Federal State Autonomous Educational Institution of Higher Education
«Peoples' Friendship University of Russia»

Medical Institute

Recommended MCSD

SYLLABUS
(STUDY GUIDE)

Subject

Medical Enzymology

Recommended for the direction of training (specialty)

31.05.01 General Medicine

Program (profile, specialization)

General Medicine

1. Purpose and objectives of the discipline: to form students' systemic knowledge of the molecular mechanisms of functioning of biological systems; to ensure the development of a theoretical basis for the further study of biomedical and clinical disciplines.

2. Place of discipline in the structure of the EP of HE:
The discipline of medical enzymology refers to the *basic* part of unit 1 (Disciplines (modules)) of the curriculum. This academic discipline is included in the section "Professional" of the principal educational program 050100.62 Pedagogical education and belongs to the optional disciplines. This course should be taken on the 3rd year of studies in the 6th semester.

Table 1 shows the preceding and subsequent disciplines aimed to form the competences of the discipline in accordance with the matrix of competencies of the **EP of HE**.

Table №1

Preceding and subsequent disciplines aimed to form the competencies

№	Code and name of competence according to FSES 3+	Preceding disciplines	ubsequent disciplines (groups of disciplines)
Universal competences (Универсальные компетенции)			
	UC (Universal Competencies, УК) -1, UK-6	Biochemistry, organic chemistry, inorganic chemistry, normal physiology, genetics	Clinical pharmacology, internal propaedeutics diseases, clinical toxicology.
General professional competencies (Общие профессиональные компетенции)			
	GPC (General Professional Competencies, ОПК)-1, 5, 10, 11	Biochemistry, organic chemistry, inorganic chemistry, normal physiology, genetics	Clinical pharmacology, internal propaedeutics diseases, clinical toxicology.

3. Requirements for the results of mastering the discipline:
The process of studying the discipline is aimed on developing of the following competencies:

Table №2

Competencies	Competency name	Competence achievement indicators
UC-1.	Able to exercise critical analysis of problem situations based on a systematic approach, to develop strategy of action	UC-1.1; analyzes scientific and technical literature and regulatory documents of medical organizations. UC-1.2; critically evaluates the reliability of information sources, works with conflicting information from various sources.
UC-6.	Able prioritize own activities and can improve it based on self-control	UC-6.1. Assesses their resources and their limits (personal, situational, temporary), uses them optimally for successful performing the assigned task. UC-6.2. Analyzes the results obtained in the course of his/her professional activity, carries out self-control and self-analysis of the process and results of professional activity, evaluates them critically, draws objective conclusions on his work, correctly defends his point of view.

GPC -1	Able to implement moral and legal norms, ethical and deontological principles in professional activity	GPC -1.1 To be able to comply with moral and legal standards in professional activities GPC -1.2 Be able to present professional information in the process of intercultural interaction, observing the principles of ethics and deontology
GPC -5.	Able to evaluate morphofunctional, physiological conditions and pathological processes in the human body to solve professional problems	GPC -5.1 Own the algorithm of clinical, laboratory and functional diagnostics when solving professional problems GPC -5.2 To be able to evaluate the results of clinical, laboratory and functional diagnostics in solving professional problems. GPC -5.3 Be able to determine morphofunctional, physiological conditions and pathological processes of the human body
GPC -10	Able to solve standard problems of a professional activities using information, bibliographic resources, biomedical terminology, information and communication technologies, taking into account the basic requirements of information safety	GPC -10.1 Be able to use modern information and communication tools and technologies in professional activities
GPC -11	Able to prepare and apply scientific, research and development (RnD), design, organizational, managerial and regulatory documentation in health care system	GPC -11.1 Be able to prepare scientific, research and production, design, organizational, management and regulatory documentation in accordance with the direction of professional activity and current requirements for their design

As a result of studying the discipline, the student should:

Know:

safety regulations and work in clinical diagnostic biochemical laboratories with reagents, instruments, laboratory animals; subject, tasks and main directions of medical enzymology, structure and physicochemical properties of enzymes; the basic principles of enzymatic catalysis and regulation of the activity of enzymes, the concept of enzymopathology, the role of enzymes and isoenzymes in enzymodiagnostics, principles of enzyme therapy (the use of enzymes in antitumor therapy, therapy of cardiovascular diseases, cosmetology and dermatology) ; the fundamental and applied aspects of engineering enzymology ; physicochemical methods of analysis in medicine (titrimetric, chromatographic, spectrophotometric, photoelectrocolorimetric); basics of computer science in medical and biological systems, the use of information computer systems.

Be able to:
use educational, scientific, popular science literature, the Internet and educational portal for professional activities;
use physical, chemical and biological equipment;
to make calculations according to the results of the experiment, to conduct elementary statistical processing of experimental data;
use measuring instruments and equipment to evaluate the activity of enzymes;
determine the activity of the enzymes that are most commonly used in enzyme diagnostics;
use the IUPAC nomenclature to names the structures of typical representatives of biologically important substances;
distinguish normal and pathological levels of metabolites in the blood serum (glucose, urea, bilirubin, uric acid, lactic and pyruvic acid, etc.), read the proteinogram and explain the reasons for the differences;
to interpret the data of enzymodiagnostic studies of blood serum.

Possess:
the knowledge of biochemical and clinical terminology within the studied discipline;
the knowledge of basic technologies of search and transformation of information, including the use of educational and learning resources;
the knowledge of the concept of limitations in the reliability and specificity of the most common laboratory tests;
the skills of making a preliminary diagnosis based on the results of biochemical tests of human biological fluids.

4. The volume of discipline and types of educational activities

Total workload of the discipline is 2 credits.

