Cofactors, Coenzymes and Prosthetic group

Cofactors

The catalytic activity of many enzymes depends on the presence of small molecules termed *cofactors*, although the precise role varies with the cofactor and the enzyme. Such an enzyme without its cofactor is referred to as an *apoenzyme*; the complete, catalytically active enzyme is called a *holoenzyme*.

Apoenzyme + cofactor = holoenzyme

Cofactors can be subdivided into two groups: metals and small organic molecules

- Most common cofactor are metal ions . (Some sources also limit the use of the term “cofactor” to inorganic substances).
- Cofactors that are small organic molecules are called coenzymes.
- If tightly bound, the cofactors are called prosthetic groups
- Loosely bound cofactors serve functions similar to those of prosthetic groups but bind in a transient, dissociable manner either to the enzyme or to a substrate.
- They are more like co substrates because they bind to and are released from the enzyme just as substrates and products are.

Prosthetic Group

Tightly integrated into the enzyme structure by covalent or non-covalent forces. It can be organic or inorganic (metal ions) e.g.

a) Organic

- Pyridoxal phosphate
- Flavin mononucleotide(FMN)
- Flavin adenine dinucleotide(FAD)
- Thiamin pyrophosphate (TPP)
- Biotin

b) Inorganic

Metals are the most common prosthetic groups

- Metal ions – Co, Cu, Mg, Mn, Zn, Fe

Role of metal ions

- Enzymes that contain tightly bound metal ions are termed – Metalloenzymes.
- Enzymes that require metal ions as loosely bound cofactors are termed as metal-activated enzymes

Metal ions facilitate

- Binding and orientation of the substrate
- Formation of covalent bonds with reaction intermediates
- Interact with substrate to render them more electrophilic or nucleophilic

Examples of Metallo enzymes- (Table-1)

Metal	Enzyme
Zn^{++}	Carbonic anhydrase
Zn^{++}	Alcohol dehydrogenase
Zn^{++}	Carboxypeptidase
Fe^{+++} or Fe^{++}	Cytochromes
Cu^{++} or Cu^{+}	Cytochrome oxidase
K^{+}	Propionyl CoA carboxylase
Mg^{++}	Hexokinase

	Superoxide dismutase
	Glutathione peroxidase
	Xanthine oxidase
Ni^{++}	Urease

Metal activated /Ion activated enzymes

In a few enzyme-controlled reactions, it is the presence of certain ions that can increase the reaction rate. Ions may combine with the enzyme or the substrate. The ion binding makes the formation of an enzyme-substrate complex happen more easily, because it can affect the *charge distribution* or the end shape of the complex.

Amylase catalyses the breakdown of maltose molecules. This enzyme will function properly only if **chloride ions** are present. Without the chloride ions, amylase cannot catalyse the reaction

Co-enzymes

Co-enzymes serve as recyclable shuttles—or group transfer agents—that transport many substrates from their point of generation to their point of utilization.

- The water-soluble B vitamins supply important components of numerous coenzymes
- Chemical moieties transported by coenzymes include hydrogen atoms or hydride ions, methyl groups (folates), acyl groups (coenzyme A), and oligosaccharides (dolichol).

Examples of Coenzymes- (Table-2)

Coenzyme	Abbreviation	Group transferred	Enzyme
Nicotine adenine dinucleotide	NAD^+ – Derived from niacin	Electron (hydrogen atom)	Lactate dehydrogenas
Nicotine adenine dinucleotide phosphate	$NADP^+$ – niacin derivative	Electron (hydrogen atom)	Glutamate dehydrogen
Flavin adenine dinucleotide	FAD – riboflavin (vit. B2) derivative	electron (hydrogen atom)	Monoamine oxidase
Coenzyme A	CoA	Acyl groups	Acetyl CoA carboxylas
Thiamine pyrophosphate	Thiamine (vit. B1)	Aldehydes	Pyruvate dehydrogena Complex
Pyridoxal phosphate	Pyridoxine (vit B6)	amino and many other	Transaminases, Decarboxylases, Glyc phosphorylase
Biotin	Biotin	Carboxyl	Pyruvate carboxylase
5′-Deoxyadenosyl cobalamine	vit. B12	alkyl groups	Methylmalonyl mutase
Tetrahydrofolate	Folic acid	One carbon compounds	Thymidylate synthase