

SUBJECT:

BIOCHEMISTRY AND MOLECULAR BIOLOGY

CREDITS:

Total: **12.5**

Theory: **6.5**

Practical: **6**

This guide to Biochemistry and Molecular Biology comprises only the information that will apply to all groups and all teaching teams for the subject. Each group and teaching team will provide its own teaching guide which will include any variable and specific content.

GENERAL OBJECTIVES

- Provide students with sufficient knowledge of biomolecular structure to understand the determining properties of biological function at the level of cells and the body. This will allow students at a later stage to understand physiology and physiopathology at the molecular level; the molecular basis of diagnosis, therapeutics, disease prevention and health promotion.
- Become familiar with and understand the basic structures and functions of cells in the human body, applying biomedical concepts and terminology.
- Apply biochemical analysis and reasoning in order to solve problems related to physiology and cellular physiopathology.
- Learn to use a biochemical approach in the study of cellular functions that will provide an understanding of future advances in the molecular bases of physiology, physiopathology, diagnostics, therapeutics, disease prevention, health promotion and the continuous updating of knowledge.
- Prepare students to acquire and apply the relevant biochemical information in order to solve potential biomedical problems.
- Provide students with basic theoretical and practical knowledge of the principal methodologies and techniques for investigation of biomolecules; operation, potential and limitations and selected personal experiences of laboratory work. Understand the theoretical and practical bases of biochemistry as applied to the investigation and measurement of cell functions.
- Assist students in understanding the scientific method. Help students develop observation and critical analysis skills: collection, evaluation and classification of data; deducing conclusions; formulating hypotheses.
- Assist students in developing self-learning and the ability to keep knowledge and skills up to date; team work and communication.

SPECIFIC OBJECTIVES

In accordance with the general objectives, students should be able to:

- Describe the structural characteristics of the inorganic components of living matter, the different types of simple organic biomolecules, their biologically important derivatives and the structural units of complex biomolecules.
- Describe the structural characteristics of the different types of complex biomolecules (glycides, lipids, nucleotides, nucleic acids and proteins) and indicate the constituent units, the links between them, and the conformation and grouping of subunits.
- Explain the classification criteria and nomenclature of the different types of simple and complex biomolecules, according to their structural characteristics.
- Formulate the molecular structure of the different types of simple biomolecules.
- Schematize the molecular structure of the different types of complex biomolecules.
- Identify from a group of molecular formulae, diagrams or models those which correspond to the different types of biomolecules.
- Explain the physicochemical properties of the different types of biologically important biomolecules.
- Discuss the biological functions of the inorganic components of simple biomolecules and explain their structural bases. Students will acquire a thorough knowledge of these functions in subsequent courses; the aim here is to provide an overall, introductory view.
- Explain the structural bases of the biological functions of the different types of oligoglycides and polyglycides, lipids and nucleotides.
- Explain the structural bases of the functions of the different types of nucleic acids in transmission and expression of genetic information.
- Describe the structural characteristics of enzymes; explain their functional properties and their role in control of metabolic fluids.
- Describe the structural characteristics of gas transport proteins.
- Explain the structural bases of their biological functions.
- Explain the molecular bases of mechanisms of transmission, recombination and protection of genetic information.
- Describe the gene structure and gene expression mechanism in eukaryotes: transcription, posttranscriptional processes and translation. Protein degradation.
- Analyze sequences of DNA and RNA and deduce the possible regulatory sequences and encoded proteins.
- Explain the foundations and medical applications of the basic techniques used in the manipulation of nucleic acids. Explain the qualitative and quantitative composition of the human genome.
- Interpret the plasmid restriction map, explain the pattern of bands obtained in an agarose electrophoresis and explain the results of a DNA hybridization experiment.
- Explain the general principals of cellular energy metabolism.
- Explain and schematize the oxidative pathways of monoglycides and fatty acids.
- Explain and schematize the final mitochondrial oxidative pathways: oxidative tricarboxylic cycle and mitochondrial respiratory chain, as well as its coupling to ATP synthesis.
- Explain the oxygen metabolism, the formation of free radicals and its consequences.
- Explain the principal structural and functional characteristics of molecular motors as energy-consuming machines.
- Describe the components of biomembranes and give a schematic representation of their structure, indicating the location of the different components.
- Schematize the metabolism of the different lipidic-glycidic components of membranes and explain their location and intracellular transport.
- Explain the processes of membrane diffusion and transport, schematize the different types of transport and the molecular characteristics of the transporter proteins.
- Name the principal types of extracellular signals, membrane and intracellular receptors and explain their distinctive properties.