№	Type of activity	**Total hours**	**Semester 6 (17 weeks)**
1.	**In-class learning (total)**	**34**	**34**
	Including:	-	-
1.1	Lectures	-	-
1.2	Other classes	-	-
	Including:	-	-
1.2.1	*Practical classes (PC)*	34	34
1.2.2	*Seminars (S)*	-	-
1.2.3	*Laboratory tasks (LT)*	-	-
	*Of these, in an interactive form (IF *):*		
2	**Self-study (total)**	**38**	**38**
	Including:	-	-
2.1	Course project	-	
2.2	Calculations and graph-making tasks	-	-
2.3	Report	-	-
2.4	Preparation for and passing the competence assessment	-	-
	Other types of self-study activities	-	-

	Type of competence assessment (pass/ no pass credit, exam)		pass / no pass credit
	Total workload, academic hours	**72**	**72**
	credits	**2**	**2**

** IF - an interactive form of classes*

5. The content of the discipline

5.1. The content of the discipline sections

SECTION 1. Medical enzymology. Targets and goals. History of development and success of medical enzymology in Russia.

Discovery of enzymes: Louis Pasteur, V. Kühne, Y. Liebig, M. Berthelot, E. Buchner, M.M. Manaseina. The history of the development of national enzymology. Establishment of leading research centers and areas of focus: Bach A.N., Kizel A.R., Gulevich V.S., Parnas Ya.O., Engelhardt VA, Braunstein, A.E., Oparin, A.I., Belozersky, A.N., Severin S.E., Ashmarin I.P.Development of Enzymology at Moscow State University Mv Lomonosov, First MGMU them. THEM. Sechenov, Institute of Biomedical Chemistry. V.N. Orekhovich, Institute of PCB them. A.N. Belozersky MSU, FIT Biotechnology RAS.

The main areas of medical enzymology: enzymopathology, enzymodiagnostics, enzyme therapy, engineering enzymology. Basic concepts. Classification of enzymopathies: primary (hereditary), secondary (acquired: alimentary and toxic). Goals of enzymatic diagnostics: early diagnosis, differential diagnosis, assessment of the dynamics of the disease, assessment of the effectiveness of treatment, assessment of the effectiveness of recovery, assessment of the prognosis of the disease. Enzymotherapy: replacement therapy and comprehensive. Engineering Enzymology. The use of immobilized enzymes in the food, chemical, pharmaceutical industry and medicine.

SECTION 2. Mechanisms of enzymatic catalysis and regulation of enzyme activity

Biocatalysts. Enzymes and ribozymes. Chemical and biological catalysis (common aspects and differences). Mechanism of action. Kinetics of chemical reactions. Michaelis constant. The structure and properties of enzymes as protein molecules. Coenzymes and their relationship with vitamins. Principles of regulation of enzyme activity. Inhibitors and activators of enzymes. Isozymes. Classification and nomenclature of enzymes.

SECTION 3. Engineering Enzymology

Fundamental and applied aspects of engineering enzymology. The main directions of development. Enzyme engineering. Rational design and directed enzyme evolution. Rational design of industrial enzymes. Site-specific mutagenesis. Ways to obtain enzymes with a stable conformation and activity: a hydrophobic core stabilization, reduction of the polypeptide chain mobility, substitution of amino acid residues in the active center. Directed evolution of enzymes: creation of a library of mutated enzyme genes, gene expression in a microbial host, recombination of genes encoding enzymes with improved properties. Method of computer molecular design (molecular docking technology): successes and prospects. The creation of heterogeneous catalysts based on immobilized enzymes and cells. Immobilization of enzymes. Microencapsulation and inclusion of enzymes in liposomes. The use of immobilized enzymes in the food and pharmaceutical industries. Production of medicines (antibiotics: penicillins, cephalosporins, tetracyclines, erythromycins**).** Production of 6-aminopenicillanic acid using penicillin

amidase. Immobilized enzymes for medicine: streptokinase, trypsin, chymotrypsin, subtilisin, collagenase. Creating Smart Biocatalysts - enzymes associated with polymers, the structure of which reversibly changes in response to the action of certain factors (temperature, pressure, pH, ionic strength, magnetic field).

SECTION 4. Enzymes, isoenzymes and their role in the diagnostics of internal organs pathologies.

Factors underlying enzymodiagnostics: uneven distribution of enzymes in tissues, the presence of organ-specific enzymes. Myocardial infarction: an increase in serum creatine kinase (CK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT). The dynamics of changes in the activity of these enzymes. Definition of isoenzymes LDH1, LDH2 and CK (MM and MB), inherent in the cardiac muscle, as a more informative analysis compared to the measurement of enzymatic activity.
Enzymodiagnostics of liver diseases. Relationship of the elevation on activity of organ-specific hepatic enzymes with the metabolic processes in the liver. Dynamics of changes in the activity of ALT and AST in the serum in liver diseases. The diagnostic value of the determination of isoenzymes LDH4, LDH5 and hepatic alkaline phosphatase.
Changes in the activity of diagnostically significant enzymes in the blood serum in diseases of the pancreas, bone tissue, muscles, prostate.
Methods for obtaining purified enzyme preparations. Ultracentrifugation. Chromatography: ion-exchange, adsorption, gel filtration, affinity (biospecific), high-performance liquid. Electrophoretic methods. Membrane methods, ultrafiltration.

SECTION 5. Laboratory tests for determination of enzyme activity in the clinical practice.

