FACULTY OF PHARMACY

STUDY PROGRAM 0916.1 PHARMACY

DEPARTMENT OF PHARMACEUTICAL AND TOXICOLOGICAL CHEMISTRY

APPROVED
at the meeting of the Commission for Quality Assurance and Evaluation of the Curriculum, Faculty of Pharmacy
Minutes No. 2 of 21.12.2017
Chairman PhD. associate professor
UNCU Livia

APPROVED
at the Council meeting of the Faculty of Pharmacy
Minutes No. 2 of 22.12.2017
Dean of Faculty PhD. associate professor
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APPROVED
at the meeting of the chair of Pharmaceutical and Toxicological Chemistry.
Minutes No. 3 of 03.11.2017
Head of chair PhD. professor
VALICA Vladimir

SYLLABUS

DISCIPLINE **MEDICINAL CHEMISTRY**

Integrated studies

Type of course: **Compulsory**

Chisinau, 2017

I. INTRODUCTION

- **General presentation of the discipline: place and role of the discipline in the formation of the specific competences of the professional / specialty training program**

Medicinal chemistry is a necessary and useful discipline for pharmacies students, as it allows for deeper integration of accumulated knowledge into basic specialties. Being an interdisciplinary field, ***Medicinal chemistry*** connects medical, chemical and pharmaceutical notions to create a clearer and clearer picture of human drug-human interaction. This knowledge is indispensable for the provision of qualitative pharmaceutical assistance and for the monitoring of therapeutic errors that may have a negative impact on the health of the patient.

As a solution to the new requirements for training the professional pharmacist's future competencies, which require knowledge of the molecular mechanisms of action of the drug on the body in direct correlation with its structure and physicochemical properties, it is proposed the course of ***Medicinal chemistry*** expected and recommended for the last year studies in the specialty of Pharmacy.

The purpose of ***Medicinal chemistry*** is to help prospective pharmacists provide extensive, reasoned and individualized consultations to each patient's individual situation as well as the development of self-training skills to meet professional requirements.

- **Mission of the curriculum (aim) in professional training**

To provide students with knowledge about the concepts of medical chemistry, as well as developing the understanding skills of rational drug design methods and methods to ensure their effectiveness and harmlessness to quality patient care.

- **Language (s) of the course:** Romanian, English.
- **Beneficiaries:** students of the V year, faculty Pharmacy, specialty PHARMACY.

II. MANAGEMENT OF THE DISCIPLINE

Code of discipline		**S.09.O.090, S.10.O.097**	
Name of the discipline		**Medicinal chemistry**	
Person(s) in charge of the discipline		PhD in Pharmaceutical Sciences, professor **Vladimir Valica** PhD in Pharmaceutical Sciences, associate professor **Livia Uncu**	
Year	**V**	Semesters	**9, 10**
Total number of hours, including:			**120**
Lectures	**29**	Practical/laboratory hours	**72**
Seminars		Self-training	**48**
Form of assessment	**C, CD**	Number of credits	**3, 4**

III. TRAINING AIMS WITHIN THE DISCIPLINE

At the end of the discipline study the student will be able to:

- ***at the level of knowledge and understanding:***

- subject of study of the subject;
- the objectives of the discipline;
- structure activity relationships in the drug groups, their mechanism of action and drug interactions;
- theoretical bases and essence of methods of synthesis of chemical and biological drugs;
- receptor drug interaction.

- ***at the application level:***

- pharmacological and chemical classification of medicinal products in pharmaceutical practice;
- mechanism of drug interactions;
- quality control of synthesis and biological substances according to DAN requirements;
- methods for determining bioavailability, solubility, bioequivalence
- the knowledge of the structure of the molecule and the physico-chemical properties of the biological effect.

- ***at the integration level:***

- knowledge of the quality of synthetic and biological drugs according to the provisions of the DAN;

- complex and reasoned qualitative pharmaceutical assistance to ensure effective treatment;
- drug interactions in pharmaceutical practice;
- procedures for excluding interactions that may have a negative impact on the health of the patient.

IV. PROVISIONAL TERMS AND CONDITIONS

It is a multidisciplinary science combining the knowledge of inorganic, organic and chemico-physical chemistry, physiology, physiopathology, biochemistry, general pharmacology previously accumulated, and fundaments other specialized disciplines such as pharmaceutical technology and clinical pharmacy.

