Discipline: "Biochemistry"

Course Code: Bio 2204

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Protocol No.1 dated 27.08. 2025 years

Head of Department, Acting Professor: _____ Daurenbekov K.N.

No. 1

1. Subject: The structure of enzymes and their biological functions.

2. Objective: Explain the properties, structure, mechanisms of action, specificity of enzymes, and the role of cofactors. Explain the kinetics and classification of enzymes. Provide an understanding of enzyme pathology, enzyme diagnostics, and enzyme therapy.

3. Lecture abstracts. Enzymes are biological catalysts made of proteins. An enzyme lowers the activation energy, i.e., reduces the barrier height. This increases the proportion of reactive molecules, thereby increasing the reaction rate. The lower the activation energy, the more effective the catalyst is and the faster the reaction.

The active site is divided into a contact region, which binds the substrate, and a catalytic region, where substrate conversion occurs after binding. The enzyme's active site is formed by 12-16 amino acid residues of the polypeptide chain. The amino acids that make up the active site are located at different points along the polypeptide chain. When folded spatially, they come together to form the active site. The remaining amino acid residues of the enzyme's polypeptide chain ensure the correct spatial configuration of the active site and influence the reactivity of its groups.

In simple enzymes, only the amino acid side chains serve as the functional groups in the contact and catalytic regions of the active site. In complex enzymes, cofactors play a key role in these processes.

The starting materials for the formation of coenzymes are vitamins, therefore, insufficient intake of them with food immediately affects the synthesis of these coenzymes, and as a consequence, the function of the corresponding complex enzymes is disrupted.

In the molecular mechanism of enzyme action, the following can be noted: the effect of reagent orientation (approach), the effect of substrate deformation (stress, bending, tension), acid-base catalysis, covalent catalysis.

The reactant orientation effect is a very characteristic property of enzymes, allowing for the acceleration of conversion (increasing the reactivity of substrates) by thousands or tens of thousands of times. Contact sites in the enzyme's active center specifically bind substrates and ensure their mutual orientation and proximity in a manner favorable to the action of the catalytic groups.

Stereochemical substrate specificity—the enzyme catalyzes the conversion of only one of the possible stereoisomers of the substrate.

Absolute substrate specificity – the enzyme catalyzes the conversion of only one substrate.

Absolute group substrate specificity – the enzyme catalyzes the conversion of a similar group of substrates.

Relative group substrate specificity – the enzyme specifically acts on the bond group of a certain group of substrates.

Relative substrate specificity – an enzyme catalyzes the conversion of substrates belonging to different groups of chemical compounds. For example, the enzyme cytochrome P450 is involved (approximately 7,000 substrates).

Enzyme kinetics is a branch of enzymology that studies the dependence of the rate of enzyme-catalyzed reactions on the chemical nature and conditions of interaction between the substrate and the enzyme, as well as environmental factors. The rate of an enzymatic reaction is determined by the amount of substance converted per unit of time. The rate of these reactions depends on external conditions (temperature, pH, and the influence of natural and foreign compounds).

All enzymes are divided into six classes, each of which has a strictly defined number: 1) oxidoreductases; 2) transferases; 3) hydrolases; 4) lyases; 5) isomerases; 5) ligases (synthetases).

The class name indicates the type of chemical reaction catalyzed by the enzyme. Consequently, there are six main types of enzymatic reactions. Classes are divided into subclasses, which in turn are divided into subsubclasses. A subclass specifies the enzyme's action by generally

indicating the nature of the chemical group of the substrate attacked by the enzyme. A subsubclass further specifies the enzyme's action by specifying the nature of the substrate bond being attacked or the nature of the acceptor involved in the reaction.

Regulation of enzyme activity can be achieved through activation of proenzymes, modification, inhibition and allosteric regulation.

The applications of enzymology in medicine are theoretically limitless, particularly in the field of enzymopathology, which studies enzymatic activity in health and disease. Many inherited metabolic disorders are the result of a defect in a specific enzyme. For example, galactosemia, a hereditary disorder characterized by abnormally high galactose concentrations in the blood, develops as a result of a hereditary defect in the synthesis of the enzyme hexose-1-phosphate-uridyltransferase, which catalyzes the conversion of galactose into easily metabolized glucose.

Enzyme diagnostics is developing both through the use of enzymes as selective reagents for the discovery and quantitative determination of normal or abnormal chemical substances in blood serum, urine, gastric juice, etc., and through the discovery and quantitative determination of the enzymes themselves in biological fluids in pathology.

Enzyme therapy, the use of enzymes and enzyme regulators as medicinal agents, is used clinically to treat gastrointestinal diseases. Pepsin, trypsin, chymotrypsin, and their mixtures (abomin, chymopsin) are used. In addition to proteinases, a number of other enzymes, including RNase, DNase, hyaluronidases, collagenases, and elastases, are used alone or in combination with proteinases to treat wounds, inflammation, burns, and to reduce swelling, hematomas, and keloid scars (pulmonary tuberculosis).