- Explain the molecular bases of signal transduction pathways, outlining the principal components of the pathways, from the membrane to the nucleus.
- Explain the molecular mechanisms behind cell proliferation and differentiation as well as their importance in the development of cancer. Explain the molecular mechanisms behind cell apoptosis.
- Explain the theoretical bases of the qualitative and quantitative analysis techniques specified in the Teaching Guide to the course.
- Resolve quantitative problems concerning the preparation of solutions and buffers.
- Formulate the protocol of a spectrometric determination. Calculate quantities and concentrations of substances from the results of spectrometric determinations.
- Create diagrams of protocols for the determination of enzymatic activities. Calculate enzymatic activities from experimental data.
- Explain the basis and general methodology of the molecular separation techniques specified in the Teaching Guide to the course. Explain the application of these techniques to the separation of mixtures with known compositions.
- Explain the basis and general methodology of the molecular characterization techniques specified in the Teaching Guide to the course.

PROGRAMME

Theory

A) INTRODUCTION

1. The molecular level in biology and medicine.

Biochemistry and Molecular Biology; the historical process of molecularization of biology.

The molecular level in medicine; clinical biochemistry, molecular pathology and molecular therapy

2. Bioelements and biomolecules

Bioelements; concept, classification and types

Biologically important properties of bioelements

Functional value of oligoelements

Biomolecules.

Immediate principles

B) INORGANIC COMPONENTS

3. Water

Electronic structure of water molecules

Electronic and structural characteristics of water molecules

Interactions between water molecules. Ionization of water; pH

Interactions of water molecules with other compounds

Biologically important physicochemical properties of water

4. Inorganic ions

Interactions between inorganic ions in solution; ionic force

Interactions between ions and water

Ionic composition of biological media

Biological functions of inorganic ions

INORGANIC BUFFER SYSTEMS; COMPOSITION, MECHANISM, EFFICACY AND BIOLOGICAL IMPORTANCE

C) GLYCIDES

5. Monoglycides

Molecular characteristics of monoglycides; Classification and nomenclature

Structural characteristics of biologically important derivatives of monoglycides: deoxysugars, acid sugars, alcohol sugars, aminosugars and acid derivatives, esters, vitamin C

Glycosidic bonds; glycosides

Biologically important physicochemical properties of monoglycides and their derivatives

Biological functions of monoglycides and their derivatives.

6. Oligoglycides and polyglycides

Structural characteristics, classification and nomenclature of oligoglycides

Biological functions of oligoglycides

Structural characteristics, classification and nomenclature of polyglycides

Reserve polysaccharides; glycogen and starch

Structural polysaccharides. Structure, properties and biological functions

Glycosamines and proteoglycans. Structure, properties and biological functions

Membrane glycoproteins and extracellular medium glycoproteins. Structure, properties and biological functions

D) LIPIDS

7. Fatty acids

Molecular characteristics of fatty acids; isomers

Classification and nomenclature

Biologically important derivatives; eicosanoids, sphingosine

Biologically important physicochemical properties

Biological functions of fatty acids and their derivatives.

8. Simple, complex and isoprenoid lipids

Classification and nomenclature of lipids

Structural, functional and biological characteristics of simple lipids; acylglycerides and cerides

Structural, functional and biological characteristics of complex lipids; sphingophospholipids, glyceroglycolipids and sphingoglycolipids.

Structural, functional and biological characteristics of isoprenoid lipids; steroids, terpenes and polyprenylquinones

E) NUCLEOTIDES AND NUCLEIC ACIDS

9. Nucleotides

Structural characteristics of the puric and pyrimidinic bases of nucleosides and nucleotides.

