Academic Year 2017-2018

Subject guide

Metabolic Biochemistry

MODULE I	CONTENT	YEAR	TERM	CREDITS	TYPE
Basic formation	Biochemistry	2nd	1st	6.0	Mandatory subject

LECTURER(S)	Postal address, telephone and e-mail address
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DEGREE IN WHICH THE MATTER IS TAUGHT	OTHER GRADES IN WHICH TO BID
Degree in Human Nutrition and Dietetics	This is a basic course in all Biology and Biomedical related degrees. Similar subjects, differently focused, are offered in Pharmacy, Food Science and Technology , Biochemistry, Biology, Medicine, Odontology, Sports and Physical Activity, etc.

PREREQUISITES and/or RECCOMMENDATIONS (if necessary)
Biology, General Chemistry and Structural Biochemistry
BRIEF ACCOUNT OF THE SUBJECT PROGRAMME (ACCORDING TO THE DEGREE)
Study of Metabolism
GENERAL AND PARTICULAR ABILITIES
CG29. Acquiring basic training for research activity, as to be able to formulate hypotheses, collect and interpret information to solve problems using the scientific method, and understanding the importance and limitations of scientific thinking in health and nutrition. *CE1 Acquiring chemical, biochemical and biological basis for implementing human nutrition human and dietetics.* *CE.2 Getting to know the structure and function of human body from the molecular level to the organism as a whole, at different stages of life.* *CE.6 Learning the basics and fundamentals of food and human nutrition.* *CE.7Acquiring teamwork skills in order to collaborate in multidisciplinary and interdisciplinary groups with other related professionals in the assessment, diagnosis and treatment of cases.*
OBJECTIVES (EXPRESSED IN TERMS OF EXPECTED RESULTS OF THE PROGRAMME)
Concept of metabolism Knowledge of major metabolic pathways occurring in humans Knowledge of oxidative metabolism Knowledge of carbohydrate metabolism Knowledge of lipid metabolism Knowledge of metabolism of nitrogen compounds Understanding metabolic integration in humans Knowledge of the most important adaptations of tissues and organs in pathophysiological situations as fasting and diabetes Use of metabolic pathways in processes for drug degradation
DETAILED SUBJECT SYLLABUS
Theorethical Programme

Chapter I. INTRODUCTION

1. **Introduction. Metabolism. An overview. Metabolic Pathways. Catabolism and anabolism. General principles of control: Control of the activity and the amount of enzyme. Compartimentalization.**

Objectives:

- Understanding the metabolic organization of living beings, differentiating the various types of pathways and enzymes.
- Understanding the importance of quantifying flows through a metabolic pathway. Enzymes involved in regulation and control processes.
- Establishing the need of having metabolic regulation systems.
- Differentiating levels of regulation , establishing their main characteristics and order of priority among them.
- Highlighting the importance of hormone regulation.
- Describing main mechanisms of regulation of enzyme activity.
- Understanding the importance of subcellular compartmentalization in the regulation of biological processes in eukaryotic cells

Chapter II. BIOENERGETICS AND OXIDATIVE METABOLISM

2. **Energetic metabolism. Sources of biological energy. High- energy compounds. Coupled reactions.**

Objectives:

- Laws of thermodynamics establishing relationships between the different state functions.
- Thermodynamic concepts applied in the analysis of biological systems.
- Knowing the role of ATP in energy metabolism.
- Distinguishing energy-rich compounds according to their potential phosphoryl transfer.
- Non-phosphorylated energy-rich compounds according to their potential acyl transfer or methyl groups.
- Understanding redox reactions as a way of biological energy utilised by cells.
- Understanding energy coupling as a mechanism to circumvent barriers in certain endergonic thermodynamic reactions.

3. **The mitochondrial electron transport system. Oxidative phosphorylation. Uncouplers. Redox shuttles. Reactive oxygen species. The microsomal electron transport system.**

Objectives:

- Defining what mitochondrial electron transport and oxidative phosphorylation are.