4. Illustrative material:
PowerPoint presentation
5. *Literature:
6.Test questions:
1. How does the structure of the active center of a simple enzyme differ from the structure of the active center of a complex enzyme?
2. Explain the specific action of enzymes.
3. Explain the mechanism of action of enzymes.
4. How can the chemical nature of enzymes be determined?
5. What is the classification of enzymes based on?
6. What groups can the class of oxidoreductases be divided into?
7. Explain the features of action of enzymes of the lyase class.
8. What causes hereditary diseases?
9. What enzymes are used in the clinic?

No. 2

1. Subject: Energy exchange.
2. Purpose Explain at the molecular level the specific and general catabolic pathways, the process of oxidative decarboxylation of pyruvate, and the Krebs cycle. Explain the transport of hydrogen from the cytoplasm to the mitochondria, the structure, and biological functions of tissue respiration enzymes. Provide an understanding of the relationship between tissue respiration and oxidative phosphorylation.
3. Lecture abstracts. The energy resources available to cells are used to provide them with energy. These energy resources include monosaccharides, amino acids, glycerol, and fatty acids, which, when passing through the cell's plasma membrane, can either be used directly as energy sources or incorporated into biopolymers (polysaccharides, lipids, proteins).

Oxidative decarboxylation of pyruvic acid is carried out by the polyenzyme pyruvate dehydrogenase complex. This complex is present in the matrix, but not in solution; rather, it is attached to proteins of the inner mitochondrial membrane facing the matrix. The pyruvate dehydrogenase complex exemplifies the structural organization of several different enzymes and possesses all the advantages of such an organization. Of the products of pyruvate oxidation, CO2 is the end product of metabolism and has no energy value. Reduced NAD is an energy-rich compound whose hydrogen is supplied to the respiratory chain. Acetyl-CoA enters the Krebs cycle, located within the mitochondria.

Acetyl-CoA, formed during the oxidation of pyruvate, fatty acids, and amino acids, enters the Krebs cycle. The first stage involves the synthesis of citric acid, with the participation of the enzyme citrate synthesis.

The second enzyme of the Krebs cycle, aconitate hydratase, catalyzes the reversible conversion of three tricarboxylic acids: citrate, cis-aconitate, and isocitrate. Isocitrate dehydrogenase catalyzes the dehydrogenation of isocitrate to form 2-oxoglutarate. 2-oxoglutarate is converted to succinyl-CoA by the multienzyme 2-oxoglutarate dehydrogenase complex. The product of this reaction, succinyl-CoA, is a highly energy-rich compound, so the next stage of the cycle involves the transfer of the high-energy bond of this substrate to high-energy phosphate bonds.

Succinate is converted to fumarate by succinate dehydrogenase. The next step involves the stereospecific addition of a proton and a hydroxyl group to fumarate, catalyzed by fumarate hydratase. The final stage of the Krebs cycle is the regeneration of oxaloacetate. This occurs through the oxidation of malate, catalyzed by malate dehydrogenase.

NADH2, formed in the cytoplasm, for example during the breakdown of carbohydrates, does not penetrate the mitochondrial membrane and therefore hydrogen transport is carried out by shuttle systems.

The respiratory chain is a unique conveyor belt for the transfer of protons and electrons from reduced NAD, formed by the action of NAD-dependent dehydrogenases on the substrate, or from reduced FAD, formed by the action of flavin-dependent dehydrogenases on sbustat, to oxygen. The respiratory chain consists of the following proton and electron carriers: flavoprotein-1 (FP), which contains FMN as a coenzyme, coenzyme Q (or ubiquinone), two iron-sulfur proteins containing non-heme iron, and cytochromes B C1, C, a, and a3. Hydrogen in NADH is attached to the flavoprotein, where its first acceptor is FMN of the flavoprotein, and hydrogen in FADH2 is attached to the section of the respiratory chain containing CoQ. The section of the respiratory chain from NADH to cytochrome B is represented by proton and electron carriers. Starting from cytochrome B and up to oxygen, the flows of hydrogen and electrons are separated, since this section of the respiratory chain contains only electron carriers (cytochromes and a special iron-sulfur protein).

ATP biosynthesis, coupled with the reverse diffusion of protons across the membrane, is carried out by H+-ATP synthetase. It has a mushroom-like shape and consists of two structural parts. The stalk of the mushroom, a protein cylinder, penetrates the entire thickness of the inner mitochondrial membrane. One end of the cylinder communicates with the external environment, while the other is attached to a spherical head at the border of the inner membrane surface. Synthesized ATP is transferred into the matrix. ATP is transported outward by a special mitochondrial membrane transport protein, which exchanges ATP for external ADP, which is needed for phosphorylation.

4.Illustrative material:

PowerPoint presentation

5. *Literature:

6. Control questions:

1. How does energy production occur anaerobically?

2. What processes are related to the general pathway of catabolism?
3. What enzymes are part of the pyruvate dehydrogenase complex?
4. What biological functions does the Krebs cycle perform?
5. What enzymes are part of tissue respiration?
6 How is proton potential formed?
7. How is ATP biosynthesis carried out?
8. How is the reducing equivalent transported into the matrix?
9. What factors cause a hypoenergetic state?

No. 3

1. Subject: Carbohydrate metabolism.

2. Objective: Explain carbohydrate metabolism at the molecular level and the use of other monosaccharides in glycolysis. Explain the pentose phosphate cycle, gluconeogenesis, and carbohydrate metabolism disorders.