Classification and nomenclature of nucleosides and nucleotides

Structure and functions of coenzyme A; related vitamins

Nucleotide function in phosphorylation reactions, adenylation, ADP ribosylation and transference. Structure and functions of cyclic nucleotides; cADP-riboses and dinucleoside polyphosphates

Structure and functions of the derivatives of folic acid; related vitamins

10. Nucleic acids

Structure of polynucleotide chains; phosphodiester bond. Complementary bases. Interactions between polynucleotide chains

Structural characteristics of DNA; forms of DNA

Supercoiling of the DNA molecule; topoisomers and superhelixes

Biologically important physicochemical properties of DNA. Denaturation of DNA

Biologically important physicochemical properties of RNA

F) PROTEINS

11. Amino acids and prosthetic groups

Molecular characteristics of amino acids; stereoisomers; classification and nomenclature

Physicochemical properties of amino acids.

Biologically important derivatives of amino acids: keto acids, amines and polyamines

Biological functions of amino acids and their derivatives

Porphyrins and ferroporphyrins; structure and functions

Corrins and cobalamines; structure, functions and related vitamins

Pyridoxal phosphate, thiamine pyrophosphate, biotin and lipoic acid; structure, functions and related vitamins

12. Peptides and proteins

Peptide bond; structural characteristics

Oligopeptides and polypeptides; structural characteristics, biologically important physicochemical properties and functions.

Peptide and non-peptide components of proteins.
 Structural levels of globular and fibril proteins
 Primary structure of proteins
 Secondary structure of proteins; characteristics and factors determining helix structures, folded sheet and twists
 Structure of the levorotatory triple helix: collagen
 Folding units (secondary superstructures); concept and types
 Tertiary structure of proteins; determining factors
 Structural domains of proteins
 Quaternary structure of proteins
 Grouping of peptide chains in the molecules of fibril proteins
 Physicochemical properties of proteins: denaturation, ionization, buffering function and solubility
 Protein interactions with other molecules
 Specific protein interaction with binders; saturation curves, cooperativity effects
 Biological functions of proteins
 Prions, effects in cells

13. Proteins with catalytic activity: enzymes

General characteristics of enzymatic catalysis; specificity of enzymes
 Thermodynamic effects of enzymes
 Classification of enzymes
 Active centre and allosteric centres
 Structural characteristics of enzymes.
 Isoenzymes; types, biological and clinical value
 ENZYME COFACTORS
 Kinetics of enzymatic reactions. stages, formation of the enzyme-substrate complex; cooperative effects. Effect of substrate concentration on reaction speed; kinetic constants. Hyperbolic and sigmoid kinetics
 Inhibitors and activators; types of inhibition and activation
 Ribozymes

14. Regulation of enzyme activity

Mechanisms of enzyme regulation and control of metabolic pathways; metabolic flows
 Allosteric effectors; mechanisms of allosteric effects
 Characteristics and patterns of allosteric control of metabolic pathways
 Interconvertible enzymes; types of interconversion reactions
 Proenzymes; activation mechanisms and regulatory value
 Control of enzyme activity through regulatory proteins and interactions between enzymes
 Regulatory value of multienzyme groups and complexes
 Regulatory value of pH, ionic force and temperature
 Effect of enzyme concentration on reaction speed
 Mechanisms of enzyme concentration control; patterns of enzyme induction and repression

15. Proteins with other functions

Gas transport proteins; structural characteristics and functions
 Soluble transport proteins; structural characteristics and functions

G) MOLECULAR GENETICS

16. Biosynthesis of nucleotides

Biosynthesis of ribonucleotides: precursors, reactions, intermediaries, enzymes and control of *de novo* biosynthesis. Recovery pathways of purine nucleotides.
 Biosynthesis of deoxyribonucleotides: ribonucleotide reductase. Biosynthesis of thymine deoxynucleotides.
 Thymidine kynase

17. DNA replication.

Structural bases of DNA as a carrier of genetic information
 DNA replication: concept and functional importance.
 General principles of DNA replication in eukaryotes.
 Molecular components of DNA replication.
 Enzyme activities of DNA polymerases
 Stages of DNA replication. Regulation of DNA replication.