- Describing the main features of cell organelle mitochondria as energy producers.
- Knowing most significant features and functions of components involved in mitochondrial electron transport chain.
- CTEM diagram indicating the electron path and proton pump in individual transfer complexes.
- Bookmark the sites of action of various respiratory inhibitors and understanding CTEM control.
- Understanding the concept of proton-motive force describing its role and mode of action
- ATP synthase and coupling between the CTEM and oxidative phosphorylation. Defining the mode of action of oxidative phosphorylation inhibitors.
- Explaining the effect of uncoupling agents on oxidative phosphorylation regarding thermogenesis and obesity.
- Overall energy balance of electron transport and oxidative phosphorylation.
- Understanding the mollecular mechanisms that allow the import of reducing power from cytosol to mitochondrial matrix.
- Understanding the harmful effects of free radicals. Removal mechanisms of reactive oxygen species.
- Describing microsomal electron transport chains and thier relation to hydroxylation processes and metabolic elimination of xenobiotics.

4. **Tricarboxylic acid cycle. Enzymes and reactions of the tricarboxylic acid cycle. Energy yield. Relations with other metabolic proccesses. Anaplerotic reactions. Regulation.**

Objectives:

- Functions, general characteristics and overall stoichiometry of TCA cycle.
- Metabolic origin of acetylCoA produced on different catabolic routes.
- Analyzing cycle reactions, individually.
- Determining the fate of the carbon atoms of the acetyl-CoA per cycle turn.
- Calculating energy balance of the cycle.
- Understanding the mechanisms regulating the cycle.
- Establishing the amphibolic nature of the cycle.
- Understanding main anaplerotic reactions and the need to maintain metabolic cycle flow.

CHAPTER III. GLUCIDIC METABOLISM

5. **Glucose Transporters. Glucose metabolic pathways.**

Objectives:

- Understanding the need of different plasma membrane glucose transporters in the diverse tissues.
- Understanding hormonal regulation of glucose transport in skeletal muscle and adipose tissue as opposed to liver .
- Knowing the role of glucose in cellular metabolism.
- Understanding the overall strategy of the carbohydrate metabolism.

6. **Glycolysis. An overview. Enzymes and reactions of glycolysis. Regulation.**

Objectives:

- Explaining glycolysis, its significance, importance, main features, indicating glycolytic phases.
- Analyzing each of the enzymatic reactions of glycolysis, the fate of carbon atoms and energy efficiency.
- Identifying substrate level phosphorylation reactions.
- Identifying irreversible steps of glycolysis as control points the route.
- Understanding the mechanisms involved in glycolysis regulation.

7. **Pyruvate metabolic pathways. Metabolic sources of Acetyl-CoA. The Pyruvate dehydrogenase complex and its regulation. Pentose phosphate pathway. Glucuronic acid. Xenobiotic metabolism: oxidation and conjugation.**

Objectives:

- Establishing the role of pyruvate as an important crossroad in aerobic metabolism (respiration) and anaerobic (fermentation).
- Understanding the differences in the production of energy by the cell depending on pyruvate destination .
- Describing the mechanism of the reaction catalyzed by pyruvate dehydrogenase complex. Regulation.
- Explaining the breakdown of sugars in pentose phosphate pathway. Physiological significance and regulation.
- Explaining key features of glucuronate biosynthesis and its relation with vitamin C.
- Understanding mechanisms of glucuronic conjugation. Removing water soluble metabolic waste products and drugs.

8. **Gluconeogenesis. Gluconeogenic substrates. Enzymes and reactions. Regulation. Glycogen metabolism. Glycogenogenesis and glycogenolysis. Regulation. Fructose, Galactose and other monosaccharides metabolism. Biosynthesis of lactose.**

Objectives:

- Explaining gluconeogenesis significance. Enzymes catalyzing specific irreversible reactions.
- Indicating the most important features of the pathway. Subcellular localization of the stages.
- Differences in the route based on subcellular compartmentalization of phosphoenolpyruvate carboxykinase and on different metabolic intermediates used as gluconeogenic substrates.
- Coordinated regulation of glycolysis and gluconeogenesis.
  Cori cycle and lactate utilization to maintain levels of glucose in animal cells ..
- Glycogen metabolism. Allosteric and hormonal regulation liver and skeletal muscle.
- Highlighting the catabolism of glycogen as an example of cascade amplification of signals.
- Describing the incorporation of different monosaccharides to the glycolitic pathway .
- Lactose biosynthesis in the mammary gland.