3. Lecture abstracts. In the human body, carbohydrates perform important functions: primarily energy, structural (an essential component of most intracellular structures), and protective (the participation of carbohydrate components of immunoglobulins in maintaining immunity).

Hydrolysis of carbohydrates in the intestine is carried out by pancreatic and intestinal enzymes. The former include pancreatic α-amylase and oligo-1,6-glucosidase. The remaining enzymes—oligosaccharidases and disaridases—are produced primarily in the intestinal mucosa. The end products of carbohydrate digestion are monosaccharides, primarily glucose, fructose, and galactose. Monosaccharides are then absorbed in the small intestine.

Phosphorolytic degradation plays a key role in the mobilization of polysaccharides. Phosphorylases convert polysaccharides (particularly glycogen) from storage to metabolically active form: in the presence of phosphorylase, glycogen is broken down to form the phosphate ester of glucose (glucose-1-phosphate) without first being broken down into larger fragments of the polysaccharide molecule. The phosphorylase enzyme exists in two forms, one of which (phosphorylase A) is active, while the other (phosphorylase B) is usually inactive. Both forms can dissociate into subunits. Phosphorylase B consists of two subunits, and phosphorylase A consists of four. The conversion of phosphorylase B to phosphorylase A is accomplished by protein phosphorylation. Maintaining a constant blood glucose concentration is the result of two simultaneous processes: the entry of glucose into the blood from the liver and its consumption from the blood by tissues, where it is used primarily as an energy source.

Fructose is converted into fructose-6-phosphate by hexokinase. 6-phosphofructokinase converts fructose-6-phosphate to fructose-1,6-bisphosphate. Fructose-1,6-bisphosphate can then undergo further conversion via glucolysis. This is the main pathway for fructose incorporation into muscle tissue, kidneys, and adipose tissue.

The biological function of the pentose phosphate cycle is associated with the production of two substances: NADPH, which serves as a reducing agent in the synthesis of various substances, and the metabolite ribose-5-phosphate, which is used as a building block in the synthesis of various substances. The pentose phosphate pathway of carbohydrate conversion is primarily active in those organs and tissues that require intensive use of NADPH in reductive synthesis reactions and ribose-5-phosphate in the synthesis of nucleotides and nucleic acids. Therefore, high activity of this pathway is observed in adipose tissue, liver, mammary gland tissue, adrenal glands, gonads, bone marrow, and lymphoid tissue. Pentose phosphate dehydrogenases are relatively active in erythrocytes. Low activity is observed in muscle tissue.

Gluconeogenesis is the synthesis of glucose from non-carbohydrate products. These products, or metabolites, primarily include lactic and pyruvic acids, so-called amino acids, glycerol, and a number of other compounds. In other words, the precursors of glucose in gluconeogenesis can be pyruvate or any compound that is converted during catabolism to pyruvate or one of the intermediate products of the tricarboxylic acid cycle. Most stages of gluconeogenesis involve the reversal of glycolytic reactions. Only three glycolytic reactions (hexokinase, phosphofructokinase, and pyruvate kinase) are irreversible, so gluconeogenesis utilizes different enzymes for these three reactions.

In humans, carbohydrate metabolism is regulated by the central nervous system and hormones at all stages of carbohydrate synthesis and breakdown. For example, it has been established that a decrease in blood glucose concentration below 3.3-3.5 mmol/L leads to reflex stimulation of higher metabolic centers located in the hypothalamus. The highest region of the central nervous system—the cerebral cortex—plays a special role in the regulation of carbohydrate metabolism. Along with the central nervous system, hormonal factors also have a significant influence on blood glucose levels. Thus, blood glucose levels are regulated by the central nervous system through a number of endocrine glands.

4. Illustrative material:

PowerPoint presentation

5. *Literature:

6. Control questions:

1. What enzymes are involved in the digestion of carbohydrates?
2. How are the enzymes phosphorylase and glycogen synthesis activated?
3. How are fructose and galactose included in the glycolysis process?
4. How does glucose enter the blood from the liver?
5. What biological functions does the pentose phosphate cycle perform?
7. How is the process of gluconeogenesis regulated?
8. For the biosynthesis of what substances is NADPH2 used?
9. What causes Gierke's disease?
10. Decreased activity of which enzyme leads to the development of galactosemia?

No. 4

1. Subject: Lipid metabolism.

2. Objective: Explain the stages of lipid metabolism in the body: digestion, absorption, intermediate metabolism, and elimination of metabolic products. Provide an understanding of the formation and metabolism of transport lipoproteins. Explain intracellular lipolysis, fatty acid metabolism, ketone body metabolism, and cholesterol metabolism at the molecular level. Explain lipid metabolism pathologies at the molecular level.

3. Lecture abstracts. Active lipase acts on the triacylglycerols of the fat droplet. The enzyme itself is dissolved in the aqueous phase and breaks down the substrate in the lipid phase. Lipase has a special hydrophobic region with which triacylglycerol contacts. Fat hydrolysis occurs at the interface. The hydrolysis products are 2-monoacylglycerol and free fatty acids. Carboxylesterases in the intestine and pancreatic juice break down 2-monoacylglycerol into free fatty acid and glycerol.