Determination of enzyme activity for use in clinical practice for the purpose of establishing a diagnosis; differential diagnosis; assessment of the dynamics of the disease; monitoring of ongoing therapy. Methods for determining the activity of enzymes: single-point and multipoint kinetics, etc. Methods for determining the concentration of product or substrate (direct photometry, staining of the substrate or product with a dye, Warburg Test). Methods for determining the activity of individual enzymes used in clinical practice (AST, ALT, LDH, CK, ALKP, ASP, CHE, amylase). ELISA (classification and principle of the method). Enzymes used in ELISA as labels.

SECTION 6. Enzymes used for replacement therapy in patients with pancreatic insufficiency.

Compounds secreted by the pancreas. Classification of pancreatic enzymes. Characteristics of individual enzymes: composition, activation mechanism, mechanism of action, substrate specificity. Possible causes of pancreatic insufficiency. Classification of enzymes used in pancreatic insufficiency: enzymes of animal and plant origin, mono- and multienzyme preparations. Characteristics of individual multienzyme preparations: composition, dosage forms, aspects of production and action, degree of purification; comparison of composition and enzymatic activity of components.

SECTION 7. Enzymes used in cosmetology and dermatology

The history of the use of enzymes in cosmetology and dermatology. Classification of enzymes used in cosmetology and dermatology. Proteolytic enzymes of animal origin - trypsin, chymotrypsin, pancreatic ribonuclease, collagenase and deoxyribonuclease, hyaluronidase; bacterial origin - collagenase, α-amylase, streptokinase, deoxyribonuclease, subtilisin, keratinase; of plant origin - ficin (from the juice of figs), bromelain (from bromeliad family plants, including pineapple), papain (from papaya fruit and melon tree leaves). The concept of cosmetic enzymology. Enzyme-based hair removal, correction of local fat deposits with the help of enzymes. Enzymes in clinical practice: nucleases, lyases, immobilized enzyme preparations, combined enzyme preparations.

SECTION 8. Thrombolytic enzymes and blood coagulation factors.

The concept of thrombolysis. The mechanism of thrombolysis. Thrombolytic enzymes: plasminogen, plasmin, tissue plasminogen activator. Thrombolytic drugs: urokinase, streptokinase, alteplase, reteplase, monteplase, lanoteplaza, palmyplaza, thrombovazim. Blood coagulation factors: structure, functions, mechanism of action, methods of activity regulation.

SECTION 9. Hereditary deficiencies of enzymes.

The concept of orphan diseases and orphan drugs. General principles of diagnosis and treatment of hereditary metabolic disorders. Enzyme replacement therapy. Disorders of carbohydrate metabolism: glycogenosis, galactosemia (biochemical pathogenesis, clinical presentation, diagnosis, treatment). Amino acid metabolism disorders: phenylketonuria, tyrosinemia, alkaptonuria, albinism, maple syrup disease, homocystinuria (biochemical pathogenesis, clinical presentation, diagnosis, treatment). Lysosomal storage disorders: Niemann-Pick disease, Gaucher disease, Fabry disease, Tay-Sachs disease (biochemical pathogenesis, clinical presentation, diagnosis, treatment). Disfunction of the ornithine cycle. Disorders of bile acids metabolism. Porphyrin metabolism disorders: acute intermittent porphyria. Disorders of purine and pyrimidine metabolism: Lesch-Nyhan syndrome. Disorders of steroid metabolism: congenital adrenal hyperplasia

SECTION 10. Enzymes used in the treatment of cancer.

Classification of enzymes with antitumor activity, as shown in clinical and experimental research. L- asparaginase: sources, mechanism of action, products on the market, features of clinical use, side effects. The role of glutaminase activity in the realization of the therapeutic effect and toxic action of L- asparaginase. The effect of pegylation on the effectiveness of L- asparaginase. The role of asparagine synthetase in tumor sensitivity determination to L- asparaginase.

SECTION 11. Enzymes of purine and pyrimidine metabolism as targets for antitumor therapy.

Dihydrofolate reductase and its inhibitors: methotrexate, pemetrexed, raltitrexed (mechanism of action, indications for use, features of clinical use). Thymidylate synthase and its inhibitors: fluorouracil, capecitabine, tegafur (mechanism of action, indications for use, features of clinical use). DNA polymerase and its inhibitors: cytarabine (mechanism of action, indications for use, features of clinical use). Ribonucleotide reductase and its inhibitors: gemcitabine (mechanism of action, indications for use, features of clinical use). Ribonucleotide reductase and its inhibitors: cladribine, fludarabine (mechanism of action, indications for use, features of clinical use). Topoisomerases and their inhibitors: irinotecan, topotecan, etoposide, doxorubicin (mechanism of action, indications for use, clinical features).

SECTION 12. Enzymes of Human Immunodeficiency Virus and Hepatitis C Virus as targets for antitumor therapy.

HIV reverse transcriptase and its inhibitors: nucleoside / nucleotide analogues: abacavir, emtricitabine, lamivudine, zidovudine, tenofovir; non-nucleotide inhibitors: efavirenz, nevirapine, etravirine, rilpivirin (mechanism of action, indications for use, clinical features). HIV protease and its inhibitors: atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir, tipranavir (mechanism of action, indications for use, features of clinical use). HIV integrase and its inhibitors: raltegravir, dolutegravir, elvitegravir (mechanism of action, indications for use, features of clinical use). Hepatitis C virus NS 3/4 A protease and its inhibitors: asunaprevir, boceprevir, paritaprevir,

simeprevir, telaprevir (mechanism of action, indications for use, features of clinical use). RNA polymerase NS 5 B of the hepatitis C virus and its inhibitors: dasabuvir, sofosbuvir (mechanism of action, indications for use, features of clinical use)

SECTION 13. Target Enzymes for the Treatment of Cardiovascular Diseases

HMG-CoA reductase inhibitors (statins). Angiotensin-converting enzyme (ACE) inhibitors. Effect of ACE inhibitors on endothelial function and oxidative stress. Endothelial NO synthase. Drugs that reduce the formation of pro-oxidant factors by acting on the sources of their formation (lipoxygenase blockers); Drugs that increase the activity and power of antioxidant enzymes (superoxide dismutase). Cytoprotectors used in cardiology: inhibitors of carnitine-palmitoyltransferase (perhexylin, etomoxir, oxfenicin, aminocarnitine); fatty acid β-oxidation inhibitors (trimetazidine, ranolazine); pyruvate dehydrogenase stimulants (dichloroacetate, left carnitine); drugs with other mechanisms of action (cocarboxylase)).

