**Approved by: ……..**

**Dean**

**Date.....**

## SOFIA UNIVERSITY "ST. KLIMENT OHRIDSKI"

**Faculty: .....Chemistry and Pharmacy…….....**

Subject area: *(code and name)*

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| C | H | L | 3 | 8 | 2 | 4 | 1 | 3 |

.....**Pharmacy**.....

**Master Program**: *(code and name)*

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| C | H | L | 3 | 8 | 2 | 4 | 1 | 3 |

.....**Pharmacy**.....

## S Y L L A B U S

| | | | |
|---|---|---|---|
| C | 2 | 8 | 7 |

Course:

*(code and name)* ***Biochemistry***

**Lecturer: Prof. Dr. Mariela Odjakova, Prof. Dr. Svetla Petrova**

Teaching assistant: Assist. Prof. Dr. Lyuben Zagorchev

| Academic work | Type | Acad. hours |
|---|---|---|
| In-class work | Lectures | 45 |
| | Seminars | 30 |
| | Practical classes (teaching assistance) | 30 |
| **Total in-class work** | | **105** |
| Out-of-class work | Topical writing /Course paper | 15 |
| | Presentation | 15 |
| | Scientific essay | |
| | Course project | |
| | Field trip | |
| | Independent literature research | |
| | Student teaching | 40 |
| **Total out-of-class work** | | **70** |
| **TOTAL ACADEMIC WORK** | | **175** |
| **ECTS credits in-class work** | | 4.2 |
| **ECTS credits out-of-class work** | | 2.8 |
| **TOTAL ECTS CREDITS** | | **7** |

| № | Grade components[1] | % of the grade |
|---|---|---|
| **1.** | Workshops {search of information and group discussions of presentations and topical writings) | |
| 2. | Participation in topical discussions during the classes | 5 |
| 3. | Demonstrations in class | |
| 4. | Field trip attendance | |
| 5. | Portfolio | |
| 6. | Quizzes throughout the semester | 15 |
| 7. | Case studies | 15 |
| 8. | Homeworks/mid-term test | 15 |
| 9. | | |
| 10. | | |
| 11. | | |
| 12. | Final exam | 50 |

**Outline of the course:**

The Biochemistry course covers the structural, functional and informational aspects of biochemical processes. The major classes of biomolecules and central metabolic pathways are considered with accent on degradation and biosynthesis of biochemically important molecules (proteins, carbohydrates, lipids and nucleic acids). Particular attention is put on the organisation and regulation of the metabolic processes. The basic principles of expression and transfer of genetic information, which explains the mechanisms of biochemical identity of organisms are considered through replication, transcription and protein synthesis in prokaryotic and eukaryotic organisms. The importance of the biochemical approach for the development of other fundamental (pharmacology, human physiology, genetics, clinical laboratory etc.) and applied (drug design) biosciences is demonstrated with appropriate examples. Laboratory exercises illustrate and expand the lectures and establish lab skills and habits, needed for the future professional realization of students.

**Preliminary requirements:**

Students must have successfuly completed the courses in organic chemistry, biology and physiology.

**Key competences acquired:**

Students acquire basic knowledge on the fundamental biochemical processes, structure and function of biomolecules and key metabolic pathways and general lab skills, needed for successful application of the knowledge acquired in different fields of biochemistry, physiology and pharmacology.

[1] Depending on the course specificity and on the requirements of the teacher, other types of activity can be added or the unnecessary ones can be removed.

