BSc II Paper III Unit V

Coenzyme

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The functional groups of the amino acid side chain of the enzymes are responsible for many of the catalytic properties of proteins. However by themselves, the sidechain functional groups are unable to catalyze all the reactions needed by a cell in metabolism. For those essential enzyme reactions that are impossible or impracticably inefficient within the repertoire of mechanism catalyzed by side chain functional groups a small structurally diverse group of molecules known as **Cofactors** is of central importance.

The catalytic activity of many enzyme depends on the presence of Cofactors, although the precise role varies with the cofactor and the enzyme. Such an enzyme without its cofactors is referred to as an apoenzyme, the complete, catalytically active enzyme is called holoenzyme. Hence

Apoenzyme + Cofactor = Holoenzyme.

Cofactors can be subdivided into 2 groups: Metals and small organic molecules

Metals can be bound to an enzyme in 2 possible manners:

(a). Tightly and rather permanently: Such enzyme, which carry a tightly bound metal group, are called Metallozyme. The metal group present are mostly transition metal ions such as, Fe^{3+}, Fe^{2+}, Mg^{2+}, Zn^{2+}, Co^{3-} etc, one of the earliest recognized metallozyme is Carbonic anhydrase with Zinc group.

(2) Loosely and often transiently: The metal ions in such associations with apoenzymes play a role of activators; hence, they are called Metal activators. They mostly belong to the earth metal group such as Na^+, K^+, and Ca^{2+}.

Associated metal cofactors play three role in enzyme's catalysis.

1. They neutralize negative change and bring about better change distribution, which can sometimes be necessary for catalysis.
2. They facilitate redox reactions by working as electron acceptor or electron donor.
3. They can promote electrostatic binding between the enz and the substrate.

Cofactors that are small organic molecules are called coenzymes. often derived from vitamins, coenzymes can be either tightly or loosely bound to the enzyme. If ~~tigh~~ tightly bound, they are called prosthetic groups. Loosely associated coenzymes are called cosubstrates because they bind to and are released from enzyme just as substrates and products are. The use of the same coenzyme by a variety of enzymes and their source in Vitamins sets coenzymes apart from normal substrates, hower. Enzymes that use the ~~co~~ same coenzyme are usually mechanistically similar.

Most coenzymes are derived from vitamins. ~~Vitamins~~. Vitamins themselves are organic molecules that are needed in small amounts in the diets of some higher animals. These molecules serve the same roles in nearly all forms of life, but higher animals lost the capacity to synthesize them in the course of evolution. For instance, whereas E. coli can ~~derive~~ thrive on glucose and organic salts, human beings require atleast 12 vitamins in the diet. The biosynthetic pathways for vitamins can be complex; thus, it is biologically more efficient to ingest vitamins than to synthesize the enzymes required to construct them from simple molecules. The efficieny comes at the cost of dependence on other organism for chemical essential for life.

Vitamins are often classified into

1. Water soluble
2. Fat ~~soluble~~ soluble.

Role of Coenzymes

Together with enzymes, coenzymes provide special chemical properties that permit exceptional chemical reactivities and reactions not otherwise possible at physiologic conditions. The role that coenzyme play in biochemistry is so extraordinary and so pivotal, it lead David Metzler to call them 'Nature's special reagents"

Coenzymes often serve as additional reagents in enzyme-catalyzed reaction, as stabilizers, or carriers of functional groups, protons, or electrons. Humans are unable to synthesize most of the coenzymes from elementary precursors, and if a dietary source is not available a deficiency with obvious clinical symptoms arises.

The functional role of coenzymes is to act as transporters of chemical groups varies from one reactant to another. The chemical groups carried can be as simple as the hydride ion (H + 2e) carried by NAD or the mole of hydrogen carried by FAD, or they can even be more complex than the amine (-NH_2) carried by pyridoxal phosphate.

but it is also source of phosphate pyrophate, phosphoribosyl, and adenosyl moieties to other reactants of a given reaction. The transfer of one carbon units by tetrahydrofolate also puts it in this class.

2. A second category of coenzymes reacts at the active site of the enzyme to modify the structure of the substrate so as to facilitate the conversion of substrate to product. Examples in this grouping include CoA, thiamine, pyridoxal phosphate and 5' deoxyadenosylcobalamin (B12)

(3) The third class consists of those coenzymes that participate in redox reactions by serving as carriers of electrons or protons. Coenzymes in this group include ascorbic acid, ~~FAD~~ FAD, FMN, and the pyridine nucleotides: NAD^+, NADH, $NADP^+$, and NADPH.

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