SECTION 14. Target Enzymes for Anti-Inflammatory Drugs

Mechanisms of development and forms of inflammation. Cycloxygeneses and their inhibitors: salicylates, pyrazolidines, derivatives of indole acetic acid, derivatives of phenylacetic acid, oxicam, alkanones, derivatives of sulfonamide (mechanism of action, indications for use, features of clinical use). The role of mTOR kinase in the development of inflammation. Inhibitors of mTOR.

SECTION 15. Tyrosine kinases that regulate tumor progression as targets for chemotherapy of malignant tumors.

The concept of a molecular target with which the drug interacts. Tyrosine kinases are enzymes that transfer phosphate group to the tyrosine residues of proteins. Effective target drugs that reduce the activity of tyrosine kinases in tumors. Biochemical mechanisms of tyrosine kinase activity regulation by small molecules - prototypes of new drugs. Experimental approaches to demonstrate targeting.

SECTION 16. Summary. Report defense by students.

SECTION 17. The final test.

5.2. Sections of disciplines and types of classes

№	The name of the section of the discipline	Lecture	Practical classes (PC) and laboratory tasks (LT)			Self-study	Total hours
			PC	LT	Of them in the IF *		
1.	Medical enzymology. Targets and goals. History of development and success of medical enzymology in Russia.	-	2	-	-	2	4
2.	Mechanisms of enzymatic catalysis and regulation of enzyme activity.	-	2	-	-	3	5
3.	Engineering Enzymology.	-	2	-	-	2	4
4.	Enzymes, isoenzymes and their role in the diagnostics of internal organs pathologies.	-	2	-	-	2	4

5.	Laboratory tests for determination of enzyme activity in the clinical practice.	-	2	-	-	2	4
6.	Enzymes used for replacement therapy in patients with pancreatic insufficiency.	-	2	-	-	2	4
7.	Enzymes used in cosmetology and dermatology.	-	2	-	-	2	4
8.	Thrombolytic enzymes and blood coagulation factors.	-	2	-	-	3	5
9.	Hereditary deficiencies of enzymes.	-	4	-	-	3	7
10.	Enzymes in the treatment of cancer.	-	3	-	-	3	6
11.	Enzymes of purine and pyrimidine metabolism as targets for antitumor therapy.	-	2	-	-	3	5
12.	Enzymes of Human Immunodeficiency Virus and Hepatitis C Virus as targets for antitumor therapy.	-	2	-	-	2	4
13.	Target enzymes for the treatment of cardiovascular diseases.	-	2	-	-	3	5
14.	Target enzymes for anti-inflammatory drugs.	-	2	-	-	2	4
15.	Tyrosine kinases that regulate tumor progression as targets for chemotherapy of malignant tumors.	-	2	-	-	2	4
16.	The final test.	-	1	-	-	2	3
	Total	-	34	-	-	38	72

6. Laboratory tasks
Not applicated

7. Material and technical support of the discipline:
Computers, multimedia projectors, projection devices

8. Information support of the discipline:
a) Software
Quiz software, university educational portal.

b) Databases, reference and search systems
SWISS-PROT, ENZYME, Medline, PubMed, etc.

9. Learning and teaching support materials of the discipline:

a) Essential literature:

1. Baynes J. W. Medical Biochemistry. - Third Edition; - London: Elsevier, 2009. - 653 p.
2. Principles of Biochemistry 4nd ed./ Lehninger, A.L., Nelson, D.L., Cox, M.M..- Worth Publishing, 2004.
3. Principles of Medical Biochemistry 2nd ed./ Gerhard Meisenberg, William H. Simmons. - Mosby Elsevier, 2006.
4. Berezov T.T., Chernov N.N. Kuznetsova O.M.Collection of biochemistry tests. – M. Изд-во «Оргсервис-2000». -2011. - 60с.
5. Principles of Biochemistry 4nd ed./ Lehninger, A.L., Nelson, D.L., Cox, M.M..- Worth Publishing, 2004.
6. Principles of Medical Biochemistry 2nd ed./ Gerhard Meisenberg, William H. Simmons. - Mosby Elsevier, 2006

b) Elective literature:

- T.T. Berezov and B.F.Korovkiv. Biochemistry. – M., Mir Publishers. -1992. -515 p.
- Berezov T.T., Chernov N.N. Kuznetsova O.M. Collection of biochemistry tests . – M. Изд-во «Оргсервис-2000». -2011. - 60с.
- T.T. Berezov and B.F.Korovkiv. Biochemistry. – M., Mir Publishers. -1992. -515 p.

10. Guidelines for students to study the discipline (module)

The study of the discipline is organized on a credit-modular system using appropriate laboratory equipment, computers, multimedia systems.

The following modules are recommended inside the discipline:

- ✓ Development and success of medical enzymology. Chemical nature of enzymes.
- ✓ Basics of biocatalysis. Enzymology problems and evaluation of the results obtained.
- ✓ Enzymopathology.
- ✓ Enzyme therapy.
- ✓ Enzymodiagnostics.
- ✓ Engineering Enzymology.