CHAPTER IV. LIPID METABOLISM

9. An Overview. Lipid transport. Lipoproteins. Triacylglycerol metabolism and its regulation.

Objectives:

- Knowing the main tissues involved in lipid metabolism.
- Knowing the composition and functions of the different lipoproteins present in plasma.
- Describing main changes in intravascular lipoprotein metabolism.
- Understanding mollecular mechanisms of lipoprotein tissue uptake , emphasizing regulatory mechanisms exerted by intracellular cholesterol .
- Metabolism of triglycerides from exogenous and endogenous origin .
- Synthesis of triglycerides.
- Discussing the endocrine functions of adipose tissue.

10. Oxidation of fatty acids. Activation of fatty acids for transport into the mitochondrion. Mitochondrial β-oxidation. Alternative pathways of fatty acid oxidation . Unsaturated and odd-chain fatty acids. Regulation. Ketogenesis. Catabolism of ketone bodies in extrahepatic tissues.

Objetives:

- Describing the pathway of fatty acid degradation. Subcellular location and redox coenzymes.
- Activation of fatty acids in the cytosol.
- Transport of long chain fatty acyl CoAs into the mitochondrion. Role of carnitine.
- Degradation of fatty acids by the β oxidation. The four basic steps. Energy balance.
- α and ω oxidation. Peroxisomal β oxidation.

- Oxidation of unsaturated fatty acids requires two additional enzymes.
- Fatty acid oxidation is tightly regulated.
- Ketone bodies. Synthesis and extrahepatic use.
- Ketone bodies in diabetes and starvation.

11. Fatty acid synthesis. An overview. Acetyl CoA carboxylase. The citrate shuttle. Structure and reactions of fatty acid synthase. Fatty acid elongation. Desaturation of fatty acids. Regulation. Essential fatty acids. Eicosanoid metabolism.

Objectives:

- Describing the pathway of fatty acid synthesis. Subcellular location and redox coenzymes as opposed to fatty acid degradation.
- Synthesis of Malonyl CoA. Mechanism of acetyl CoA carboxylase. Enzyme regulation.
- Fatty acid synthase complex. Mechanism of the synthesis to palmitate.
- Mechanisms involved in regulating lipogenesis. Short- and long-term effects.
- Synthesizing other fatty acids from palmitate by elongation and unsaturation reactions.
- Essentiality of linolenic and linoleic acids for humans. Reasoning.
- Knowing the main polyunsaturated fatty acids of the n-9, n-6, n-3 series and their biological importance.
- Biosynthesis of eicosanoids .Main enzymes involved. Involvement of eicosanoids in various pathophysiological processes and synthesis modulation by dietary or pharmacological interventions

12. Biosynthesis of membrane lipids. Phosphatidic acid biosynthesis. Glycerophospholipid metabolism. Plasmalogens. Sphingolipid metabolism.

Objetives:

- Knowing the biosynthetic pathways of glycerophospholipids and interconversion reactions.
- Describing the role played by cytosine nucleotides in activation of biosynthetic intermediates.
- Knowing the biosynthetic pathway of sphingosine.
  Sphingolipidosis as serious hereditary diseases.

13. Isoprenoid compounds. Sterols. Sterol biosynthesis. Cholesterol biosynthesis. Regulation. Bile acid metabolism. Biosynthesis of steroid hormones.

Objectives:

- Main aspects of cholesterol biosynthesis. From Acetyl CoA to HMGCoA. From HMGCoA to Isopentenyl PP . From Isopentenyl PP to Squalene. From Squalene to Cholesterol.

