MEDICINAL CHEMISTRY AND BIOCHEMISTRY 2	
GENERAL INFORMATION	
Course coordinator	Professor Ljubica Glavaš-Obrovac, PhD
Assistant/Associate	Assistant Professor Marijana Leventić, PhD Assistant Professor Katarina Mišković Špoljarić, PhD Assistant Professor Teuta Opačak-Bernardi, PhD Assistant Professor Barbara Viljetić, PhD
Study Programme	Integrated undergraduate and graduate university study of Medicine
Status of the course	Mandatory
Year of study, semester	2nd Year, 3rd Semester
ECTS	**9**
Workload (hours)	Lectures (40); Seminars (30); Exercises (30)
Expected number of students	70
COURSE DESCRIPTION	
Course objectives	
Students will learn about biochemical mechanisms and their regulation in the human body, which form the basis for understanding life processes in the healthy and diseased state of the organism. They will also learn how metabolic disorders affect the human body. The aim of the course is to provide students with knowledge of biochemical processes that enable living organisms to function normally, maintain optimal concentrations of constituents in cells and body fluids, and processes involved in growth and reproduction.	
Enrolment requirements and entry competencies	
This program is a continuation of the program of Medicinal Chemistry and Biochemistry 1 and Medical Biology courses. To successfully complete and pass the exam in Medicinal Chemistry and Biochemistry 2, it is necessary to pass the previously mentioned courses.	
Learning outcomes at the Program level	
1.1., 2.1., 2.2., 2.3., 3.4., 3.5., 4.2.	
Learning outcomes (5-10)	
After completing lectures, seminars and exercises, independent study and passing the exam, students will be able to: 1. explain the principles of biochemical and energetic changes in the human body; 2. integrate knowledge of biochemical reactions in metabolism and metabolic changes at the level of cells, tissues and the whole organism; 3. evaluate the mechanisms of regulation of metabolism of carbohydrates, lipids, proteins, information and signaling molecules; 4. critically evaluate the metabolic background of disorders caused by defects in the structure of molecules and in biochemical reactions or biochemical processes; 5. evaluate the application of biochemical methods in biochemistry and various biochemical laboratory tests in the diagnosis and treatment of disease; 6. select IT tools and databases to solve problems in metabolism and metabolic disorders; 7. independently perform qualitative and quantitative methods of biochemical analysis to detect pathological or normally present constituents in biological fluids or simple solutions; 8. apply knowledge in the interpretation of the obtained results.	
Course content	

Lectures

Introduction to biochemistry: the relationship between biochemistry and medicine. The dependence of health on the balance of biochemical reactions occurring in the body. Basic settings of metabolism and signal transduction: what is metabolism. Anabolism and catabolism. The change of free energy as a prerequisite for biochemical reactions. Entropy of the system. Energy conservation and transfer. The role of ATP. Oxidative reduction systems in the cell. NADH, NADPH and FADH2 as activated electron transporters. Types of reactions in the cell. The role of signaling molecules in maintaining homeostasis in the body, cell response to external stimuli, wound healing, response to viruses and bacteria, response to stress, and in establishing cyclic and developmental processes such as sexual differentiation, maturation, etc. ***Overview of intermediate metabolism.*** Biosynthetic and degradative metabolic pathways. Cellular compartments. Sources and consumption of metabolic fuels.

Carbohydrate metabolism:

Citric acid cycle. Oxidative decarboxylation of pyruvate. Acetyl-CoA catabolism. Structure and catalytic activity of pyruvate dehydrogenase. Synthesis and isomerization of citrate. Oxidative decarboxylation of isocitrate. Oxidative decarboxylation of α-ketoglutarate. Succinate oxidation. Hydration of fumarate. Oxidation of malate - formation of oxaloacetate. By-products of glycolysis and the citric acid cycle. Regulation of the citric acid cycle.