Prophospholipase A2 is activated in intestinal juice, where trypsin cleaves a hexapeptide from the proenzyme. Phospholipase A2, the primary digestive phospholipase, produces extremely toxic lysophosphatides, which are immediately hydrolyzed by lysophospholipase. Phospholipases C and D complete the hydrolysis of phosphoglycerides. The end products of their hydrolysis are glycerol, fatty acids, inorganic phosphate, and one of the residual alcohols (choline, ethanolamine, inositol, serine).

The absorption of lipid digestion products has its own characteristics. For example, the absorption of fatty acids depends on the length of their hydrocarbon chain. Short-chain fatty acids with up to 10-12 carbon atoms are absorbed by simple diffusion into the intestinal epithelium. Long-chain fatty acids (more than 14 carbon atoms) form complexes with bile acids. In this form, the fatty acids pass through the intestinal epithelial membrane.

Lipids resynthesized in the intestine are transported as chylomicrons. Chylomicrons pass from the intestinal epithelium into the thoracic lymphatic duct. After ingesting large amounts of fatty foods, the lymph takes on a milky appearance from suspended chylomicrons. From the thoracic duct, chylomicrons enter the blood, which becomes turbid and highly opalescent (this type of blood plasma is called lipemic). In the blood, chylomicrons, or more precisely, the triacylglycerols they contain, are broken down by lipoprotein lipase.

Activation of fatty acids occurs in the cytoplasm with the participation of acyl-CoA synthetase. Since this process occurs outside the mitochondria, further transport of acyl-CoA across the membrane into the mitochondria is necessary. This transport is mediated by carnitine, which transfers the acyl from the acyl-CoA on the outer surface. Acylcarnitine diffuses to the inner surface of the membrane, where it releases its acyl-CoA to the matrix.

Fatty acid oxidation occurs in the matrix via the Knoop-Linen cycle. This cycle involves four enzymes that act sequentially on acyl-CoA. As a result of this reaction, fatty acids are converted into acetyl-CoA.

The oxidation of odd-carbon fatty acids is unique in that, in addition to the usual oxidation products (as with even-carbon fatty acids)—acetyl-CoA, FADH2, and NADH2—one propionyl-CoA molecule is formed per oxidized fatty acid molecule. Propionyl-CoA is converted to succinyl-CoA, which enters the Krebs cycle.

The oxidation characteristics of unsaturated fatty acids are determined by the position and number of double bonds in their molecules. An additional enzyme, Δ3,4-cis-Δ2,3-transenoyl-CoA isomerase, is involved in the oxidation process, facilitating the movement of the double bond to the desired position and changing its configuration from cis to trans.

Ketone bodies, or acetone bodies, are three substances: acetoacetate, β-hydroxybutyrate, and acetone. The formation of ketone bodies, or ketogenesis, occurs in the liver. In the first stage, two acetyl-CoA molecules condense with the help of acetyl-CoA acetyltransferase. Next, acetoacetyl-CoA condenses with another acetyl-CoA molecule with the help of hydroxymethylglutaryl-CoA synthetase. β-hydroxy-β-methylglutaryl-CoA is broken down into acetyl-CoA and acetoacetate. Acetoacetate is the end product of the hydroxymethylglutarate cycle. The remaining ketone bodies are formed from acetoacetate: β-hydroxybutyrate is formed through its reduction by NAD-dependent hydroxybutyrate dehydrogenase, and acetone is formed through the decarboxylation of acetoacetate. In the liver, ketone bodies are not further converted but enter the bloodstream. Other tissues and organs (heart, lungs, kidneys, muscles, and even nervous tissue), unlike the liver, use them as energy substrates.

Fat synthesis occurs during the absorptive period in the liver and adipose tissue. The immediate substrates for fat synthesis are acyl-CoA and glycerol-3-phosphate.

The first reaction in fatty acid synthesis is the conversion of acetyl-CoA to malonyl-CoA. After malonyl-CoA is formed, fatty acid synthesis continues in a multienzyme complex called fatty acid synthase (palmitoyl synthetase). This enzyme consists of two identical protomers, each with a domain structure and, accordingly, seven sites with different catalytic activities. This complex sequentially extends the fatty acid radical by two carbon atoms, donated by malonyl-CoA. The end product of this complex is palmitic acid, hence the former name of this enzyme, palmitoyl synthetase.

The complex pathway of cholesterol synthesis can be divided into three stages. The first stage ends with the formation of mevalonate (mevalonic acid).

In the second step, mevalonate is converted into a five-carbon isoprenoid structure containing pyrophosphate – isopentyl pyrophosphate.

In the third stage of cholesterol synthesis, squalene is converted through epoxide formation by the enzyme cyclase into the lanosterol molecule, which contains four fused rings and 30 carbon atoms. Twenty subsequent reactions occur, converting lanosterol into cholesterol. In the final stages of synthesis, three carbon atoms are removed from lanosterol, giving cholesterol a total of 27 carbon atoms.

Cholelithiasis is a pathological process in which cholesterol-based stones form in the gallbladder. The release of cholesterol into bile must be accompanied by a proportional release of bile acids and phospholipids, which keep the hydrophobic cholesterol molecules in the bile in a micellar state. If these proportions are disrupted, cholesterol begins to precipitate in the gallbladder, initially forming a viscous sediment that gradually becomes more solid. Sometimes, this sediment becomes impregnated with bilirubin, a breakdown product of heme, proteins, and calcium salts. Gallstones can consist solely of cholesterol (cholesterol stones) or a mixture of cholesterol, bilirubin, proteins, and calcium. Cholesterol stones are usually white, while mixed stones are brown in various shades.

