Bio-organic chemistry

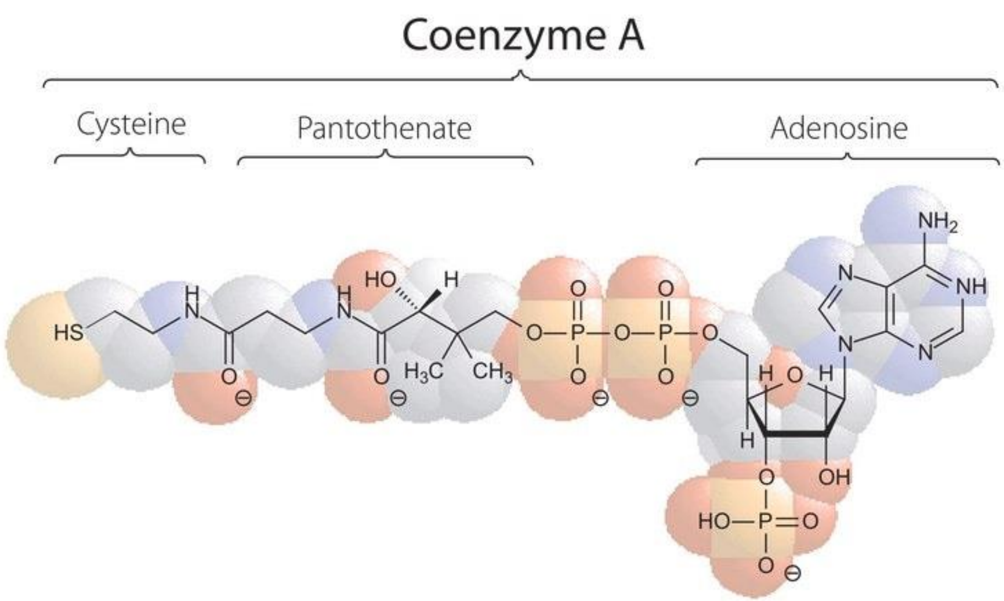
Lecture #6

Coenzymes. Chemical structure, properties and physiological role in the body

Lecturer:
Dr. Gulnaz Seitimova
Associate Professor

A **coenzyme** is a molecule required by a particular enzyme to carry out the catalysis of a chemical reaction. Many are derived from vitamins, particularly those that are phosphorylated derivatives of water-soluble vitamins. Coenzymes participate in catalysis when they bind to the active site of the enzyme (called apoenzyme) and subsequently form the active enzyme (called holoenzyme). Although coenzymes activate enzymes they are not considered as substrates of the reaction. The main function of the coenzyme is to act as an intermediate carrier of transferred electrons or functional groups in a reaction.

Examples of coenzymes: nicotineamideadenine dinucleotide (NAD), nicotineamide adenine dinucelotide phosphate (NADP), and flavin adenine dinucleotide (FAD). These three coenzymes are involved in oxidation or hydrogen transfer. Another is coenzyme A (CoA) which is involved in the transfer of acyl groups.



Coenzyme A (CoA, CoASH or HSCoA) is the key cofactor in first step of the TCA cycle, responsible for transferring the acetyl group from pyruvate oxidation to oxaloacetate yielding citrate.

Coenzyme A is also a critical cofactor in fatty acid metabolism. Coenzyme A carries fatty acids through the catabolic/oxidation process in the mitochondria and transfers acetyl groups during the elongation process of fatty acid synthesis in the cytosol.

Coenzyme Definition

Coenzymes play a vital role in several biochemical pathways such as breaking down macronutrients into smaller molecules (Catabolism) or the formation of new biological compounds in the body (Anabolism).

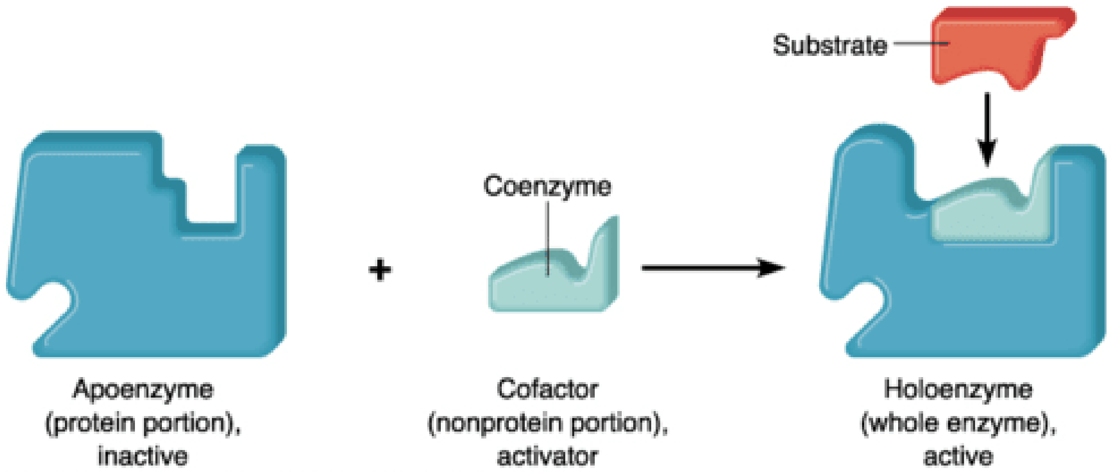
What is a coenzyme? Sometimes, a coenzyme is referred to as a co-substrate because it binds to the enzyme along with the substrate at the beginning of a chemical reaction and they leave the enzyme altered at the end of the reaction. However, they are called coenzymes because they bind to the enzyme before other substrates will. Moreover, coenzymes are reconverted by other enzymes found in the cell to their original form to be reused. A coenzyme is usually a form of activated vitamin that is essential for biochemical pathways. Coenzymes form complexes with enzymes. These complexes convert nutrients into useful forms of energy. They produce biomolecules that are considered to be the basis of our life.