***Lessons plan***

| № | Topic: | Acad. hours |
|---|---|---|
| | **Lectures** | |
| 1 | **Subject of biochemistry**. Molecular organization of living matter. Basic principles. Water — structure, properties and functions. Buffer systems in living organisms. | 1 |
| 2 | **Proteins.** Amino acids, peptides and polypeptides. Levels of organization of the protein molecule. Domain structure. Structure-function relationship. Protein folding, native conformation. Denaturation and renaturation, chaperones. Protein modifications. Principles of protein purification and analysis. Oxygen-binding proteins — hemoglobin. Proteins of the interstitial matrix: collagens, proteoglycans, glycoproteins, adhesive proteins. | 5 |
| 3 | **Biocatalysts.** Enzymes and ribozymes. Cofactors. Active site – structure and properties. Enzymes classification. Mechanisms of the enzymatic catalysis. Enzyme-substrate complex. Enzyme kinetics – Michaelis-Menten model; Km, Vmax, kcat, kcat/Km criteria. Regulation of enzyme activity, impact of temperature and pH. Inhibition, irreversible reversible inhibition. Allosteric enzymes. Analogues of the transit state, catalytic antibodies (abzymes). Clinical importance of enzymes. | 4 |
| 4. | **Catalytic strategies.** Basic principles of catalysis. Catalysis of hardly proceeding reactions: proteases – serine proteases (chymotripsin, tripsin, elastase), aspartate-containing (pepsin, HIV-protease), metal-containing. Drugs – protease inhibitors. Catalytic mechanism of cyclooxygenase – drugs - inhibitors | 2 |
| 5. | **Regulatory strategies.** Allosteric control, product inhibition. Symmetry and sequential models of allosterism. Cooperative effect. Hemoglobin, oxygen binding, effect of 2,3-bisphosphoglycerate. Bor effect. Isoenzymes – lactat dehydrogenase. Regulation of the enzyme activity through covalent modifications. Regulation of the enzyme activity through proteolysis – digestive and blood clotting enzymes. | 2 |
| 6. | **Metabolic strategies** Metabolism – general characteristics, metabolic chains, reversible and irreversible reactions, key metabolites. Compartmentalization. Entropy and laws of thermodinamics. Exergonic and endergonic reactions. Biological oxidation. High energy compounds. Anabolitic and catabolitic, aerobic and anaerobic processes. Role of ATP, NAD and NADP. Energetical status of the cell. Basic principles of metabolic regulation. | 1 |
| 7. | **Carbohydrates.** Monosaccharides, disaccharides and polysaccharides. Glycoproteins – O and N-linked. Proteoglycans. Biologically active glycosides. | 1 |

| | | |
|---|---|---|
| 8. | **Carbohydrate metabolism.** Glycolysis. ATP synthesis at the substrate level. Glycolysis and metabolism of erytrocytes. Anaerobic glycolysis, lactic acidosis and Cori cycle. Cancer and glycolysis. Lactose, fructose and ethanol metabolism. Galactose, galactosemia. Glycogen metabolism, regulation, metabolic disorders, glycogenosis. Gluconeogenesis. Regulation of glycolysis and gluconeogenesis. Substrate cycles and heat production. Blood sugar control, hypoglycemia. Pentose-phosphate pathway. Citric acid cycle. Piruvate dehydrogenase complex. Anaplerotic reactions. Regulation. | 6 |
| 9. | **Oxidative phosphorylation and bioenergetics.** Energy accumulation in the cell. High energy compounds as mediators between exergonic and endergonic reactions. Importance of ATP for the energetic turnover in the cell. Redox systems with biological importance. Substrate chains of the biological oxidation. Molecular design of the electron transport chains. Electron transport chain linked dehydrogenases. Mechanisms of oxidative phosphorylation. ATP synthase. Shuttle mechanisms for electron and metabolites transport. Regulation of cellular respiration. Oxidative phosphorylation inhibitors. Mitochondria and apoptosis. Electron transport chains in the endoplasmic reticulum, generation and scavenging of superoxide, hydrogen peroxide and free radicals. | 3 |
| 10. | **Lipids.** Fatty acids, phospholipids, sphingolipids, glycolipids, steroids, lipoproteins. Biological membranes, properties. Membrane proteins. Transport accross membrane channels and pumps. Liposomes. Application for drug therapy. | 2 |
| 11. | **Biosignaling.** General features of signal transduction. G-protein coupled receptors and second messengers. Receptor tyrosine kinases. Receptor guanylyl cyclases. Regulation of the cell cycle by protein kinases. Oncogenes, tumor suppressor genes and programmed cell death. Development of protein kinases inhibitors for cancer treatment. | 2 |
| 12. | **Lipid metabolism.** Degradation of triacylglycerols. Chilomicrones. Degradation of triacylglycerols in fatty tissues. Fatty acids oxidation. Peroxisomal oxidation. Ketogenesis, regulation of lipid metabolism. Metabolism of phospholipids, sphingolipids and eicosanoids. Lipid transport. Lipoprotein complexes, types, formation and biological importance. Receptor-mediated endocytosis of lipoproteins. Metabolism of cholesterol. Bile acids, steroid hormones, vitamin D. Metabolism of arachidonic acid. Regulation of lipid metabolism. Drugs, inhibitors of lipid biosynthesis. | 3 |
| 13. | **Amino acids metabolism.** Oxidative deamination, transamination, decarboxylation. Biogenic amines. Detoxificaiton of ammonia. Urea cycle. Degradation of carbon | 2 |

