model of the biomineralization of ferritin determined by X-ray diffraction. $[Fe_6(OMe)_4(\mu\text{-}OMe)_8(\mu_4\text{-}O)_2L_2]^{2+}$

While the structures of ferritin is established, the manner in which iron is transposed in and out of the protein cavity is still under investigation. It is proposed that iron enters as Fe^{2+} and is oxidized once inside the protein. The formation of the crystalline core is an example of biomineralization and it is a remarkable achievement of evolution that iron can be stored in mammals effectively as hydrated iron (III) oxide.

Formulation of the core of ferritin[2]

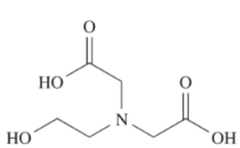
$$Fe(OAc)_2 + LiOMe \xrightarrow[\text{in MeOH}]{\text{in presence of } O_2} Fe_{12}(OAc)_3(\mu\text{-}OAc)_3(MeOH)_4(\mu\text{-}OMe)_8(\mu_3\text{-}OMe)_{10}(\mu_6\text{-}O)_2$$

a

$$Fe(O_3SCF_3)_2 + L \xrightarrow{\text{in MeOH}} [Fe_6(OMe)_4(\mu\text{-}OMe)_8(\mu_4\text{-}O)_2L_2][O_3SCF_3]_2$$

$$\text{where } L = N(CH_2CH_2NH_2)_3$$

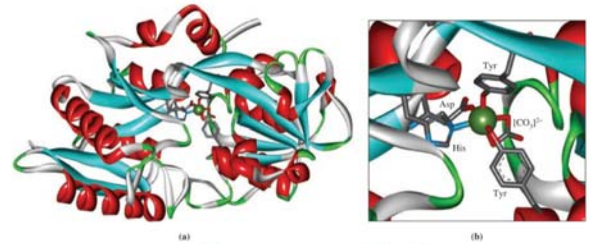
b

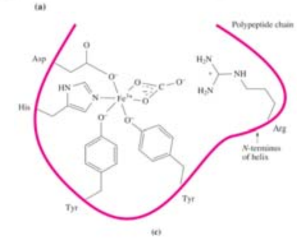


(H3L)

The synthesis of large iron-oxido clusters from mono- and dinuclear precursors is in relation to modelling the formation of the core of ferritin. Reaction (a) and (b) give two an example. The product of reaction (a) is a mixed oxidation state iron species $(Fe(III)_4Fe(II)_8)$. The Fe_6O_{14}-core of the product of reaction (b) is the model at left. For the model complex to mimic the characteristics if iron(III) – containing ferritin, it should contain an $Fe(III)_xO_y$ – core surrounded by an organic shell. The latter should contain C, N, H and O to reproduce the protein chains , and appropriate ligands include H3L in the model complexes $[Fe_{17}(\mu3\text{-}O)_6(\mu3\text{-}OH)_6(\mu\text{-}OH)_8L_{10}(OH_2)_{12}]^+$ and $[Fe_{17}(\mu3\text{-}O)_4(\mu3\text{-}OH)_6(\mu\text{-}OH)_{10}L_8(OH_2)_{12}]^{3+}$.

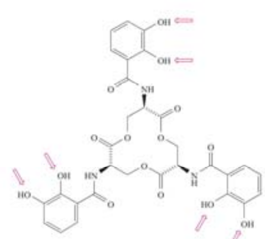
Essential Features of Transferrin[2]



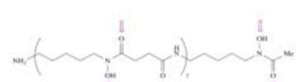


(a) The structure of human serum transferrin determined by X-Ray diffraction.
(b) An enlargement of the coordination environment of Fe^{3+}
(c) Schematic representation of the Fe^{3+} binding site in transferrin; the coordinated $[CO_3]^{2-}$ points towards the positively charged Arg residue and the N-terminus of helix.

In humans, serum transferrin transports ≈ 40 mg of iron per day to the bone marrow. It contains a single polypeptide chain (molecular weight of ≈ 80000) coiled in such a way as to contain two pockets suitable for binding Fe3+. The stability constant for the Fe3+ complex is very high, making transferrin extremely efficient as an iron trans- porting and scavenging agent in the body. The exact mechanism by which the Fe3+ enters and leaves the cavity has not been elucidated, but protonation of the carbonate ion and a change in conformation of the protein chain are probably involved.



Aerobic microorganisms also require iron, but cannot simply absorb it from their aqueous environment since Fe3+ is precipitated as $Fe(OH)_3$ Evolution has provided these organisms with O-donor poly- dentate ligands called siderophores which scavenge for iron. Examples of siderophores are the anions derived from enterobactin (left) desferrichrome (right) and desferrioxamine (blow). Enterobactin, H6Ent, is derived from three L-serine residues, each carrying a 2,3- dihydroxybenzoyl group. The deprotonated form, Ent6-, binds Fe3+ to give the complex [Fe(Ent)]3- in which Fe3+ is in an approximately octahedral environment.



Conclusions

➔Ferritin serves to store iron in a non-toxic form, to deposit it in a safe form, and to transport it to areas where it is required.[1]
➔Transferrin is a well-characterized plasma glycoprotein where the majority of cells in the organism acquire iron from.

References

1. "Ferritin." Wikipedia, Wikimedia Foundation, 1 Feb. 2019, en.wikipedia.org/wiki/Ferritin#cite_note-14.

2. "Inorganic Chemistry", Catherine E. Housecroft, Alan G. Sharpe, 4th edition, Pearson Education, ISBN: 978-0-273-74275-4