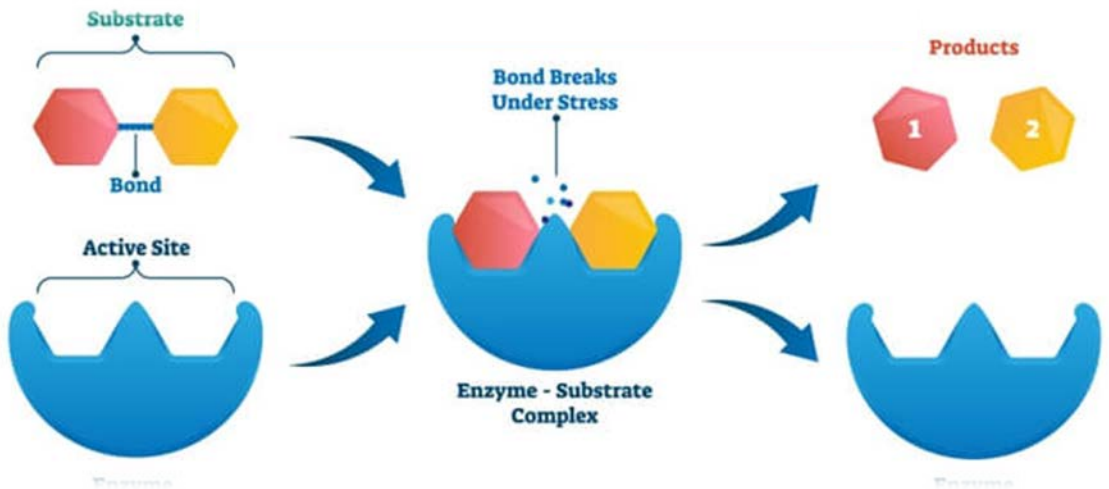
BIOCHEMISTRY - YEAR 2



Enzymes
Part 2
Lecture No: 15

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Enzyme Catalyzed Reaction

- The proper alignment of a substrate within the active site forms an enzyme-substrate (ES) complex. This combination of enzyme and substrate provides an alternative pathway for the reaction that has a lower activation energy. Within the active site, the amino acid side chains take part in catalyzing the chemical reaction. For example, acidic and basic side chains remove protons from or provide protons for the substrate. As soon as the catalyzed reaction is complete, the products are quickly released from the enzyme so it can bind to a new substrate molecule. We can write the catalyzed reaction of an enzyme (E) with a substrate (S) to form product (P) as follows:

Enzyme Kinetics

$$E + S \longrightarrow ES \longrightarrow E + P$$

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

E = enzyme
S = substrate
P = product
ES = enzyme-substrate complex
k = rate constant

Isoenzymes as Diagnostic Tools

Isoenzymes are different forms of an enzyme that catalyze the same reaction in different cells or tissues of the body. They consist of quaternary structures with slight variations in the amino acids in the polypeptide subunits. For example, there are five isoenzymes of lactate dehydrogenase (LDH) that catalyze the conversion between lactate and pyruvate.

Each LDH isoenzyme contains a mix of polypeptide subunits, M and H. In the liver and muscle, lactate is converted to pyruvate by a LDH_5 isoenzyme with M subunits designated M_4. In the hart, the same reaction is catalyzed by a LDH_1 isoenzyme (H_4) containing four H subunits. Different combinations of the M and H subunits are found in the LDH isoenzymes of the brain, red blood cells kidney, and white blood cells.

The different forms of an enzyme allow a medical diagnosis of damage or disease to a particular organ or tissue. In healthy tissues, isoenzymes function within the cells. However, when a disease damages a particular organ, cells die, which releases cell contents including the isoenzymes into the blood. Measurements of the elevated levels of specific isoenzymes in the blood serum help to identify the disease and its location in the body.