Glycolysis and oxidation of pyruvate: glycolysis as the main metabolic pathway of glucose utilization in the body. Different catalytic activities of glucokinase and hexokinase. Glucose entry into the cell. Energy balance of glycolysis. Regulation of glycolysis. Metabolism of galactose and fructose in the cell.

Gluconeogenesis. Corri cycle. Glucose biosynthesis from non-carbohydrate precursors. The substrate cycle. Energy balance of gluconeogenesis. Regulation of gluconeogenesis. Cooperation between glycolysis and gluconeogenesis.

Pentose phosphate metabolic pathway and other metabolic pathways of hexoses. Metabolic pathways for which NADPH is required. Oxidative branch of the pentose phosphate cycle. Non-oxidative branch of the pentose phosphate cycle. Directions of the pentose phosphate cycle depending on the current needs of the cell. Clinical aspects of pentose phosphate pathway disorders. Pathways of hexose metabolism.

Glycogenesis and glycogenolysis. The importance of glycogen as an energy reserve and the advantage of using glycogen over fat. Glucose-6-phosphate as a key intermediate in carbohydrate metabolism. Function and regulation of glycogen in the liver. Regulation of glycogen metabolism. Clinical aspects of disorders of glycogen metabolism.

Lipid metabolism:

Lipid digestion; fatty acid catabolism. Classification of lipids. Triacylglycerols as energy stores. Degradation of triacylglycerols from food. Mobilization and degradation of triacylglycerols from adipocytes. Glycerol metabolism. Transport of fatty acids into the mitochondrial matrix. Degradation of straight-chain saturated, unsaturated, branched, and fatty acids with an odd number of C atoms. Biosynthesis of fatty acids and eicosanoids. The main reactions involved in the synthesis of fatty acids. Fatty acid synthase (multienzyme complex) and reactions on fatty acid synthase. The regulation of fatty acid biosynthesis. Sources of NADPH for fatty acid synthesis. Synthesis of long-chain fatty acids and unsaturated fatty acids. Essential fatty acids. Symptoms of essential fatty acid deficiency in humans. Biosynthesis of eicosanoids from polyunsaturated fatty acids. Cyclooxygenase (COX). Biosynthesis of leukotrienes, prostaglandins, and thromboxanes. Metabolism of acylglycerols and sphingolipids. Clinical significance. Biosynthesis of triacylglycerols and typical (ester) glycerophospholipids. Biosynthesis of ether glycerophospholipids. Structure and synthesis of complex lipids, phospholipids and glycolipids. Biosynthesis of ceramide. Synthesis of complex

sphingolipids from ceramides. Synthesis of gangliosides. Clinical significance of disorders in lipid metabolism.

Cholesterol biosynthesis, transfer and excretion. Bile acids. Synthesis of mevalonate from acetoacetyl-CoA and acetyl-CoA. Synthesis of isopentenyl pyrophosphate. Mechanism of condensation. Synthesis and cyclization of squalene. Conversion of lanosterol to cholesterol. Regulation of cholesterol biosynthesis. Transport of cholesterol by lipoproteins. Lipoprotein receptors. Disorder in the metabolism and transport of cholesterol. Bile salt synthesis cytochrome P450 system.

Ketone body formation (ketogenesis). Biomedical significance. Formation of ketone bodies. Acetoacetate as a metabolic fuel. Regulation of ketogenesis. Clinical aspects of impaired fatty acid oxidation.

Lipid transfer and storage. Structure of lipoprotein particles. Classification of lipoproteins. Composition and properties of human lipoproteins. Apolipoproteins. Lipoprotein metabolism. Lipid storage in adipocytes.