Examples of assessment tools to monitor the progress:

- ✓ Quizzes
- ✓ Discussion of theoretical material

Examples of assessment materials for midterm performance monitoring:

- ✓ Defense of reports by students
- ✓ Final computer assisted quiz

11. Database of assessment materials to monitor the progress of students in the discipline (module)

11.1. List of essential structures, terms and concepts

1. Kuznetsova O.M., Smirnova I.P., Chernov N.N., Neborak E.V., Ivanova-Radkevich V.I., Lobaeva T.A. Practical guide to learning Biochemistry M.: Digitpress 2018.-64p.

11.2. Guidance materials for students:

1. Kuznetsova O.M., Berezov T.T., Chernov N.N. Laboratory Manual on Biochemistry. Part 1. -M.: DIGITPRESS. - 2017. -58 p.
2. Kuznetsova O.M., Berezov T.T., Chernov N.N. Laboratory Manual on Biochemistry. Part 2. -M.: DIGITPRESS. - 2018. -58 p.

11.3. The composition of the laboratory workshop
Laboratory workshop is not conducted

11.4. Description of grading system

Tab. 1. Distribution of the workload (hours and credits) in the semester and the stages of student assessment

Distribution of in-class activities in the semester	36 hours of lab. classes
Final assessment	Pass / No pass credit

Total: 36 in-class hours (18 weeks * 2-hour of lab. classes) + 18 hours of self-study activities of students.
Total: 54 hours, which corresponds to 1.5 credits, which the student must master during the semester (100 points).

The student will not be credited, if the student gains less than 51 points (out of 100) during the course of study in in-class and self-study activities.

The total amount of points a student receives at the end of the semester is made up of:
1) Quizzes after sections
2) Final quiz

Tab. 2. The distribution of points for the semester and the calculation of the final grade

№	***Types of assessment***	***Points for the assessment***	***Total points***
1.	Thematic tests	*3 points for one practical class (15 lessons are taken into account)*	45 points
2.	Final test	*55 points for computer assisted quiz*	55 points
3.	Summarization		Total: 100 points

The final grade is to be written in the record (credits) book according to the table:

Points converted into grades	**ECTS grades**
95-100	A
86-94	B
69-85	C
61-68	D
51-60	E

31-50	FX
0-30	F

11. 5. Questions for self-control and discussion.

- ✓ Describe the properties of enzymes as biological catalysts.
- ✓ What are the properties and nomenclature of enzymes?
- ✓ Describe the mechanism of action of enzymes
- ✓ What are the key aspects of the kinetics of enzymatic reactions?
- ✓ Name effectors of enzymes.
- ✓ List the enzymes that are most relevant in the diagnostics of particular diseases.
- ✓ What are the main achievements and successes of medical enzymology in our country?
- ✓ Name the challenges of enzymology.
- ✓ How results are evaluated in medical enzymology?
- ✓ What are the key aspects of tumor enzyme therapy?
- ✓ How the diagnosis is made after determination of the activity of enzymes in biological fluid?
- ✓ How the cell redox status is regulated in health and disease?
- ✓ What is the role of glutathione and glutathione-dependent enzymes in the redox-dependent mechanisms of the development of drug resistance of tumor cells?
- ✓ Explain the redox-dependent regulation of mechanisms of cancer cell death.

11. 6. Questions for self-study.

- ✓ Brief history of biochemistry. The value of biochemistry for the doctor.
- ✓ History of Enzymology. Physicochemical properties of enzymes. The similarity and difference between enzymatic and non-enzymatic catalysis.
- ✓ Evidence of the protein nature of the enzyme. Isolation and purification of enzymes.
- ✓ Structural and functional organization of enzymes. Cofactors and coenzymes.
- ✓ The mechanism of action of enzymes. The theory of enzymatic catalysis.
- ✓ Factors affecting the rate of enzymatic reactions.
- ✓ Kinetics of enzymatic reactions. Michaelis constant: definition, physiological meaning.
- ✓ Mechanisms of regulation of enzyme activity. Types of inhibition.
- ✓ Allosteric enzymes. Features of the structure and functioning, properties and biological role.
- ✓ Qualitative detection and quantitative determination of enzyme activity. Units of measurement of quantity and activity of enzymes.
- ✓ Nomenclature and classification of enzymes.
- ✓ Localization of enzymes in the cell. Organ-specific and marker enzymes.
- ✓ Isozymes, their biological role and origin. The use of isoenzymes in the diagnosis of diseases.
- ✓ Enzymopathies, their classification, causes. The degree of clinical manifestations of enzymopathies.
- ✓ The mechanism of development of defects in enzymopathies.
- ✓ Enzymodiagnostics. Principles, objectives and objects of study.
- ✓ The use of enzymes in diagnostics.
- ✓ Enzymotherapy, methods and uses. Immobilized enzymes, liposomes.
- ✓ Enzymes and coenzymes of biological oxidation.
- ✓ Enzymatic and non-enzymatic antioxidant protection.