, five isoenzymes of LDH that occurs as a dimer of 2 different subunits H &M

Isoenzymes of lactate dehydrogenase	Highest levels found in the following:	Isoenzymes of lactate dehydrogenase	Highest levels found in the following:
H M		H_2M_2 (LDH_3)	Brain, lung, white blood cells
H_4 (LDH_1)	Heart, kidneys	HM_3 (LDH_4)	Lung, skeletal muscle
H_3M (LDH_2)	Red blood cells, heart, kidney, brain	M_4 (LDH_5)	Skeletal muscle, liver

For example elevation in the serum LDH_5, which is the M_4 isoenzyme of lactate dehydrogenase, indicates liver damage or disease. When a myocardial infarction (MI), or heart attack, damages the cells in heart muscle, an increase in the level of LDH_1 (H_4) isoenzyme is detected in the blood serum.

Another isoenzyme used diagnostically is creatine kinase (CK). which consists of two types of polypeptide subunits. One subunit (B) is prevalent in the brain and the other predominates in skeletal muscle (M). Normally only the CK_3, is present in low amounts in the blood serum. However, in a patient who has suffered an MI, the levels of CK_2, will be elevated soon after the heart attack.

Factors Affecting Enzyme Activity

The activity of an enzyme describes how fast an enzyme catalyzes the reaction that converts a substrate to product. This activity is strongly affected by reaction conditions, which include the temperature, pH, concentration of the substrate, and concentration of the enzyme.

Temperature

- Enzymes are very sensitive to temperature. At low temperatures, most enzyme show little activity because there is not a sufficient amount of energy for the catalyzed reaction to take place. At higher temperatures, enzyme activity increases as reacting molecules move faster to cause more collisions with enzymes. Enzymes are most active at optimum temperature, which is 37°C or body temperature for most enzymes. At temperatures above 50°C, the tertiary structure and thus the shape of most proteins is destroyed causing a loss in enzyme activity. For this reason, equipment in hospitals and laboratories is sterilized in autoclaves where the high temperatures denature the enzymes in harmful bacteria.

pH

Enzymes are most active at their optimum pH, the pH that maintains the proper tertiary structure of the protein. A pH value above or below the optimum pH causes a change in the three-dimensional structure of the enzyme that disrupts the active site. As a result the enzyme cannot bind substrate properly and no reaction occurs.

Enzymes in most cells have optimum pH values at physiological pH values around 7.4. However, enzymes in the stomach have a low optimum pH because they hydrolyze proteins at the acidic pH in the stomach. For example, pepsin, a digestive enzyme in the stomach has an optimum pH of 2. Between meals, the pH in the stomach is 4 or 5 and pepsin shows little or no digestive activity. When food enters the stomach, the secretion of HCI lowers the pH to about 2, which activates pepsin.

If small changes in pH are corrected, an enzyme can regain its structure and activity. However, large variations from optimum pH permanently destroy structure of the enzyme.

Enzyme and Substrate

In any catalyzed reaction, the substrate must first bind with the enzyme to form the substrate-enzyme complex. Increasing the enzyme concentration when the substrate concentration remains constant increases the rate of the catalyzed reaction and thus enzyme activity. At higher concentrations more enzyme molecules are available to bind and catalyze the reaction of substrate molecules. When the enzyme concentration is increased to twice the initial concentration, the rate of the catalyzed reaction is twice as fast. If the enzyme concentration is increased to three times the initial enzyme concentration, the rate of reaction will increase also to three times as fast. There is a direct relationship between the enzyme concentration and enzyme activity. When enzyme concentration is kept constant, increasing the substrate concentration increases the rate of the catalyzed reaction as long as there are more enzyme molecules present than substrate molecules. At some point an increase in substrate concentration saturates the enzyme. With all the available enzyme molecules bonded to substrate, the rate of the catalyzed reaction reaches its maximum. Adding ore substrate molecules cannot increase the rate further.

The End

Thank You All

Reference: General, organic,& biological chemistry structures of life.
Timberlake. Pearson Education. 2002