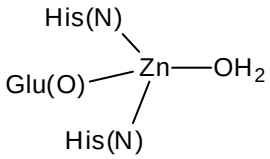
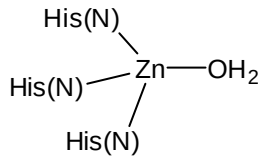
15.1. Active sites of metalloenzyme



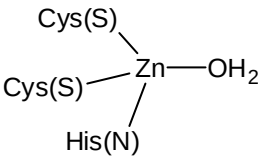
Peptide hydrolysis
(removes terminal amino
acids from proteins)

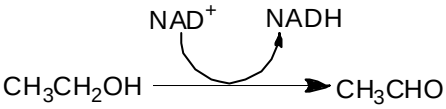
Carboxy peptidase



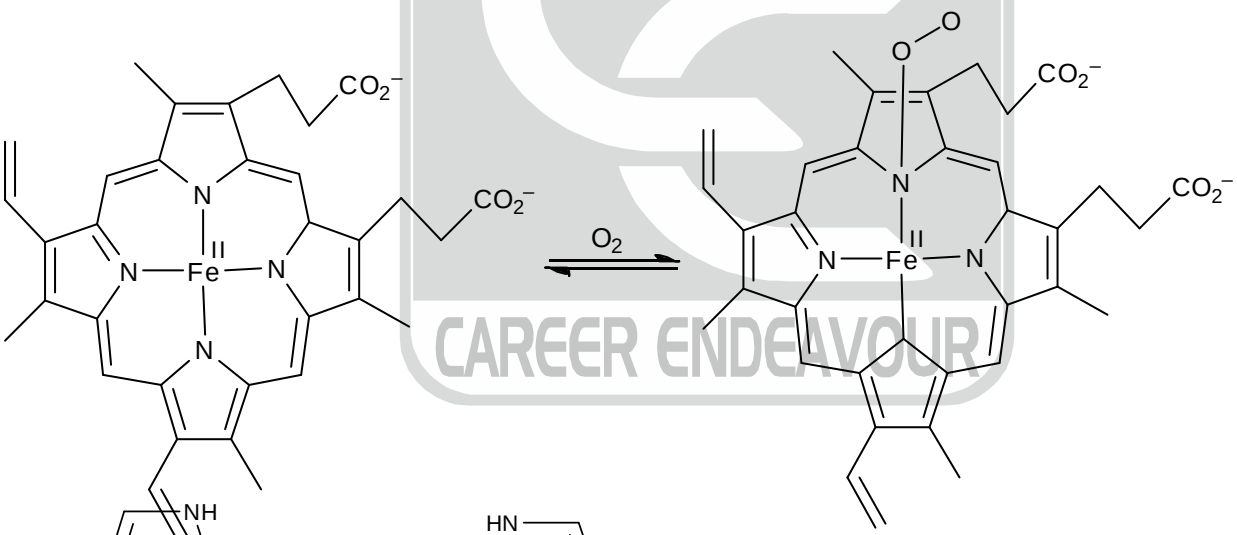
$H_2O + CO \longrightarrow H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