| | | |
|---|---|---|
| | skeleton – glucogenic and ketogenic amino acids. Role of folic acid in single carbon radicals transfer. Biosynthesis of amino acids, essential and non-essential amino acids. Amino acids as biosynthetic precurssors. Porphyrins and bile pigments. Drugs, targeting amino acids metabolism. | |
| 14. | **Nucleotidic metabolism.** Synthesis of purine and pirimidine nucleotides. Degradation of nucleotides. Drugs, targeting nucleotidic metabolism. | 1 |
| 15. | **Nucleic acids.** Types, structure, level of organization, functions. | 2 |
| 16. | **DNA metabolism.** Biosynthesis of DNA (replication). Enzymatic machinery. Mechanism of replication. Inhibitors of replication. | 2 |
| 17. | **RNA metabolism.** Biosynthesis of RNA (transcription). Inhibitors of transcription. | 2 |
| 18. | **Protein metabolism.** Biosynthesis of proteins (translation). Major stages. Posttranslational modifications. Degradation of proteins. Inhibitors of translation. | 2 |
| 19. | **Integration of metabolism.** Strategies for metabolic regulation. Interrelation between metabolism of carbohydrates,, fats and amino acids. Metabolism at molecular, cellular and organ level. | 2 |
| | **Seminars/Practical exercises** | |
| 1 | Calculating concentrations problems. Buffer solutions. Amino acids properties. Titration curves. Isoelectric point calculation. | 6 |
| 2 | Isolation of protein by fractional precipitation, methods for desalting of fractions (dialysis, gel filtration, ultrafiltration). | 6 |
| 3 | Protein characterization. Determination of the absorbance spectrum. Methods for quantitative characterization. Standard curves. | 6 |
| 4. | Protein characterization. Protein fractionation with electrophoresis in polyacrylamide gel (PAGE) in denaturing and native conditions. Molecular weight determination - SDS PAGE, gel filtration, FPLC, HPLC. Sediment analysis. | 8 |
| 5. | Carbohydrates. Standard curves — DNS and Somogyi-Nelson methods. | 4 |
| 6. | Enzyme kinetics. Initial rate determination. Effect of enzyme concentration on the reaction rate. Units for enzyme acitivity. | 6 |
| 7. | Effect of subtrate concentration on the reaction rate. Michaelis-Menten constant (Km) determination. Substrate inhibition. Kinetics of product inhibition. | 6 |
| 8. | Effect of inhibitors on the reaction rate. Determination of ID50 of drugs. | 6 |
| 9. | Genomic and plasmidic DNA isolation from E. Coli. Spectrophotometrical and electrophoretical characterization of nucleic acids. | 6 |
| 10. | Lipids. Quantitation of cholesterol. | 6 |

## *Topics Covered on the Final Exam*

| № | Topic |
|---|---|
| 1 | Chemical bonds. Water – structure and functions. Properties. pH. Buffers. |
| 2 | Proteins. Amino acids, peptides and polypeptides. Levels of organization of th protein molecule. |
| 3 | Link between strucutre and functions. Globular and fibrillar proteins. Domain structur Structure-function relationship. Protein folding, native conformation. Denaturatio and renaturation, chaperones. |
| 4. | Oxygene-transfer proteins. Hemoglobin – oxygen binding, effect of 2,3 bisphosphoglycerate. Bor effect. Protein modifications. Principles of protei purification and analysis. |
| 5. | Biocatalysts. Enzymes and ribozymes. Cofactors. Active site – structure an properties. Enzymes classification. |
| 6. | Mechanisms of the enzymatic catalysis. Enzyme-substrate complex. Enzyme kinetic – Michaelis-Menten model; Km, Vmax, kcat, kcat/Km criteria. |
| 7. | Regulation of enzyme activity, impact of temperature and pH. |
| 8. | Inhibition, irreversible and reversible (competitive and non-competitive) inhibitio Allosteric enzymes. Allosteric control, product inhibition. Cooperative effec Analogues of the transit state, catalytic antibodies (abzymes). |
| 9. | Catalytic strategies. General catalytic mechanisms. Serine proteinases as example for catal of hardly proceeding reactions and catalytic mechanims of lyzosyme. |
| 10. | Metabolic strategy. Metabolism – general characteristics, metabolic chains, reversi and irreversible reactions, key metabolites. Compartmentalization. Anabolitic catabolitic, aerobic and anaerobic processes. Entropy and laws of thermodinam Exergonic and endergonic reactions. |
| 11. | Energetical status of the cell. Role of ATP. High energy compounds. Role of NA NADP and FAD. Basic principles of metabolic regulation. |
| 12. | Carbohydrates. Monosaccharides, disaccharides and polysaccharides. Glycoproteins – O and N-linked. |
| 13. | Carbohydrate metabolism. Glycolysis. ATP synthesis at the substrate level. Glycoly and metabolism of erytrocytes. Anaerobic glycolysis, lactic acidosis and Cori cy Cancer and glycolysis. |
| 14. | Glycogen metabolism, regulation. |
| 15. | Gluconeogenesis. Regulation of glycolysis and gluconeogenesis. Substrate cycles heat production. |
| 16. | Pentose phosphate pathway. |
| 17. | Citric acid cycle. Piruvate dehydrogenase complex. Anaplerotic reactions. Regulatio |
| 18. | Oxidative phosphorilation and bioenergetics. Electron transport chains, proton pun transmembrane proton transport – Q cycle. |
| 19. | Mitochondria and apoptosis. Electron transport in the endoplasmic reticulum, generation scavenging of superoxide, hydrogen peroxide and free radicals. |
| 20. | Lipids. Fatty acids, phospholipids, sphingolipids, glycolipids, steroids, lipoproteins. Biological membranes. |
| 21. | Membrane proteins. Transport accross membrane channels and pumps. Liposomes. Application for drug therapy. |