11. 7. Quiz assessment on topics (for current and midterm self-control)

Examples of quiz questions:

1. Match the class with the enzyme:

1. Catalase	A. Oxidase
2. Transketolase	B. Transferase
3. Amylase	C. Hydrolase
4. Glycogen synthase	D. Lyase
5. Phosphoglucomutase	E. Isomerase
6. Glutamine Synthetase	F. Ligase

Answer: 1A 2D 3C 4D 5E 6F

2. The enzyme that catalyzes the conversion of aldoses to ketoses should be classified as:
1. Oxidoreductase
2. Transferase
3. Hydrolases
4. Isomerase
5. Lyase
Answer: 4

3. Cholinesterase enzyme hydrolyzes bonds:
1. Ester
2. Glycosidic
3. Peptide
4. Disulfide
5. Hydrogen
Answer: 1

4. One katal unit is
1. Amount of enzyme catalyzing the formation of 1 mole of product per second under standard conditions
2. Number of substrate molecules turning on 1 enzyme molecule in 1 second
3. The number of units of enzyme per 1 mg of protein in the preparation of the enzyme
4. The amount of enzyme that causes the conversion of 1 μmole of substrate per minute under standard conditions
5. Enzyme activity related to the most favorable substrate
Answer: 1

5. Competitive Inhibitors
1. Increase K_M of enzyme
2. Lower K_M of enzyme
3. Increase Vmax
4. Lower Vmax
5. Do not change K_M and Vmax
Answer: 1

6. One international unit of enzyme activity is
1. Amount of enzyme catalyzing the formation of 1 mole of product per second under standard conditions
2. Number of substrate molecules converted with 1 enzyme molecule in 1 second
3. The number of units of enzyme per 1 mg of protein in the preparation of the enzyme
4. The amount of enzyme that causes the conversion of 1 μmole of substrate per minute under standard conditions
5. Enzyme activity related to the most favorable substrate

Answer: 4

7. The specific activity of the enzyme is
1. Amount of enzyme catalyzing the formation of 1 mole of product per second under standard conditions
2. Number of substrate molecules converted with 1 enzyme molecule in 1 second
3. The number of units of enzyme per 1 mg of protein in the preparation of the enzyme
4. The amount of enzyme that causes the conversion of 1 μmole of substrate per minute under standard conditions
5. Enzyme activity related to the most favorable substrate
Answer: 3

8. The speed of the enzymatic reaction increases with
1. Decrease of temperature
2. Increase in the amount of enzyme
3. Enzyme denaturation
4. Lack of coenzyme
5. Addition of allosteric activator
Answer: 2, 5

9. If the substrate concentration is K_M, then the reaction rate is
1. 0.25 Vmax
2. 0.33 Vmax
3. 0.50 Vmax
4. 0.67 Vmax
5. 0.75 Vmax
Answer: 3

10. Which of the following CANNOT bind in the active site of an enzyme
1. Substrate
2. Product
3. Coenzyme
4. Competitive inhibitor
5. Allosteric effector
Answer: 5

11. Match the substrate and the enzyme acting on it:

1. Amber acid	A. Succinate dehydrogenase
2. Glucose	B. Hexokinase
3. Starch	C. Phosphorylase
4. Phosphoenolpyruvate	D. Amylase
5. Glycogen	E. Pyruvate kinase

Answer: 1A 2B 3D 4E 5C

12. Match the enzyme and the organ in which it functions:

1. Acid phosphatase	A. Prostate gland
2. Glucokinase	B. Stomach
3. Pancreatic Amylase	C. Gut
4. Pepsin	D. Liver

Answer: 1A 2D 3C 4B

13. What will increase in a tumor cell?

1. Ribonucleotide reductase activity
2. The rate of catabolism of purines and pyrimidines
3. Speed of synthesis of DNA and RNA
4. Concentration of polyamines (putrescine, spermidine and spermine)
Answer: 1,3,4

14. What will increase in tumor tissue?
1. Oxygen concentration
2. pH
3. Glycolysis rate
4. Lactate concentration
Answer: 3.4

15. What is used in the therapy of cancer?
1. Methionine gamma-lyase
2. L-lysine-alpha oxidase
3. L-asparaginase
4. Tyrosine phenolase
Answer: 3

16. The action of potential anticancer enzymes is aimed to develop the lack of
1. Lactate
2. Amino acids
3. Folic acid
4. RNA
Answer: 2,3,4

17. What kind of interactions determines the specificity of an enzyme-linked immunosorbent assay (ELISA)?
1. Enzyme - substrate
2. Antigen - “first” antibody
3. Antigen - “second” antibody
4. Product - dye
Answer: 2

18. Multienzyme complexes catalyze the following reactions:
1. Pyruvate → Lactate
2. Pyruvate → Acetyl-CoA
3. Isocitrate → Alpha-ketoglutarate
4. Alpha-ketoglutarate → Succinyl-CoA
Answer: 2.4

19. Match the enzyme and its localization in the cell:

1. Succinate dehydrogenase	A. Cytoplasm
2. Lactate dehydrogenase	B. Mitochondria
3. Acid phosphatase	C. Lysosomes
4. 5’-nucleotidase	D. Plasma membrane

Answer: 1B, 2A, 3C, 4D

20. The activity of which enzyme is determined in urine and serum to diagnose acute pancreatitis?
1. Amylase
2. Aminotransferase
3. Lactate dehydrogenase
4. Alkaline phosphatase
5. Creatine Kinase
Answer: 1

21. In case of myocardial infarction, it is necessary to determine the activity of the following enzymes in blood serum:
1. Amylase
2. Aminotransferase
3. Lactate dehydrogenase
4. Alkaline phosphatase
5. Creatine kinase
Answer: 2 3 5

22. Match the enzyme and its location in the body:

1. Ornithine-carbamoyltransferase	A. Intestine
2. Pepsin	B. Liver
3. Chymotrypsin	C. Stomach
4. Ureaza	D. No in human tissues

Answer: 1B, 2C, 3A, 4D

23. Which enzymes could be used for treatment of necrotic areas in patients with burns?
1. Collagenase
2. Trypsin
3. Lipases
4. Amylase
Answer: 1 2

24. Enzymopathies cause the following diseases:
1. Diabetes
2. Phenylpyruvic oligophrenia (phenylketonuria)
3. Type 1 glycogenosis (von Gierke disease)
4. Pancreatitis
Answer: 2 3

25. Match the enzyme and its inhibitor used in clinical practice:

1. Cyclooxygenase (prostaglandins synthase)	A. Allopurinol
2. Xanthine oxidase	B. Aspirin
3. Carboanhydrase	C. Diakarb (acetazolamide)
4. Monoamine oxidase	D. Nialamide

Answer: 1B 2A 3C 4D

11. 8. The list of questions for the final assessment

1. The discovery of enzymes. The history of the development of national enzymology. Establishment of leading research centers and areas of focus.
2. The main directions of medical enzymology: enzymopathology, enzymodiagnostics, enzyme therapy, engineering enzymology. Basic concepts.