- Regulatory role of HMG-CoA reductase Several factors regulating enzyme activity..
- Alternative fates of Cholesterol. Biosynthetic pathway of bile acid formation.
- Synthesis of steroidal hormones. Principal aspects.

14. An overview of nitrogen metabolism. Amino acid metabolic reactions. Transamination reactions: Aminotransferases. Oxidative deaminations. Glutamate dehydrogenase. Dehydratases enzymes.

Objectives:

- Incorporation of nitrogen into living organisms.
- Importance of the lack of nitrogen storage compounds in animals. Importance of a standard nitrogen balance.
- Protein turnover.
- General reactions involved in removal of nitrogen from amino acids prior to carbon skeleton metabolism.
- Metabolic fates of amino groups. Transamination and deamination reactions.
- Role of pyridoxal phosphate, in amino acid metabolism. Mechanism.

15. Nitrogen transport from peripheral tissues to liver: Role of Glutamine and Alanine. Urea Cycle. Degradation of aminoacids. Carbon skeleton of aminoacids as sources of metabolic intermediates.

Objectives:

- Central role of glutamine and alanine in the transport of nitrogen and carbon between different tissues.
- Knowing the importance of the urea cycle and nitrogen excretion.
- Sequence of individual reactions in urea cycle with special emphasis on its regulation in different physiological situations.
- Interconnections between urea and TCA cycles.
- Main points of entry of the standard amino acids into the citric acid cycle.
- Gluconeogenic and ketogenic amino acids.
- Genetic disorders affecting amino acid catabolism. Biochemical basis of the treatment of these diseases.

16. Biosynthesis of aminoacids. Essential and nonessential aminoacids. Metabolites derived from aminoacids. One-carbon unit metabolism. Tetrahydrofolate and S-Adenosylmethionine: The one-carbon carriers. B12 Coenzyme.

Objectives:

- Identify nutritionally essential amino acids. Semiessential and nonessential.
- Knowing the general pathways for biosynthesis of non-essential amino acids from

different metabolic intermediates.

- Precursor role of amino acids for the biosynthesis of other nitrogen compounds of biological interest.
- Functions of folic acid, vitamin B12 and S-adenosylmethionine in the one-carbon fragment metabolism. Their relation to megaloblastic anemia and other pathological conditions such as atherosclerosis.

17. **Heme biosynthesis. Enzymes involved in heme biosynthesis. Regulation. Heme catabolism. Bile pigments.**

Objetives:

- Knowing the route of porphyrin ring formation from amino acids and its regulation.
- Describing certain alterations in this biosynthetic pathway.
- Analyzing formation of bile pigments, bilirubin conjugation in the liver for disposal via bile. Relationship with jaundice.

18. **Synthesis of purine nucleotides. Regulation. Synthesis of pyrimidine nucleotides. Regulation. Salvage pathways in nucleotide metabolism. Deoxyribonucleotide formation. Degradation of nucleotides. Uric acid.**

Objectives:

- Understanding the need for cells to synthesize purine and pyrimidine nucleotides.
- Understanding why nucleotides do not constitute reserve, neither energetic mollecules.
- Comparing *de novo* biosynthesis route *of* purine nucleotides versus pyrimidine establishing differences with salvage pathways..
- Deoxyribonucleotide formation. Regulation of ribonucleotide reductase.
- Pathways of nucleic acid degradation to nucleotides, nucleosides and nitrogen bases as well as their use in different tissues by salvage pathways.
- Base degradation. Nitrogenous end products of nucleotide degradation. Uric acid. Accumulation of uric acid. Gout.