Some nutrients act as cofactors and coenzymes. Others are being broken down by the help of coenzymes. Therefore, it is essential to maintain the dietary intake of trace elements to produce the energy required for life.

Enzymes that require the presence of coenzymes to function will not be able to maintain the normal metabolic processes or to maintain the activity of the natural biochemical processes that keep the normal functions of the cell activated such as cell growth, differentiation, division, and repair.

Additionally, coenzymes function to keep the integrity of some regulatory proteins and hormone structures.

Some vitamins act as coenzymes participating in biochemical processes such as catabolism, anabolism, and the production of energy. Vitamins A and K are two fat-soluble vitamins that act as coenzymes or cofactors, while all the water-soluble enzymes can act as cofactors or coenzymes. In addition to their action as cofactors, vitamins have a critical role in several vital processes such as the production of hormones, the integrity of collagen in bones, blood coagulation, and proper vision.



A cofactor is a non-protein chemical compound that is required for the protein's biological activity. Many enzymes require cofactors to function properly.

Examples of Coenzymes

Coenzymes are not specific to substrates, instead, they act as a carrier to the reaction products. Coenzymes are regenerated to be reused. An important example of coenzymes is nicotinamide adenine dinucleotide (NAD) which is used to activate the lactic dehydrogenase enzyme.

In the dehydrogenation of pyruvate to lactate, NAD itself is reduced by accepting hydrogen atoms for catalytic reactions, whereas some enzymes require the nicotinamide adenine dinucleotide phosphate (NADP) phosphate which is likewise reduced.

For the synthesis of steroids, NADP coenzyme is required. The reduced enzyme is, then, re-oxidized by transferring the introduced hydrogen along a hydrogen acceptors chain to be combined with molecular oxygen forming a water molecule.

NAD+ is the first molecule that binds to the enzyme, and it is the last molecule to be unbound from the complex. Therefore, it is the rate-limiting step of the biochemical reaction. As such, it is considered to be a coenzyme, not a substrate.

Nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP) help enzymes that remove hydrogen (dehydrogenases) to assist in the catabolic process of amino acids, fats, and carbohydrates as well as the enzymes participating in the synthesis of steroids, fats, and other metabolites.

Types of Coenzymes

Table 1: Vitamins as examples of coenzymes.

Water-Soluble Vitamins	Coenzyme	Coenzyme Function
vitamin B_1 (thiamine)	thiamine pyrophosphate	decarboxylation reactions
vitamin B_2 (riboflavin)	flavin mononucleotide or flavin adenine dinucleotide	oxidation-reduction reactions involving two hydrogen atoms
vitamin B_3 (niacin)	nicotinamide adenine dinucleotide or nicotinamide adenine dinucleotide phosphate	oxidation-reduction reactions involving the hydride ion (H^-)
vitamin B_6 (pyridoxine)	pyridoxal phosphate	variety of reactions including the transfer of amino groups
vitamin B_{12} (cyanocobalamin)	methylcobalamin or deoxyadenoxylcobalamin	intramolecular rearrangement reactions
biotin	biotin	carboxylation reactions
folic acid	tetrahydrofolate	carrier of one-carbon units such as the formyl group
pantothenic Acid	coenzyme A	carrier of acyl groups
vitamin C (ascorbic acid)	none	antioxidant; formation of collagen, a protein found in tendons, ligaments, and bone

Functions of Coenzymes

Minerals and vitamins play an important role in the anabolic and catabolic pathways that lead to the synthesis of biomolecules such as lipids, nucleic acids, proteins, and carbohydrates as coenzymes or cofactors.

Vitamins as coenzymes: Vitamin A metabolite form, retinoic acid, functions as genes regulator, therefore, it is very important for the normal development of cells. Vitamin K is a coenzyme for enzymes that move —CO2 groups (g-carboxylases). The released carboxylic group binds to calcium, this step is important for the formation of osteocalcin, an important protein for bone remodelling. Additionally, it is important for the formation of prothrombin, which plays a crucial role in blood coagulation.

Minerals as cofactors and catalysts: Minerals can function in biological processes as cofactors and catalysts. When minerals act as catalysts they do not integrate with an enzyme or its substrate. However, they accelerate the biochemical reaction between the enzyme and its substrate. Alternatively, when minerals act as cofactors, they become a part of the enzyme or protein structure that is essential for the biochemical reaction to proceed. Minerals that act as cofactors include manganese, selenium, magnesium, and molybdenum. Some minerals, such as cobalt, iodine, calcium, and phosphorus, act as cofactors for certain non-enzymatic proteins. Others, like copper, zinc, and iron, act as cofactors for both non-enzymatic and enzymatic proteins.