3. Classification of enzymopathies: primary (hereditary), secondary (acquired: alimentary and toxic).
4. Tasks of enzymatic diagnostics: early diagnosis, differential diagnosis, assessment of the dynamics of the disease, assessment of the effectiveness of treatment, assessment of the effectiveness of recovery, assessment of the prognosis of the disease.
5. Enzymotherapy: replacement therapy and comprehensive.
6. Engineering Enzymology. The use of immobilized enzymes in the food, chemical, pharmaceutical industry and medicine.
7. Biocatalysts. Enzymes and ribozymes. Chemical and biological catalysis (common aspects and differences). Mechanism of action.
8. Kinetics of chemical reactions. Michaelis constant. The structure and properties of enzymes as protein molecules. Coenzymes and their relationship with vitamins.
9. Principles of regulation of enzyme activity. Inhibitors and activators of enzymes.
10. Isozymes. Classification and nomenclature of enzymes.
11. Fundamental and applied aspects of engineering enzymology. The main directions of development. Enzyme engineering. Rational design and directed enzyme evolution.
12. Rational design of industrial enzymes. Site-specific mutagenesis.
13. Ways to obtain enzymes with a stable conformation and activity: a hydrophobic core stabilization, reduction of the polypeptide chain mobility, substitution of amino acid residues in the active center.
14. Directed evolution of enzymes: creation of a library of mutated enzyme genes, gene expression in a microbial host, recombination of genes encoding enzymes with improved properties.
15. The method of computer molecular design (molecular docking technology): successes and prospects.
16. The creation of heterogeneous catalysts based on immobilized enzymes and cells. Immobilization of enzymes.
17. Microencapsulation and inclusion of enzymes in liposomes.
18. The use of immobilized enzymes in the food and pharmaceutical industries.
19. Production of medicines (antibiotics: penicillins, cephalosporins, tetracyclines, erythromycins). Preparation of 6-aminopenicillanic acid using penicillin amidase.
20. Immobilized enzymes for medicine: streptokinase, trypsin, chymotrypsin, subtilisin, collagenase.
21. Creation of smart biocatalysts - enzymes associated with polymers, the structure of which reversibly changes in response to the action of certain factors (temperature, pressure, pH, ionic strength, magnetic field).
22. Factors underlying enzymodiagnostics: uneven distribution of enzymes in tissues, the presence of organ-specific enzymes.
23. Myocardial infarction: an increase in serum creatine kinase (CK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT). The dynamics of changes in the activity of these enzymes.
24. Determination of isoenzymes LDH1, LDH2 and CK (MM and MB), inherent in the heart muscle, as a more informative analysis compared with the measurement of enzymatic activity.
25. Enzymodiagnostics of liver diseases. Relationship of the elevation on activity of organ-specific hepatic enzymes with the metabolic processes in the liver. Dynamics of changes in the activity of ALT and AST in the serum in liver diseases.
26. The diagnostic value of the determination of isoenzymes LDH4, LDH5 and hepatic alkaline phosphatase.
27. Changes in the activity of diagnostically significant enzymes in the blood serum in diseases of the pancreas, bone tissue, muscles, prostate gland.

28. Methods for obtaining purified enzyme preparations. Ultracentrifugation. Chromatography: ion-exchange, adsorption, gel filtration, affinity (biospecific), high-performance liquid. Electrophoretic methods. Membrane methods, ultrafiltration.
29. Determination of enzyme activity for use in clinical practice for the purpose of establishing a diagnosis; differential diagnosis; assessment of the dynamics of the disease; monitoring of ongoing drug therapy.
30. Methods for determining the activity of enzymes: single-point and multi-point kinetics, etc. Methods for determining the concentration of product or substrate (direct photometry, staining of the substrate or product by the dye, Warburg Test).
31. Methods for determining the activity of individual enzymes used in clinical practice (AST, ALT, LDH, CK, ALKP, ASP, CHE, amylase. ELISA (classification and principle of the method). Enzymes used in ELISA as labels.
32. Compounds secreted by the pancreas. Classification of pancreatic enzymes. Characteristics of individual enzymes: composition, activation mechanism, mechanism of action, substrate specificity.
33. Possible causes of pancreatic insufficiency. Classification of enzymes used in pancreatic insufficiency: enzymes of animal and plant origin, mono- and multienzyme preparations.
34. Characteristics of individual multienzyme preparations: composition, dosage forms, features of production and action, degree of purification; comparative characteristics of the composition and enzymatic activity of the components.
35. The history of the use of enzymes in cosmetology and dermatology. Classification of enzymes used in cosmetology and dermatology.
36. Proteolytic enzymes of animal origin - trypsin, chymotrypsin, pancreatic ribonuclease, collagenase and deoxyribonuclease, hyaluronidase.
37. Proteolytic enzymes of bacterial origin - collagenase, α-amylase, streptokinase, deoxyribonuclease, subtilisin, keratinase.
38. Proteolytic enzymes of plant origin - ficin (from fig juice), bromelain (from bromeliad family plants, including pineapple), papain (from papaya fruit and melon tree leaves).
39. The concept of cosmetic enzymology. Enzyme-based hair removal, the correction of local fat deposits with the help of enzymes.
40. Enzymes in clinical practice: nucleases, lyases, immobilized enzyme preparations, combined enzyme preparations.
41. The concept of thrombolysis. The mechanism of thrombolysis.
42. Thrombolytic enzymes: plasminogen, plasmin, tissue plasminogen activator. Thrombolytic drugs: urokinase, streptokinase, alteplase, reteplase, monteplase, lanoteplaza, palmyplaza, thrombovazim.
43. Blood coagulation factors: structure, functions, mechanism of action, methods of activity regulation.
44. The concept of orphan diseases and orphan drugs. General principles of diagnosis and treatment of hereditary metabolic disorders. Enzyme replacement therapy.
45. Disorders of carbohydrate metabolism: glycogenosis, galactosemia (biochemical pathogenesis, clinical presentation, diagnosis, treatment).
46. Disorders of amino acid metabolism: phenylketonuria, tyrosinemia, alkaptonuria, albinism, maple syrup disease, homocystinuria (biochemical pathogenesis, clinical presentation, diagnosis, treatment).
47. Lysosomal storage disorders: Niemann-Pick disease, Gaucher disease, Fabry disease, Tay-Sachs disease (biochemical pathogenesis, clinical presentation, diagnosis, treatment). Disfunction of the ornithine cycle.
48. Disorders of bile acid metabolism. Porphyrin metabolism disorders: acute intermittent porphyria.
49. Disorders of purine and pyrimidine metabolism: Lesch- Nyhan syndrome. Disorders of steroid metabolism: congenital adrenal hyperplasia