V. THEMES AND ESTIMATE ALLOCATION OF HOURS

Lectures, practical hours/ laboratory hours/seminars and self-training

Nr. d/o	THEME		Number of hours		
			Lectures	Practical hours	Self-training
1.	**Medical chemistry. Fundamental concepts.**	Medical Chemistry: Definition and Purpose. Basic steps to finding and rational building of the drugs.	2	2	-
		Targets for drug action - lipids, enzymes, receptors, nucleic acids. Biological membranes, structure, transport of drugs.	2	2	-
		Drug-receptor interactions. Types of receptors, their chemical nature. Kinetic interactions. Basic theories of reception ligands. Transmission systems and mediators: the adenylate cyclase. Metabolic products of phospholipids. Calcium ions. Enzymes; principles of action and regulatory activity. Inhibitors of enzymes in the arsenal of drugs. Target nucleic acids as biologically active substances	2	2	4
2.	**Relationship between the physico-chemical properties of the active principle and its pharmacological action.**	Relationship between the physico-chemical properties of the active principle and its pharmacological action. Solubility and lipophilia, ionization of drug molecules. Chemical bonds and biological activity of molecules. Stereochemical aspects of drugs. Chirality and biological activity. Isosteroism and bioisosterism.	4	4	4
3.	**Relationship structure of activity. QSAR.**	Drug design. QSAR. Main stages of drug design. Total screening.	2	2	2
		Molecular mechanics and its applications. The design of ligands. Ligands homo and heterodimers: twin	2	2	2

Nr. d/o	THEME		Number of hours		
			Lectures	Practical hours	Self-training
		study drug. Structural concepts in forecasting of toxicity of medicinal preparations.			
		Natural compounds that produced leaders for designing new drugs.	2	2	4
	Control assessments.		-	2	-
4.	**Bioavailability and bioequivalence of drugs**	Principles of bioavailability and bioequivalence of drugs. Optimization of bioavailability. Factors influencing bioavailability and bioequivalence. Bioequivalence studies.	2	2	8
		Biotransformation of drugs and physico-chemical properties of drug substances. The influence of drug structure on the degree of absorption. Metabolism of biologically active substances: C phase metabolic reactions, CYP450-catalyzed reactions and ferments. Phase II reactions. Reduction and hydrolysis processes.	3	4	4
		Modifying the structure to increase the solubility of the drug and improve pharmacological action. Pro-drugs and bioprecursors. Changes in structure after hydroxy-, mercapto-, carboxy-, amino-, carbonyl. Cycling of linear analogs in body conditions.	2	3	4
	Control assessments.		-	4	-
5.	**Drug interactions.**	Drug interactions. Classification and mechanisms. Food -drug interactions, drug - alcohol, drug-tobacco. Principles. Examples.	2	4	8
	Control assessments.		-	1	-
6.	**Biological Medicines.**	Biological Medicines. Particularities of obtaining and control. Hormonal biological preparations. Preparations of animal extracts. Medicines used in hemorrhagic diseases. Blood and products derived from blood. Vaccines. Immunological products.	4	4	8
	Control assessments.		-	1	-
7.	***Diferentiated colloquium*.**		-	2	-
Total			**29**	**43**	**48**

VI. REFERENCE OBJECTIVES OF CONTENT UNITS

Objectives	Content units
Theme (chapter) 1. Medical chemistry. Fundamental concepts.	
• Define the basic concepts of medical chemistry; • be familiar with the rational design of medicines; • demonstrate abilities to analyze and systematize the theoretical knowledge; • apply the criteria for differentiating the methods used in the rational design of medicines; • integrate in the pharmaceutical activity the knowledge about the interaction of the drug with the human body. Fundamental concepts of medical chemistry.	Methods of rational drug design in medical chemistry. Differentiating rational design methods, highlighting the advantages / disadvantages. Practical applications of medical chemistry.
Theme (chapter) 2. Relationship between the physico-chemical properties of the active principle and its pharmacological action.	
• To define the main notions (solubility, lipophilicity, molecular size, polymorphism); • to know the theoretical bases for the calculation of the most representative indices that influence the pharmacokinetic parameters; • apply the knowledge acquired to solve the problems and tasks proposed; • explain the role of spatial conformation in the ligand-receptor relationship.	Main concepts of physico-chemical parameters. Calculation formulas of the main parametrifico-chemical ones. Spatial conformation and influence on biological activity.
Theme (chapter) 3. Relationship structure of activity. QSAR.	
• Define the structure of activity relationships in the drug groups, their mechanism of action and drug interactions; • to know the theoretical bases and the essence of synthetic methods of chemical and biological drugs; • apply the knowledge gained for the analysis of case studies; • explain the role of descriptors in creating a QSAR model; • to critically assess the quality of synthetic and biological drugs according to the dan provisions.	Processes and methods to optimize the activity structure relationship. Examples. The notions of isostere, bioisosteres and their methods of production. Indicators used to create the QSAR model. Classification. Importance. Practical applications of the QSAR method and the utility of the method in drug design.
Theme (chapter) 4. Bioavailability and bioequivalence.	
• Define the main pharmacokinetic parameters and explain the importance of their knowledge; • demonstrate ability to analyze analytical	Main concepts of pharmacokinetic parameters. Formulas for the calculation of the main pharmacokinetic parameters.