Protein and amino acid metabolism

Protein catabolism. Amino acid catabolism. Urea biosynthesis. Protein exchange. Degradation of proteins from food. Proteases and peptidases. Degradation of cellular proteins. Ubiquitin road. Proteosomes. Ubiquitination damage. Amino acid catabolism. Amino groups removal reactions. Aminotransferases and the mechanism of transamination. Alanine cycle. Urea cycle. Metabolic disorders associated with the urea cycle. The fate of carbon atoms in amino acid catabolism. The formation of pyruvate from amino acids. Reversible degradation of glycine. Threonine catabolism. Reduction of cystine to cysteine. Direct oxidation and transamination of cysteine. Oxaloacetate as an entry point into metabolism. Formation of α-ketoglutarate from amino acids. Histidine degradation. Conversion of proline and arginine. Formation of succinyl-CoA. Metabolism of methionine. Metabolism of branched-chain amino acids. Degradation of aromatic amino acids. Congenital defects in amino acid metabolism. Biosynthesis of nutritionally non-essential amino acids. Amino acid cleavage. Synthesis of glutamate and glutamine. Amino acid biosynthesis by transamination. The role of tetrahydrofolate in amino acid metabolism. Regeneration of methionine. Mechanisms of regulation of amino acid biosynthesis. Regulation by a variety of enzymes. Feedback control. Cumulative feedback inhibition. Regulation of adenylation. Conversion of amino acids into specialized products; porphyrins and bile pigments. Amino acids as precursors of many biomolecules. Synthesis of NO. Glutathione. Peptide hormones. Porphyrin biosynthesis. Disruption of porphyrin biosynthesis - porphyria. Degradation of heme.

Structure, function and replication of information macromolecules

Metabolism of purine and pyrimidine nucleotides. De novo biosynthesis of purine and pyrimidine nucleotides. Nucleotide synthesis by alternative pathways. Deoxyribonucleotide biosynthesis. Regeneration of tetrahydrofolate. Thymidylate synthesis inhibitors as antitumor drugs. Regulation of nucleotide biosynthesis. Degradation of purine nucleotides. Defects in nucleotide catabolism. The biological role of uric acid.

RNA and DNA - the flow of genetic information. Organization, replication and repair; RNA synthesis, regulation of gene expression, molecular genetics, recombination. DNA and genomic technology.

Biochemistry of extracellular and intracellular communication

Membranes and transport across the cell membrane. Membrane channels and pumps. Structure of biological membranes. Kinetics and mechanisms of transport across biological membranes. Passive and active transport. Types of active transport: P-type ATPase (Na + -K + ATPase and sarcoplasmic Ca2 + -ATPase); ATP-binding cassettes (ABC) - transporters that use ATP hydrolysis to transport ions across the membrane (MRP, CFTCR). Secondary transporters. Types of passive transport: voltage-dependent-Na and K ion channels; ligand-dependent-acetylcholine receptor; cotransport; simport;

antiport.
Hormones and mediators. Intercellular communication mechanisms. The concept of target cell. Factors determining the response of the target cell to the hormone. The central role of hormone receptors. Specificity and selectivity of hormone receptors. Comparison of receptors and protein carriers. Classification of hormones. Classification of hormones according to the mechanism of actin fibers. Mechanism of motor kinesin movement. Chemotaxis and signaling pathways that stop the flagellar motor. Chemical diversity of hormones. Synthesis of steroid and peptide hormones.

Selected Chapters:

Molecular motors: Movement within the cell. Structure of myosin, kinesin, and dynein. Actin polymerization. Muscle contraction - movement of myosin along actin fibers. Mechanism of movement of kinesin and dynein through microtubules. The role of microtubules in the cell. The structure of flagelin. Components of the flagellar motor. Chemotaxis and signaling pathways that stop the flagellar motor.
Xenobiotic metabolism: pharmacokinetic availability. Xenobiotics enter the body. Cytochromes P450 (structure, division, substrate specificity). Metabolism of xenobiotics with CYP (cytochrome P450). Monoxigenation of substrates. Metabolism of organochlorohydrocarbons, aromatic compounds, ethanol. Toxic effects of xenobiotics. Activity of enzymes involved in xenobiotics metabolism. Some important drug reactions due to mutant or polymorphic forms of enzymes or proteins. Pharmacogenomics.
Nutrition, digestion and absorption. Micronutrients and macronutrients. Extracellular space: the structure of the extracellular space. Molecules of the extracellular matrix. Classes of macromolecules: collagen, elastic fibers, proteoglycans, hyaluronic acid, adhesion glycoproteins. Collagen - structure of molecule, types, assembly. Defects in collagen biosynthesis and their modifications. Elastic fibers - types, material, structure. Disorders in structure and degradation.
Regulation of metabolic pathways and interrelationships in intermediate metabolism. Biosynthetic and degradative metabolic pathways. Metabolic relationships between tissues in a well-fed organism, after a meal and in a state of starvation.