4. Illustrative material:

PowerPoint presentation

5. *Literature:

6. Test questions:

1. Explain the process of lipid digestion in the body.
2. How are lipid digestion products absorbed?
3. How does chylomicron metabolism occur?
4. Explain the features of oxidation of fatty acids with an odd number of carbon atoms.
5. Name the ketone bodies.
6. How is fatty acid biosynthesis carried out?
7. Which enzyme is a regulatory one in the metabolic pathway of cholesterol synthesis?
8. What causes gallstone disease?

No. 5

1. Subject: Protein and amino acid metabolism. Chromoprotein metabolism.

2. Objective: Explain at the molecular level the stages of protein metabolism in the body.

3. Lecture abstracts. Pepsin is produced as a proenzyme (pepsinogen) in the principal cells of the gastric mucosa. Pepsinogens are activated by hydrochloric acid, which is secreted by the parietal cells of the stomach autocatalytically, i.e., by the pepsin molecules formed. Pepsin is an endopeptidase that rapidly cleaves internal peptide bonds in proteins formed by the carboxyl groups of aromatic amino acids. The optimal pH of gastrixin is approximately 3.5. Gastrixin hydrolyzes peptide bonds formed by dicarboxylic amino acids.

Proteolytic enzymes enter the intestine from the pancreas in the form of proenzymes: trypsinogen, chymotrypsinogen, procarboxypeptidases A and B, and proelastase. These enzymes are activated by partial proteolysis of their polypeptide chain. Aminopeptidases and dipeptidases are present in the intestinal mucosa. Under the action of these enzymes, protein is hydrolyzed into free amino acids. Free amino acids are absorbed by secondary active transport.

Oxidative deamination is typical in humans, although some amino acids, such as histidine, undergo intramolecular deamination. The biological purpose of transamination reactions is to assemble the amino groups of all degraded amino acids into molecules of a single amino acid, namely glutamic acid. Glutamic acid enters the cell's mitochondria, where the second stage of

transdeamination—the actual deamination of glutamic acid—occurs. This reaction is catalyzed by glutamate dehydrogenase.

The decarboxylation product of amino acids produces amines, which have high biological activity and are therefore called biogenic amines. Histamine is synthesized from histidine by histidine decarboxylase.

Serotonin is produced from tryptophan. It acts as a neurotransmitter in the nervous system and a local regulator of peripheral organ and tissue function.

GABA is formed from glutamic acid by the action of glutamate decarboxylase. Synthesis occurs in inhibitory synapses of the nervous system, where it acts as a neurotransmitter. The largest quantities of GABA are found in the subcortical structures of the brain (the substantia nigra, globus pallidus, and hypothalamus).

After performing their biological functions, biogenic amines are rendered harmless by oxidative deamination.

Chromoprotein metabolism: Chromoproteins are complex proteins containing colored prosthetic groups (chromophores), which impart their specific color and determine their biological function. The most well-known examples are hemoproteins (hemoglobin, myoglobin, cytochromes, catalase, peroxidase), flavoproteins, and rhodopsin. They play a key role in respiration, oxygen transport, oxidation-reduction reactions, and light perception.

Hemoproteins contain a heme group with an iron atom capable of reversibly binding oxygen. Hemoglobin transports oxygen and carbon dioxide in the blood, while myoglobin stores it in muscles. Cytochromes participate in the mitochondrial respiratory chain, catalyzing electron transfer. Catalase and peroxidases protect cells from the toxic effects of peroxides.

Flavoproteins contain riboflavin derivatives (FAD, FMN) and participate in dehydrogenation reactions, being important links in energy metabolism.

Rhodopsin (the light-sensitive retinal pigment) is an example of a chromoprotein with vitamin A aldehyde (retinal) as a chromophore, essential for visual perception.

Chromoprotein metabolism includes their synthesis, catabolism, and the disposal of prosthetic groups. Heme synthesis occurs in the liver and bone marrow. During the breakdown of hemoglobin, heme is converted to biliverdin, then to bilirubin, which is excreted in bile. Disruptions in this metabolism lead to pathologies such as anemia, porphyria, hyperbilirubinemia, and jaundice.

Thus, chromoproteins are essential biomolecules that ensure cellular respiration, protection from oxidative stress, and sensitivity to light. Their metabolism is closely linked to the body's overall energy and plastic metabolism, and disruptions are accompanied by severe clinical manifestations.

4. Illustrative material:

PowerPoint presentation

5. *Literature:

6.Test questions:

1. How are zymogens activated?
2. What biological functions does hydrochloric acid perform in the process of protein digestion?
3. What process is impaired by the excretion of a large amount of animal indican in the urine?
4. Why do the amino groups of all degraded amino acids collect in glutamic acid molecules?

No. 6

1. Topic: Biochemistry of hormones.

2. Objective: Explain the mechanisms of hormonal action and the biological functions of hypothalamic and pituitary hormones. Explain the molecular structure and biological functions of insulin and glucagon.