18. DNA repair and recombination.

Structural characteristics of RNAs; mRNA, tRNA and rRNA
Structural bases of the functions of RNA in the expression of genetic information
DNA repair: concept and functional importance.
Damage to the DNA molecule.
DNA repair by photoreactivation and excision
Repairing disrupted pairs.
DNA recombination: concept and functional importance.
Mechanisms of recombination in human cells

19. Transcription and processing of RNA.

DNA transcription: concept and functional importance.
Stages of transcription, enzymes and participating proteins.
Regulation of transcription; transcription factors and other regulatory proteins and metabolic regulators.
Structural and functional characteristics of transcription factors.
Processing and maturation of the different types of pre-RNA
Processing and maturation of ribosomal pre-RNA, pre-tRNA and pre-mRNA, regulation of processing and maturation.
Degradation of mRNA.

20. Translation and posttranslational modifications.

Translation: concept and functional importance.
The genetic code.
Activation of amino acids.
Translation: stages of translation, molecular components of translation and regulation of translation.
Principal types of posttranslational modifications; intracellular protein transport

21. Degradation of proteins.

Concept of intracellular exchange of proteins
Mechanisms of proteolysis.
Intracellular proteases: lysosomal and cytoplasmic
The proteasome and other intracellular proteases.
Regulation of intracellular proteolysis.

22. Investigation of the human genome

Concept and obtention of cDNA
Techniques for obtaining recombinant DNA.
Polymerase chain reaction (PCR).
Genetic isolation and cloning techniques.
Nucleic acid hybridization techniques.
DNA sequencing:
Techniques for obtaining proteins through recombinant DNA.
Techniques for obtaining transgenic animals and gene disruption.
Medical applications of recombinant DNA techniques.
The human genome.

H) CELLULAR ENERGY METABOLISM

23. Principles of bioenergy and cellular oxidative metabolism

Energy requirements of cells and cellular energy sources.
High-energy nucleotides; structural characteristics and functions
Energy changes coupled to the synthesis and hydrolysis of ATP
Functions of nicotinamide and flavin nucleotides
Concept of metabolism and metabolic pathways

24. Tricarboxylic oxidative cycle.

Functional significance of the tricarboxylic oxidative cycle (TOC)
Entrance of acetyl-CoA and reactions
Material and energy balance.
Anaplerotic reactions of TOC.
The TOC as a biosynthesis pathway. Anaplerotic reactions

25. Mitochondrial respiratory chain and oxidative phosphorylation.

Functional significance of the mitochondrial respiratory chain and oxidative phosphorylation.

Electron transport chain: structural components of the chain, complexes, free elements
Structure and functional properties of cytochromes, ferro-sulphurated proteins and CoQ.
Generation of the electrochemical proton gradient: Chemiosmosis
ATP synthesis: structural and functional properties of ATP synthesis
Inhibitor agents and decoupling agents of the respiratory chain and ATP synthesis
Transport processes across the internal mitochondrial membrane.

26. Metabolism of oxygen radicals and other free radicals.

Principle types of free radicals: superoxide ion, hydroxyl radical. Nitrogen radicals
Generating mechanisms of free radicals.
Consequences of the generation of radicals.
Molecular mechanisms of the destruction of free radicals. superoxide dismutase, catalases, glutathione peroxidases

27. Molecular bases of molecular motors and energy consumption

Molecular bases of cellular work.
Intracellular contractile proteins: kinesin, dinein, myosin, actin.
Molecular coupling between ATP hydrolysis and molecular movement
Function of calcium in the control of cell movement.

I) BIOMEMBRANES

28. Components and metabolism of biomembranes

Molecular components of biomembranes.
Biosynthesis of phospholipids: precursors, stages and enzymes involved; subcellular localization and control
Biosynthesis and degradation of glycolipids: stages and enzymes involved; subcellular localization and control
Biosynthesis of glycosil-glycerides

29. Molecular bases and mechanisms of mediated transport

Ionic channels: general characteristics of ionic channels, types of ionic channels and structural characteristics.
Ionophores: properties and types.
Passive mediated transport: structural and functional characteristics of the permeases. Stages of passive mediated transport
Active mediated transport: ion pumps and cotransport systems. Structural characteristics of ion pumps; stages of transport by ion pumps
Transport via group translocation.