| | |
|---|---|
| 22. | Biosignaling. General features of signal transduction. G-protein coupled receptors and second messengers. Receptor tyrosine kinases. Receptor guanylyl cyclases. |
| 23. | Regulation of the cell cycle by protein kinases. Oncogenes, tumor suppressor genes and programmed cell death. Development of protein kinases inhibitors for cancer treatment. |
| 24. | Degradation of triacylglycerols. Chilomicrones. Degradation of triacylglycerols in fatty tissues. Fatty acids oxidation. Peroxisomal oxidation. Ketogenesis, regulation of lipid metabolism. |
| 25. | Fatty acids biosynthesis. Lipid metabolism regulation. Metabolism of phospholipids, sphingolipids and eicosanoids. |
| 26. | Lipid transport. Lipoprotein complexes, types, formation and biological importance. Receptor-mediated endocytosis of lipoproteins. Metabolism of cholesterol. Bile acids, steroid hormones, vitamin D. |
| 27. | Metabolism of arachidonic acid. Regulation of lipid metabolism. Drugs, inhibitors of lipid biosynthesis. |
| 28. | Amino acids metabolism. Oxidative deamination, transamination, decarboxylation. Biogenic amines. Detoxificaiton of ammonia. Urea cycle. |
| 29. | Degradation of carbon skeleton – glucogenic and ketogenic amino acids. Role of folic acid in single carbon radicals transfer. |
| 30. | Biosynthesis of amino acids, essential and non-essential amino acids. Amino acids as biosynthetic precurssors. Porphyrins and bile pigments. Drugs, targeting amino acids metabolism. |
| 31. | Nucleotidic metabolism. Synthesis of purine and pirimidine nucleotides. Degradation of nucleotides. Drugs, targeting nucleotidic metabolism. |
| 32. | Nucleic acids. Types, structure, level of organization, functions. |
| 33. | DNA metabolism. Biosynthesis of DNA (replication). Enzymatic machinery. Mechanism of replication. Inhibitors of replication. |
| 34. | RNA metabolism. Biosynthesis of RNA (transcription). Inhibitors of transcription. |
| 35. | Protein metabolism. Biosynthesis of proteins (translation). Major stages. Posttranslational modifications. Degradation of proteins. Inhibitors of translation. |
| 36. | Integration of metabolism. Strategies for metabolic regulation. Interrelation between metabolism of carbohydrates, fats and amino acids. Metabolism at molecular, cellular and organ level. |

## *Bibliography*

***Main sources:***

J.M. Berg., L. Stryer., J.C. Tymoczko et al., 2011, **Biochemistry.** W.H.Freeman & Co.
D. Voet & J. Voet, 2010, **Biochemistry**. J. Wiley & Sons Inc.
A. Lehninger, D.Nelson., M.Cox., 2008, **Lehninger Principles of Biochemistry**. Worth Publishers
C.K. Mathews., K.E. van Holde., K.G. Ahern et al., 2012, **Biochemistry**. Benjamin.Cummings Publ
L. A. Moran, R.A. Horton, G.Scrimgeour and M. Perry., 2011, **Principles of Biochemistry**. Prentice Hall Publ.