3. Lecture abstracts. Hormones act as integrating regulators that link various regulatory mechanisms and metabolism in different organs. They function as chemical messengers, transmitting signals from the central nervous system to organs. A cell's response to a hormone is highly diverse and is determined by both the chemical structure of the hormone and the cell type it targets.

Based on their chemical structure, hormones are divided into 3 groups: peptide (or protein), steroid, and non-peptide – amino acid derivatives.

Based on their mechanism of action, hormones can be divided into two groups. The first group includes hormones that interact with membrane receptors (peptide hormones, adrenaline, as well as locally acting hormones such as cytokines and eicosanoids). The second group includes hormones that interact with intracellular receptors.

Hormones whose interaction with a target cell receptor leads to the formation of cAMP act through a three-component system that includes a receptor protein, a G protein, and the enzyme adenylate cyclase.

Another system that generates cGMP as a second messenger is coupled to guanylate cyclase.

The hypothalamus occupies a crucial position in the hierarchical system, uniting the higher divisions of the central nervous system and the endocrine glands. Two types of peptide hormones are synthesized in the cells of hypothalamic neurons. Some enter the anterior pituitary gland via the hypothalamic-pituitary vascular system, where they stimulate or inhibit the synthesis of tropic hormones. Others, such as oxytocin and vasopressin, enter the posterior pituitary gland via nerve cell axons, where they are stored in vesicles and secreted into the blood in response to appropriate signals.

The pituitary gland secretes a large number of hormones involved in the regulation of various biochemical processes and physiological functions. The anterior pituitary gland (adenohypophysis) synthesizes so-called tropic hormones, which stimulate the synthesis and secretion of hormones from other endocrine glands or influence metabolic reactions in other target tissues.

The posterior pituitary gland, or neurohypophysis, secretes hormones that primarily regulate water balance and lactation.

The α-cells of the islet part of the pancreas biosynthesize glycagon, and the β-cells biosynthesize insulin.

Glucagon's effects are largely opposite to those of insulin. The primary target cells of glucagon are the liver and adipose tissue. By binding to receptors on the plasma membrane of target cells, glucagon increases cAMP levels. In hepatocytes, this leads to the activation of glycogen phosphorylase and a decrease in glycogen synthesis. As a result, glycogen mobilization is accelerated. Phosphorylation of pyruvate kinase inhibits glycolysis and accelerates gluconeogenesis. Furthermore, glucagon stimulates gluconeogenesis by inducing the synthesis of the enzymes glucose-6-phosphatase, phosphoenolpyruvate carboxykinase, and fructose-1,6-bisphosphatase. In adipose tissue cells, glucagon activates hormone-sensitive TAG lipase via the adenylate cyclase cascade and stimulates lipolysis.

Insulin accelerates glycolysis in hepatocytes due to increased activity and levels of key enzymes: glucokinase, phosphofructokinase, and pyruvate kinase. At the same time, gluconeogenesis is inhibited due to the inactivation of fructose-1,6-bisphosphatase and a decrease in the levels of phosphoenolpyruvate carboxykinase, key enzymes in gluconeogenesis. Increased glucose-6-phosphate concentrations in hepatocytes during the absorptive period are accompanied by active use of NADPH for fatty acid synthesis, which promotes stimulation of the pentose phosphate pathway.

Insulin-dependent diabetes mellitus is a disease caused by the destruction of β-cells of the islets of Langerhans in the pancreas.

Non-insulin-dependent diabetes mellitus is a general name for several diseases that develop as a result of a relative deficiency of insulin, which occurs due to impaired insulin secretion, impaired conversion of proinsulin to insulin, increased rate of insulin catabolism, and damage to the

mechanisms of insulin signal transmission to target cells (for example, a defect in the insulin receptor, damage to intracellular insulin signal mediators, etc.).

Possible causes of NIDDM include: the formation of antibodies to insulin receptors; a genetic defect in the post-receptor apparatus of insulin-dependent tissues; and impaired regulation of insulin secretion. Factors that determine the development and clinical course of the disease include obesity, poor diet, a sedentary lifestyle, and stress.

4. Illustrative material:

PowerPoint presentation

5. *Literature:

6. Control questions:

1. How are hormones classified by chemical structure?
2. By what mechanisms do hormones act?
3. What hormone deficiency causes dwarfism?
4. What diseases does loss of gonadotropic function of the pituitary gland lead to?
5. How does insulin biosynthesis occur?
6. How does the mechanism of action of the hormone glucagon work?
7. What causes non-insulin-dependent diabetes mellitus?
8. What is the difference between insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus?

No. 7

1. Subject: Biochemistry of the liver and kidneys.

2. Objective: Explain the biochemical functions of the liver at the molecular level. Explain the mechanism of ethanol metabolism in the liver.

3. Lecture abstracts. The liver functions as the body's biochemical laboratory and plays a vital role in protein, carbohydrate, and lipid metabolism. The liver synthesizes key plasma proteins, including albumin, fibrinogen, prothrombin, ceruloplasmin, transferrin, angiotensinogen, and others. These proteins mediate the liver's role in such important processes as maintaining oncotic pressure, regulating blood pressure and circulating blood volume, blood clotting, iron metabolism, and more.

The liver's most important function is detoxification. It is essential for maintaining the body's life. The liver detoxifies substances such as bilirubin and amino acid catabolism products in the intestine, and also inactivates medications and toxic substances of exogenous origin.