Objectives	Content units
documentation and scientific studies; • apply the knowledge gained in formulating recommendations on drug treatment; • integrate the critical analysis skills of prescribed treatment to prevent therapeutic errors.	The practical role of these parameters. The importance of knowledge by the pharmacist.
Theme (chapter) 5. Drug interactions.	
• Define the main notions of drug interactions; • know the classification of interactions with eloquent examples; • to describe the factors that favor the emergence of drug interactions; • demonstrate the ability to relate theoretical material previously studied with new concepts; • explain in detail the mechanism of drug interactions; • contribute to the exclusion of interactions that may have a negative impact on the health of the patient.	Drug-drug, drug - alcohol, drug – tobacco interactions. Case studies discussion. Practical applications of knowledge about drug interactions. Analyzing methods to minimize / exclude the emergence of drug interactions.
Theme (chapter) 6. Biological drugs.	
• to define and describe the main notions: biopharmaceuticals, biosimilar, bioscientists; • be familiar with the classification of biological drugs; • explain the influence of different factors on the stability of biological drugs; • propose a reasoned opinion on the use of vaccines; • demonstrate critical analysis skills during case studies.	Particularities of obtaining biopharmaceuticals. Methods of control and standardization of biopharmaceuticals. Immunogenicity and procedures to minimize this phenomenon. Case studies discussion.

VII. PROFESSIONAL (SPECIFIC (SC)) AND TRANSVERSAL (TC) COMPETENCES AND STUDY OUTCOMES

✓ Professional (specific) (SC) competences

- PC1. Identification, knowledge and use of concepts, principles and theories of medical chemistry in professional activities.
- PC2.Good knowledge, understanding and operation with theoretical knowledge and basic practical methods of medical chemistry.
- PC3. Thorough knowledge, design and application of specialist knowledge in relation to the patient, taking into account age, gender, diagnosis, the presence / absence of chronic diseases in order to ensure therapeutic compliance.
- PC4. Professional possession of the theoretical principles of rational drug development.
- PC5. Application of theoretical and practical knowledge in solving complex situational problems

and providing qualified pharmaceutical assistance.Etc.

✓ Transversal competences (TC)

- TC1. Application of rigorous and efficient working rules, manifestation of a responsible attitude towards the scientific and didactic field, optimal and creative a of their own potential in specific situations, observing the principles and norms of professional ethics;
- TC2. Ensure effective deployment and effective engagement in group activities. Identifying training needs according to the evolution of chemical and medical science; determining the priorities in the continuing professional training of the pharmacist.
- TC3. Identifying opportunities for continuous training and efficient use of learning resources and techniques for their own development.

✓ Study outcomes

Upon completion of the course the student will be able to:

- to know the general methods and procedures of rational drug design, the factors that influence the action of the drug, the biological drugs;
- to know the principles of interaction of the drug with the human organism for the successful fulfillment of professional responsibilities;
- be able to identify and avoid the main types of mistakes commonly encountered during medical treatment;
- to propose and provide complex and reasoned qualitative pharmaceutical support;
- apply the methods for determining the bioavailability, solubility, bioequivalence in professional activity;
- detect and contribute to the exclusion of drug interactions, which may have a negative impact on the patient's health.

Note. Study outcomes (are deduced from the professional competencies and formative valences of the informational content of the discipline).

VIII. STUDENT'S SELF-TRAINING

No.	Expected product	Implementation strategies	Assessment criteria	Implementation terms
1.	Working with lecture materials, methodical indication	Work systematically in the library and mediate. Exploring the current electronic sources on the topic under discussion	1. Quality of formed judgments, logical thinking, flexibility. 2. The quality of the systematization of the informational material obtained through its own activity.	During the semester
2.	Report	Analysis of relevant sources on the topic of the paper. Analysis, systematization and synthesis of information on the	1. The quality of systematization and analysis of the informational material obtained through	During the semester

		proposed theme. Compilation of the paper according to the requirements in force and presentation to the chair.	its own activity. 2. Concordance of information with the proposed theme. 3. Quality of PPT presentation and answers to questions. During the semester	
3.	Case study analysis	Choice and description of the case study Analysis of the causes of the issues raised in the case study. Prognosis of the case investigated. Deduction of the expected outcome of the case.	1. Ability to analyze, synthesize, generalize data obtained through its own investigation. 2. Formation of an algorithm of knowledge based on the obtained conclusions.	Semester X