Seminars: Problem solving problems in metabolism and disorders in the metabolism of carbohydrates, lipids, proteins, and nucleic acids, and the application of methods of biochemistry and various biochemical laboratory tests in diagnosis and treatment.

Exercises: Rules of operation and protection in the medical biochemical laboratory. Application of various biochemical methods for determination of proteins and detection of enzyme activity, carbohydrates, lipids and metabolic degradation products. Application of rtPCR, RT PCR and capillary electrophoresis.

Mode of teaching

Lectures, Problem solving seminars, Laboratory exercises

Student obligations

Attendance at all forms of classes is mandatory and the students are obligated to attend all knowledge exams. A student may justifiably miss 30% of the lectures. Exercises: taking entrance exams, keeping a work diary, writing a term paper, taking the concluding exercise exam. Part of the seminars is conducted in the form of a directed discussion, so students should prepare for the seminar in advance. Taking a partial and final written exam, and an oral exam.

Monitoring student work *(alignment of learning outcomes, teaching methods and grading)*

Teaching activity	ECTS	Learning outcome	Student activity	Assessment methods	Grade points	
					Min.	Max.
Attending classes	0.5	1-8	Class attendance	Attendance record	1	6
Seminars	1.5	1-6	Preparation of seminar	Seminar presentation	8	16
Exercises	1	7-8	entrance exams, performing exercises, keeping work diary	work diary, entrance exam	2	8
Knowledge test (partial exams)	2	1-8	Studying for partial exams	2 partial exams	15	30
Final exam	4	1-8	Studying for the final exam	Written exam	12	20
				Oral exam	12	20
Total	**9**				**50**	**100**

Evaluation of the final written exam:

Percentage of correct answers (%)	Ocjenski bodovi
60.00-64.99	12
65.00-69.99	13
70.00-74.99	14
75.00-79.99	15
80.00-84.99	16
85.00-89.99	17
90.00-94.99	18
95-100	20

Calculation of final grade:
Grade points earned in the final exam are added to the grade points earned during the course. Grading in the ECTS system is done by absolute distribution, i.e. based on total achievement and is compared to the numerical system in the following manner: A - excellent (5): 90-100 grade points; B - very good (4): 80-89.99 grade points; C - good (3): 65-79.99 grade points; D - sufficient (2): 50-64.99 grade points.

Required reading (available in the library and through other media)

Title	Number of copies in the library	Availability through other media
1. R.K. Murray, D.A. Bender, K.M. Botham, P.J. Kennelly, V. W. Rodwell, P.A. Weil. Harperova ilustrirana biokemija, 28 izdanje Medicinska naklada 2011.	21	-
2. Glavaš-Obrovac Lj. i sur. Priručnik za seminare i vježbe iz Medicinske kemije i biokemije 2, Medicinski fakultet Osijek, 2021.	80	-

Additional reading

J.M. Berg, J.L. Thymoczko, L. Stryer: Biokemija, 1. Izdanje (hrvatsko), Školska knjiga, 2013.

Course evaluation procedures

Anonymous, quantitative, standardised student survey on the course and the teacher's work implemented by the Quality improvement office of the Faculty of Medicine Osijek.

Note /Other

E-learning is not included in the class quota, but it is used in teaching and it contains links to various sites and video and audio materials available on websites.