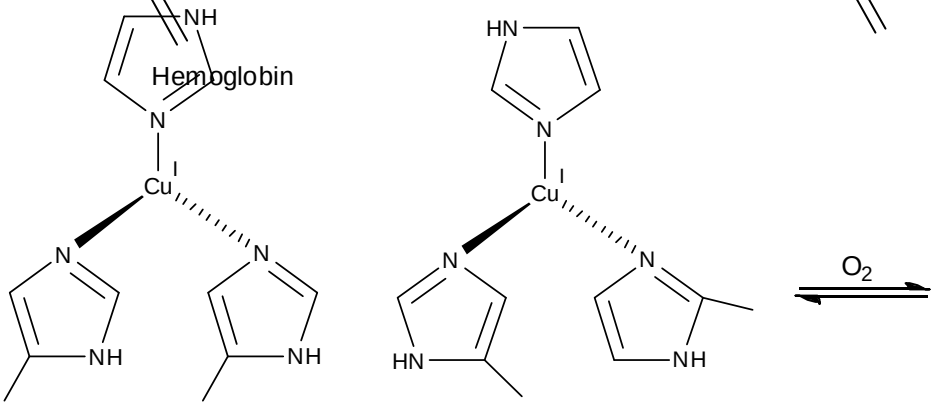
Carboxy anhydrase



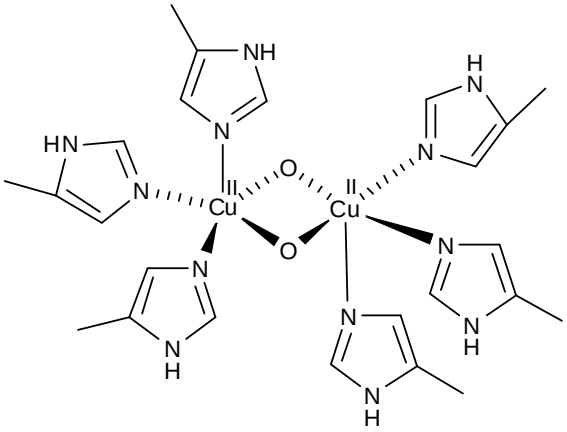


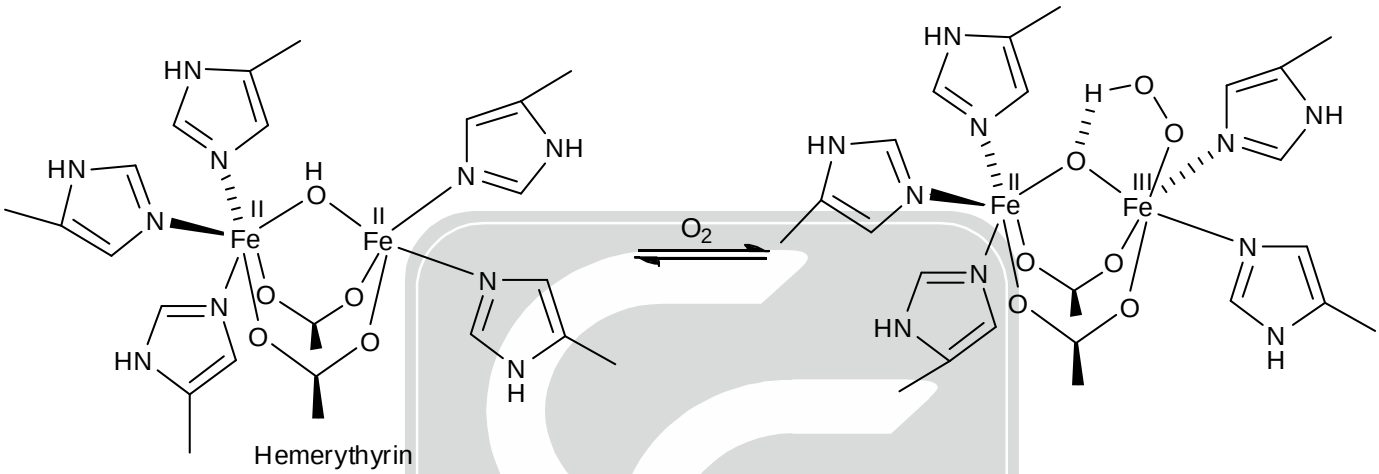
Liver alcohol dehydrogenase

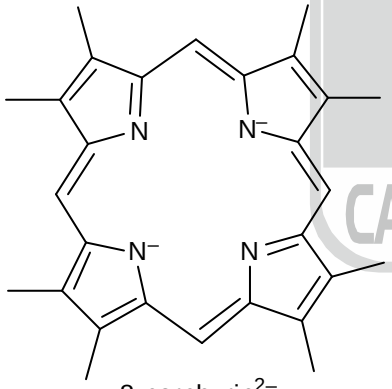




Hemocyanin







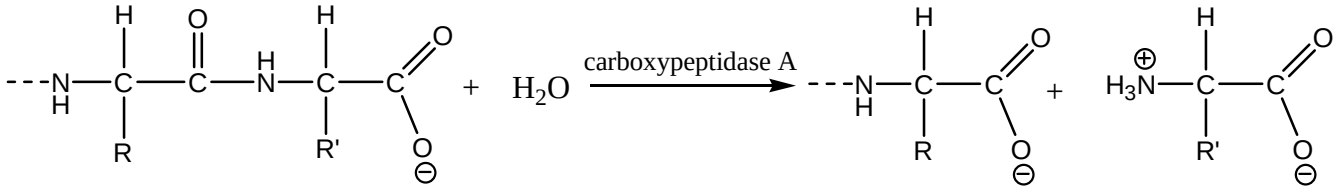
METALLOENZYMES

A metalloenzyme is an enzymatic protein in which a metal as metal ion is embedded in the cavity of the enzyme and forms strong bonds with the donor atoms of the protein. The donor atoms of proteins may be either soft bases such as S or hard bases such as O and N. In the similar way the metals may be either soft metals such as Cu^{+}, Hg^{+} and Cd^{2+} or hard such as Fe^{3+}, Zn^{2+}. The protein prat is called as an apoenzyme and a metal ion or complex metal ion is called a prosthetic group. For example, heme is prosthetic group in hemoglobin. A reversible bound group that combines with an enzyme for a particular reaction and then is released to combine with another is called as coenzyme. Both the prosthetic group and coenzyme are sometimes called cofactors.

ZINC METALLOENZYMES

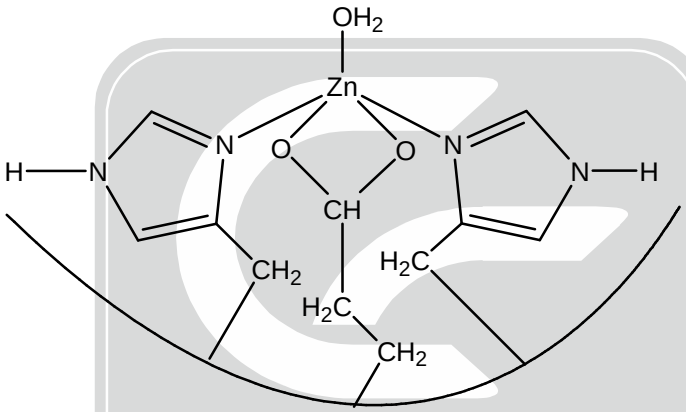
Carboxypeptidase-A:

Carboxypeptidase A is a pancreatic metalloenzyme which catalyses the hydrolysis of peptide bonds in protein during the process of digestion.



The enzyme consists of a single protein chain of 307 amino acids and one Zn^{2+} ion. Molar mass of this enzyme is about 34, 800.

The metal ion is coordinated to two N-atoms of two histidine residues (His-69 and His-196), to an oxygen atom of a glutamate residue (Glu-72) that acts as bidentate ligand and to a water molecule.



Protein portion of enzyme