IX. METHODOLOGICAL SUGGESTIONS FOR TEACHING-LEARNING-ASSESSMENT

- ***Teaching and learning methods used***

Exposure, interactive lecture, heuristic conversation, problem-solving, brainstorming, group work, individual study, work with textbook and text, debate, problem solving, role play, simulation, interactive listening**.**

- ***Applied teaching strategies / technologies*** *(specific to the discipline)*

Inductive, deductive strategies, teaching and learning strategies are developed using models (analogue strategies), algorithmic strategies: explicative-demonstrative, intuitive, exponential, imitative and algorithmic; heuristic strategies - to develop knowledge through his or her own thinking effort, using problem-solving, discovery, modeling, hypothesis formulation, heuristic dialogue, investigative experiment, assault of ideas, which stimulate creativity.

- ***Methods of assessment*** *(including the method of final mark calculation)*

Current: front and / or individual control via:

(a) application of docimological tests;
(b) solving problems / exercises;
(c) analysis of case studies;
(d) playing role plays on the topics discussed;
(e) control assesments – 4;
(f) the current assessment of self-training at the end of the semester.

The average mark is calculated by average of the marks obtained at control assesments

and the mark of self-training.

Final: Colloquium, the "pass" rating – test-control and oral answer.

Diferentiated colloquium – test-control and oral answer.

Funal mark is caiculated by the average mark (50%), test-control (20%) and oral answer (30%).

Method of mark rounding at different assessment stages

Intermediate marks scale (annual average, marks from the examination stages)	National Assessment System	ECTS Equivalent
1,00-3,00	**2**	**F**
3,01-4,99	**4**	**FX**
5,00	**5**	**E**
5,01-5,50	**5,5**	
5,51-6,0	**6**	
6,01-6,50	**6,5**	**D**
6,51-7,00	**7**	
7,01-7,50	**7,5**	**C**
7,51-8,00	**8**	
8,01-8,50	**8,5**	**B**
8,51-8,00	**9**	
9,01-9,50	**9,5**	**A**
9,51-10,0	**10**	

The average annual mark and the marks of all stages of final examination (computer assisted, test, oral) - are expressed in numbers according to the mark scale (according to the table), and the final mark obtained is expressed in number with two decimals, which is transferred to student's record-book.

Absence on examination without good reason is recorded as "absent" and is equivalent to 0 (zero). The student has the right to have two re-examinations.

X. RECOMMENDED LITERATURE:

A. Compulsory:

1. Course support.
2. Abraham D.J. *Burger's medicinal chemistry and drug discovery*, 6th ed., vol I – VI, Wiley & Sons Inc. – pe CD
3. Block J.H., Beale J.M. *Wilson and Gisvold's, Textbook of Organic Medicinal and Pharmaceutical Chemistry,* ed. a XI-a, Ed. Lippincott Williams &Wilkins, 2004 – pe CD
4. Methodical indications.

B. Additional:

1. Lista medicamentelor esenţiale. Ordinul MS RM Nr. 162 din 23.04.07.
2. Matcovschi C., Safta V. Ghid farmacoterapeutic (medicamente omologate în Rep. Moldova) – 2010, Chişinău, 1340 p.
3. Haţieganu E., Stecoza C. Chimie terapeutică. Vol. II. – Bucureşti: Editura Medicala, 2006-2008. – 253 p.
4. Mureşan A., Palage M. *Chimie Terapeutică. Medicamente utilizate în afecţiuni cardiovasculare,* Ed. Accent, Cluj-Napoca, 2000.
5. Mureşan A., Palage M., *Medicaţia afecţiunilor sistemului nervos central,* Ed. Medicală Universitară Iuliu Haţieganu, Cluj-Napoca, 2006.
6. Oniga O., Tiperciuc B. *Antiseptice şi dezinfectante*, Ed. Medicală Universitară Iuliu Haţieganu, Cluj-Napoca, 2002.
7. Oniga O., Tiperciuc B. *Antibiotice antibacteriene*, Ed. Medicală Universitară Iuliu Haţieganu, Cluj-Napoca, 2003.
8. Neidle S. *Cancer Drug Design and discovery*, Elsevier Inc., 2008 – pe CD.
9. Newton D. *Chemistry of drugs*, Fact on File Inc., New York, 2007.
10. Williams D.A., Lemke T.L. *Foye's principles of Medicinal Chemistry*, ed. a V-a , Ed. Lippincott Williams & Wilkins, 2002.
11. Ziwei Huang, *Drug discovery research. New frontiers in the post-genomic era*, Wiley Interscience, 2007 – pe CD.