The microsomal system does not contain cytosolic protein components; all enzymes are membrane proteins with active sites located on the cytoplasmic surface of the ER. The system includes several proteins that make up electron transport chains (ETCs). The ER contains two such chains: the first consists of two enzymes, NADH-P450 reductase and cytochrome P450, and the second includes NADH-cytochrome B5 reductase, cytochrome B5, and another enzyme, steraoyl-CoA desaturase.

The most important properties of microsomal oxidation enzymes are: broad substrate specificity, which allows them to neutralize substances with a wide variety of structures, and regulation of activity by an induction mechanism.

As a result of the first phase of detoxification with the participation of cytochrome P450, modification of substances occurs with the formation of functional groups that increase the solubility of the hydrophobic compound.

The second phase of detoxification of substances is the conjugation reaction, during which other molecules or groups of endogenous origin are added to the functional groups formed in the first stage, increasing hydrophilicity and reducing the toxicity of xenobiotics.

In clinical practice, the rate of formation and excretion of hippuric acid after the introduction of the xenobiotic benzoic acid (sodium benzoate) into the body is determined using the Quick test.
Biochemical transformations of medicinal substances in the human body, ensuring their inactivation and detoxification, are a common manifestation of the biotransformation of foreign compounds. The biotransformation of medicinal substances can result in: a decrease in their pharmacological activity; an increase in the activity of medicinal substances; and the formation of toxic metabolites.

4. Illustrative material:

PowerPoint presentation

5. *Literature:

6. Control questions:

1. What biochemical functions does the liver perform?
2. Where are the enzymes of the microsomal oxidation system localized?
3. How does the first phase of detoxification with the participation of cytochrome P 450 occur?
4. What reaction is involved in the second phase of detoxification of substances?

No. 8

1. Subject: Blood biochemistry.

2. Objective: Explain the processes of blood biochemistry.

3. Lecture abstracts. Blood is involved in the regulation of metabolism, delivering signaling molecules from endocrine organs to target tissues.

Blood's protective function is twofold. First, it contains cellular (leukocytes) and humoral (antibodies) elements of the immune response, which protect the body from any foreign molecule. Second, it has the ability to clot.

Blood maintains the body's acid-base and water balance. Normally, blood pH is 7.36-7.4. Maintaining a constant pH is crucial, as large amounts of acidic (e.g., lactate, ketone bodies, carbonic acid) and basic (ammonia) metabolic products are released into the blood.

pH regulation is carried out by blood buffer systems.

By performing a thermoregulatory function, blood maintains a constant body temperature in its different parts.

Blood plasma contains 7% of all body proteins at a concentration of 60-80 g/L. Plasma proteins perform many functions. One of them is maintaining osmotic pressure, as proteins bind water and retain it in the bloodstream.

When a blood vessel is damaged, a cascade of reactions is initiated that results in the formation of a blood clot—a thrombus—which prevents bleeding. Platelets and a number of plasma proteins play a key role in blood coagulation. Three stages are distinguished in stopping bleeding. In the first stage, the blood vessel contracts. Then, platelets adhere to the site of injury, layering on top of each other to form a platelet plug (white thrombus). A white thrombus is fragile and can only block a small blood vessel. In the third stage, the soluble plasma protein fibrinogen is converted to the insoluble protein fibrin, which is deposited between the platelets, forming a strong fibrin thrombus. This thrombus contains red blood cells and is therefore called a red thrombus.

The formation of a fibrin thrombus is preceded by a cascade of proteolytic reactions leading to the activation of the enzyme thrombin, which converts fibrinogen into fibrin.

Fibrinolysis is the hydrolysis of fibrin within a thrombus, producing soluble peptides that are removed from the bloodstream. This stage of hemostasis prevents vessel occlusion by a fibrin clot.

The anticoagulant system limits the spread of blood clots and keeps the blood fluid. It includes inhibitors of blood clotting enzymes and the anticoagulant system (anticoagulant pathway). (Antithrombin III, tissue factor inhibitor (anticonvertin), α2-macroglobulin, α1-antitrypsin)

4. Illustrative material:

PowerPoint presentation

5. *Literature:

6.Test questions:

1. In the development of which pathological processes is cryoglobulin determined?
2. What biological functions do interferons perform?
3. What groups are blood plasma enzymes divided into?
4. What buffer systems function in the blood?
5. When does acidosis and alkalosis occur?
6. What are the main factors involved in blood clotting processes?

Lecture 9

1. Subject: Biochemistry of nervous, muscle and dental tissues.

2. Objective: Explain the biochemical processes of nervous tissue. Explain the biochemical processes of muscle tissue at the molecular level.

3. Lecture abstracts.A distinctive feature of the chemical composition of nerve cells is the presence of unusual proteins such as neuroglobulin, neurostromin, neurokeratin, neurocollagen, and clathrin. Neuroglobulin is a DNA-containing nucleoprotein, neurostromin is an RNA-containing nucleoprotein, and neurocollagen is a proteolipid. DNA and RNA are also present in free form. It has been established that RNA levels increase and DNA levels decrease with age.