J) CELL COMMUNICATION. SIGNAL TRANSDUCTION. CELL PROLIFERATION AND DIFFERENTIATION AND APOPTOSIS

30. Molecular bases of signal transduction.

Extracellular signals: definition and classification.
Intracellular receptors: localization, types and interaction with other proteins. Action mechanisms
Membrane receptors: principal types of receptors with enzyme activity. Receptors without enzyme activity: association with G proteins and other strategies
Concept of signal transduction pathways. Principal strategies
The most important protein kinase cascades
Connection with gene regulation: signal arrival at the nucleus

31. Molecular bases of cell proliferation, differentiation and apoptosis

Growth factors and other mitogenic signals.
Growth factor receptors.
Signal transduction pathways.
Oncogenes and antioncogenes.
Apoptosis execution program: caspases.
Apoptosis modulator proteins: Bcl-2/Ced9 and Ced-4/APAF-1 families.
Signal transduction pathways and apoptosis: receptors associated with cell death and survival pathways.

K) METHODOLOGY OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

32. Qualitative and quantitative analysis techniques

Units of substance quantity; mole, equivalent and derivatives

Units of concentration; molarity and normality
Calculation of ionic force and activity (apparent concentration)
Preparation of solutions
Colorimetric determination of pH; pH indicators
Electrometric determination of pH; electrodes
Preparation of buffer solutions
Spectrometric techniques; foundations and applications
Optical techniques; foundations and applications
Immunochemical techniques; foundations and applications
Units of enzyme activity; Katal, international unit (IU), molar activity and specific activity
Determination of enzyme activity

33. Separation and purification techniques

Chromatographic techniques; foundations, general methodology and applications
Chromatography types; distribution, ion exchange, affinity, immunoaffinity, hydrophobic, covalent, exclusion
Gas chromatography, high-resolution liquid chromatography (HPLC)
Electrophoretic techniques; foundations, general methodology and applications
Discontinuous gel electrophoresis; foundations, general methodology and applications
Selective precipitation techniques; foundations, general methodology and applications
Dialysis, filtration and ultrafiltration; applications
Centrifugation and ultracentrifugation; applications
General methodology for protein purification

34. Molecular characterization techniques

Determination of the amino acid sequences of peptide chains
Prediction and determination of the conformation of peptide chains
Investigation of the quaternary structure of proteins
Analysis of essential residues; chemical modifications and directed mutations
Artificial peptide synthesis
Determination of the sequence of nucleotide chains
Determination of the conformation of nucleotide chains.

PRACTICAL TRAINING

Seminars

pH, indicators and buffers
Structure and properties of amino acids
Structure of proteins; tridimensional conformation of proteins
Structure of nucleic acids
Enzyme activity
Analysis of nucleic acid sequences

The following IT applications will be used:

- Seqaid: analysis of protein and DNA sequences
- Protein Explorer: tridimensional structure of proteins and nucleic acids.
- Nucleic and gencode: programmes for the study and simulation of gene expression processes.
- Internet search engines to access molecular databases and biomedical literature

Practical laboratory work

Determination of pH. Buffer solutions
Colorimetric reactions
Gel filtration chromatography and thin-layer chromatography
Cellulose acetate electrophoresis and polyacrylamide electrophoresis
Determination of molecular weight through chromatography and electrophoresis
Determination of enzyme activity

Introduction to techniques for genome study.

LEARNING RESOURCES AND TEACHING METHODOLOGIES

Theoretical teaching

This will be carried out through classes and lectures on current topics of particular interest and importance in the field of molecular pathology. Classes and lectures will be given to the entire year group. These classes will introduce students to the principal aspects of the programme to prepare them for private study and for the work to be developed in seminars and tutorials

Practical teaching

This will be carried out in small groups through seminars, computer classes, practical laboratory sessions, guided study and visits.

The seminars are one-hour sessions with small groups to discuss and solve problems.

The course Teaching Guide details the schedule and content for each activity.

Videos

The course Teaching Guide includes a list of videos available in the video-library of the Faculty of Medicine.

LEARNING REQUIREMENTS

Knowledge of Biology and Chemistry corresponding to higher secondary education level.