The cavity has a hydrophobic pocket close to Zn^{2+} ion that can accommodate organic group of the peptide undergoing hydrolysis and therefore accounts for the higher efficiency with which hydrophobic C-terminal peptides are cleaved. The hydrophobic C-terminals peptides containg branched side chain or aromatic side chain such as $C_6H_5–CH_2–$or$–CH_2C_6H_4OH$. The carboxyl group of the substrate hydrogen bonds to an arginine (Arg-145) whereas the Zn^{2+} ion bonds to the oxygen of the peptide carbonyl group. The Arg-127 bonds to oxygen of carbonyl group of peptide of substrate. The oxygen of the water molecule coordinate to Zn^{2+} ion bonds to the carbon of the carbonyl group of the peptide and free glutamate residue of the enzyme hydrogen bonds to hydrogen of the water ligand and H^+ ion transfer from water to glutamate residue (Glu-270) leaving –OH group coordinated to Zn^{2+} ion.

In the next step C = O of carboxylic group Glu-270 hydrogen bonds to H of –OH group coordinated to Zn^{2+} and H^+ from –COOH group of Glu-270 is transferred to –NH group of the substrate with breaking of C–N peptide bond of the substrate. The glutamate residue abstract a proton from –OH group coordinated to Zn^{2+} ion to form glutamic acid. The hydrogen bonding to the carboxyl group by the Arg-145 and amide linkage by the Tyr-248 residues not only holds the substrate to the enzyme but also helps to break the C–N bond. In the final product of Zn^{2+}, the carbonyl of substrate binds in the bidentate fashion. Therefore, five coordination is maitained by switching the Glu-72 metal ligand from bidentae to monodentate becauase the metal moves toward Arg-127.