The primary mechanism generating a nerve impulse is the membrane potential formed across nerve cell membranes by the concentration gradient of Na+ and K+ ions. The primary functional systems of this process are Na+ and K+-ATPase and two types of ion-conducting channels—sodium and potassium channels. The Na+ and K+-ATPase enzymes, which utilize ATP energy, pump Na+ ions out of the cell in exchange for K+ ions. As a result of this so-called sodium-potassium pump, the Na+ concentration inside the cell becomes approximately ten times lower than outside, while the K+ concentration is significantly lower outside than inside the cell. The resulting difference in Na+ and K+ ion concentrations generates an electrochemical membrane potential.

The axon of any neuron terminates in a synaptic button, which forms a synapse with the membrane of the effector cell. Various mechanisms of synaptic transmission of nerve impulses exist. The simplest and fastest way to transmit a signal from neuron to neuron is through direct electrical interaction via gap junctions. Such electrical synapses between neurons are found in some areas of the nervous system. The main advantage of electrical synapses is that the signal is transmitted without delay. However, these synapses are not adapted to certain functions and cannot be regulated as finely as chemical synapses, where signal transmission occurs through a chemical messenger. This messenger, a neurotransmitter, is released into the synaptic cleft by exocytosis, diffuses to the postsynaptic membrane, and thereby transmits the nerve signal to the effector cell.

The mechanisms of nerve impulse transmission at the neuromuscular, acetylcholine, and adrenergic synapses have been studied most thoroughly. A group of neurotransmitters—amino acid derivatives—biogenic amines and neuropeptides have been identified. The presence of excitatory and inhibitory synapses has also been established. Glycine and aminobutyric acids are neurotransmitters at inhibitory synapses, while glutamic and aspartic acids, in addition to biogenic amines, are neurotransmitters at excitatory synapses.

Thus, methylated derivatives of dopamine or norepinephrine—dimethoxyphenylethylamine (DMPE), structurally reminiscent of the psychomimetic drug mescaline—have been detected in schizophrenia and manic-depressive psychosis. DMPE has also been found in large quantities in the urine of patients with Parkinson's disease.

GABA is an inhibitory neurotransmitter, which simultaneously acts as a synaptic modulator at the level of the olfactory tubercle of the brain and causes behavioral anomalies resembling psychosis.

Skeletal and cardiac muscles exhibit striations when examined microscopically, but smooth muscles lack such striations. Unlike striated muscles, smooth muscles do not contain the protein troponin. The myosin β-light chain inhibits actin-myosin interactions in smooth muscles, while troponin J inhibits striated muscles. Smooth muscles have higher cholesterol levels than cardiac and skeletal muscles.

Each myofibril is composed of numerous sarcomeres, ranging in length from 1500 to 2300 nm, separated from each other by Z-lamellae formed by the protein α-actinin. The sarcomere is the functional unit of muscle. Each sarcomere is composed of protein filaments of two types: thick and thin filaments. The main protein of the thick filaments is myosin, while the main protein of the thin filaments is actin, troponin, and tropomyosin.

According to modern data, the biochemical cycle of contraction and relaxation of any type of muscle consists of five stages:

1. Myosin heads are loaded with ATP molecules.

2. Freely rotating at large angles, the myosin heads contact the F-actin, forming an angle of about 90 0 with the fibril axis.

3. The association of myosin heads with actin leads to the activation of ATPase, leading to the hydrolysis of ATP and the release of ADP and inorganic phosphate. This changes the angle of the myosin heads' interaction with actin from 90° to 45° and leads to actin movement by 10-15 nm toward the center of the sarcomere. This alters the conformation of the proteins in the B-actin-myosin complex, resulting in contraction.

4. New ATP molecules bind to the myosin heads of the myosin-F-actin complex.

5. The myosin-ATP complex has a low affinity for actin, which leads to the separation of the myosin heads from the actin - the original state of the proteins of the thick and thin filaments of the sarcomeres is restored - relaxation occurs.

These principles govern the contraction and relaxation of any muscle. The only limiting factor in muscle contraction and relaxation is ATP, and the main regulator of these processes are Ca++ ions, which accumulate in the cisterns of the sarcoplasmic reticulum in complex with the special Ca-binding protein calsequestrin.

Muscle diseases associated with atrophy are characterized by elevated creatine levels in the blood and its appearance in the urine (creatinuria). Creatine levels depend on the rate of its synthesis and conversion to creatinine. Creatinine is also excreted in the urine. Creatinine is formed by the non-enzymatic dephosphorylation of creatine phosphate. In muscular dystrophies, creatine excretion from the body increases, while creatinine levels decrease. This is likely due to a decrease in the rate of creatine phosphate formation in the muscles.

4. Illustrative material:

PowerPoint presentation

5. *Literature:

6. Control questions:

1. What unusual proteins are part of the chemical composition of nerve cells?
2. What are the mediators of synapses that transmit inhibitory signals?
3. How does a nerve impulse arise?
4. How is a nerve impulse transmitted through synaptic systems?
5. What is the mediator of sensory and facilitatory neurons?
6. What proteins are found in muscle tissue?
7. Explain the structural features of the myosin molecule.

8. What proteins make up the thin filament of muscle tissue?
9. How do skeletal muscles contract and relax?
10. In what muscle tissue disease is creatinuria observed?

Note: 5. *Literature:
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