19. **Integration and hormonal regulation of mammalian metabolism.**

LABORATORY PRACTICE

Metabolite and enzyme determinations in serum and tissues of animals in order to evaluate different metabolic situations such as fasting and the well-fed state.
Determinations include metabolites and / or enzymes of carbohydrate, lipid and nitrogen metabolism
Determination of plasma glucose concentration. GOD-POD method
Extraction of lipids and separation by thin layer chromatography

Determination of free glycerol in plasma
Determination of β-hydroxybutyrate in plasma
Determination of enzymatic activity of Glucose 6-phosphatase in liver

Recommended texbooks:

- Devlin TM. “Bioquímica”. 4ª Edición. Reverté, Barcelona, 2004.
- Elliott WH, Elliott DC. “Bioquímica y Biología Molecular”. Ariel, Barcelona, 2002.
- Feduchi E, Blasco I, Romero CS, Yáñez E. “Bioquímica. Conceptos esenciales”. Editorial Panamericana. Madrid. 1ª edición, 2010.
- Gil A. “Tratado de Nutrición, Tomo I” 3ª Edición. Editorial Médica Panamericana, 2017.
- Mathews CK , Van Holde KE, Appling DR, Anthony-Cahill SJ. “Bioquímica”. Pearson, Madrid, 2013.
- Nelson DL, Cox MM. “Lehninger. Principios de Bioquímica”. 6a Edición. Ediciones Omega, Barcelona, 2015.
- Sánchez-Medina F y Vargas AM. “Bioquímica Estructural y Metabólica”. 2ª Edición. Editorial Técnica AVICAM, Granada, 2015.
- Stryer L, Berg JM, Tymoczko JL. “Bioquímica”. 7ª Edición. Reverté, 2012.
- Tymoczko JL, Berg JM, Stryer L. “Bioquímica. Curso básico”. Reverté, 2014
- Voet D y Voet J. “Bioquímica”. 3ª edición Ediciones Panamericana, Barcelona, 2006.
- Voet D, Voet J. y Pratt CW “Fundamentos de Bioquímica”. Ediciones Panamericana, Barcelona, 2007.

RECOMMENDED INTERNET LINKS

http://www.biorom.uma.es/indices/index.html
http://expasy.org/cgi-bin/show_thumbnails.pl
http://www.genome.jp/kegg/pathway.html
http://www.sigmaaldrich.com/lifescience/metabolomicshttp://www.sigmaaldrich.com/life-science/metabolomics

METHODOLOGY

EVALUATION (EVALUATION TOOLS, EVALUATION CRITERIA ,PERCENTAGE ON FINAL MARKS ETC.)

According to the guidelines for evaluation and assessment of students at the University of Granada, (May 20, 2013), students will be evaluated in a continuous system except for

specifical statement made by the student. In this case, a single final exam will be held.

CONTINUOUS ASSESSMENT
It is based on the assessment of the student's work throughout the course and assess the active participation in lectures and practical realization of proposed activities, seminars, tutorials, etc. The greatest percentage in evaluation lies on written examinations.

THEORY
Two similar written tests, one at mid-semester and one at the end of the semester will take place. Students who do not pass the first test will have the opportunity of repeating it at end semester.

All exams will be composed, partly, by multiple choice questions on basic contents of thesubject and, partly, by various more specific questions by which synthesis capabilities and general comprehension of the subject by the student, will be assessed . The student must show abilities and capabilities in relating the different metabolic pathways studied.

To pass the subject it is necessary to obtain a minimum score of 5 points of a total of 10, having sufficiently answered issues in both parts, which means reaching in each part a minimum score of 40%.

PRACTICE
Immediately after the completion of the internship, students will perform a written examination to demonstrate the achievement of the objectives. In case of not succeeding, the student will be called for a new examination . A final exam will take place at end semester.

The essential requirements to pass are:
- To complete the practice in the lab, successfully passing the exam. In case
- of a student not performing lab practices a theoretical and practical examination is needed to be passed in the laboratory.
- Succeed both written examinations, either at the time or at the end semester.

Relative percentage in the final grade for the different sections are:

Practice: 10%; Various activities: 10%; First test: 40%; Second test: 40%

FINAL UNIQUE EVALUATION
Students choose this evaluation and have been admitted into it during the first two weeks of the semester, will have to pass a multiple choice examination (90% of score) and a practical exam (10% of score).

Additional Information
Additional information can be found on the website of the Department of Biochemistry and Molecular Biology II: http://farmacia.ugr.es/BBM2/