50. Classification of enzymes with antitumor activity, as shown in clinical and experimental studies. L- asparaginase: sources, mechanism of action, products on the market, features of clinical use, side effects.
51. The role of glutaminase activity in the realization of the effect and toxic action of L- asparaginase. The effect of pegylation on the effectiveness of L- asparaginase. The role of asparagine synthetase in determining the sensitivity of a tumor to L- asparaginase.
52. Dihydrofolate reductase and its inhibitors: methotrexate, pemetrexed, raltitrexed (mechanism of action, indications for use, features of clinical use). Thymidylate synthase and its inhibitors: fluorouracil, capecitabine, tegafur (mechanism of action, indications for use, features of clinical use).
53. DNA polymerase and its inhibitors: cytarabine (mechanism of action, indications for use, features of clinical use).
54. Ribonucleotide reductase and its inhibitors: gemcitabine (mechanism of action, indications for use, features of clinical use).
55. Ribonucleotide reductase and its inhibitors: cladribine, fludarabine (mechanism of action, indications for use, features of clinical use).
56. Topoisomerase and their inhibitors: irinotecan, topotecan, etoposide, doxorubicin (mechanism of action, indications for use, features of clinical use).
57. HIV reverse transcriptase and its inhibitors: nucleoside / nucleotide analogues: abacavir, emtricitabine, lamivudine, zidovudine, tenofovir; non-nucleotide inhibitors: efavirenz, nevirapine, etravirine, rilpivirin (mechanism of action, indications for use, clinical features).
58. HIV protease and its inhibitors: atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir, tipranavir (mechanism of action, indications for use, features of clinical use).
59. HIV integrase and its inhibitors: raltegravir, dolutegravir, elvitegravir (mechanism of action, indications for use, features of clinical use). Hepatitis C virus NS 3/4 A protease and its inhibitors: asunaprevir, boceprevir, paritaprevir, simeprevir, telaprevir (mechanism of action, indications for use, features of clinical use).
60. Hepatitis C virus NS 5 B RNA polymerase and its inhibitors: dasabuvir, sofosbuvir (mechanism of action, indications for use, features of clinical use)
61. HMG-CoA reductase inhibitors (statins).
62. Inhibitors of the angiotensin-converting enzyme (ACE). Effect of ACE inhibitors on endothelial function and oxidative stress.
63. Endothelial NO-synthase.
64. Drugs that reduce the formation of prooxidant factors by acting on the sources of their formation (lipoxygenase blockers);
65. Drugs that increase the activity and power of antioxidant enzymes (superoxide dismutase).
66. Cytoprotectors used in cardiology: inhibitors of carnitine-palmitoyltransferase (perhexylin, etomoxir, oxfenicin, aminocarnitine).
67. Inhibitors of β-oxidation of fatty acids (trimetazidine, ranolazine).
68. Stimulants of pyruvate dehydrogenase (dichloroacetate, levocarnitine).
69. Mechanisms of development and forms of inflammation. Cycloxygeneses and their inhibitors: salicylates, pyrazolidines, derivatives of indole acetic acid, derivatives of phenylacetic acid, oxicam, alkanones, derivatives of sulfonamide (mechanism of action, indications for use, features of clinical use).
70. The role of mTOR kinase in the development of inflammation. MTOR inhibitors.

The program is compiled in accordance with the requirements of the FSES HE.

Developers:

Professor
of the Temirbolat T. Berezov Department of Biochemistry PhD, DSc, Elena V. Kalinina

Associate Professor
of the Temirbolat T. Berezov Department of Biochemistry PhD, Tatyana A. Lobaeva

Assistant Professor
of the Temirbolat T. Berezov Department of Biochemistry MD, Marsel M. Basharov

Head of the Temirbolat T. Berezov Department
of Biochemistry MD, PhD, DSc, prof. Vadim S. Pokrovsky

Head of the Program **PhD, DSc, Ivan V. Radysh**