Approved

At the meeting of the Council of Faculty of Pharmacy
Minutes No. 4 of 12.06.2014

Dean of the Faculty of Pharmacy
PhD, associate professor N. Ciobanu

Approved

At the meeting of the chair of General Chemistry
Minutes No. 11 of 06.06.2014

Head of the chair,
PhD, associate professor C. Cheptănaru

SYLLABUS FOR STUDENTS OF

FACULTY OF PHARMACY

Name of the course: **Organic Chemistry**

Code of the course: **F03O027 F04O036**

Type of course: **compulsory**

Total number of hours – 187

lectures 68 hours, practical lessons 119 hours

Number of credits provided for the course: 10 hours

Lecturers teaching the course:

PhD, associate professor – Constantin Cheptanaru

PhD, associate professor – Ion Santevoi

Lecturer – Elena Globa

Chisinau 2014

I. Aim of the discipline

The aim of the Organic Chemistry course is the formation of the chemical structure – function – reactivity approach based on the concepts of chemical bonding, hybridization, molecular geometry, movement of electrons through the effect field, inductive effect, conjugation etc. At the same time it aims to form at a current scientific level the systemic knowledge concerning the laws of organic compounds transformations according to the chemical structure of the molecule and also the obtaining of practically useful activity skills in the field of medicinal chemistry.

II. Objectives obtained in teaching the discipline

- Acquiring knowledge of contemporary theoretical and practical organic chemistry necessary for understanding the specialty disciplines, highlighting the importance of organic chemistry for biochemistry and pharmacy.
- The obtaining of knowledge for understanding the relationship between the compounds and the physical, chemical and biological characteristics, assimilation of knowledge required for the synthesis of organic compounds, their structural analysis for understanding chemical reactivity and reaction mechanisms for achieving modulation in the functional groups.
- The obtaining of practical skills and acquiring working methods useful both for work in other laboratories (pharmaceutical chemistry, biochemistry, toxicology, pharmaceutical technology, drug control, pharmacognosy, etc.) and for the practice of the future pharmacist.

- <u>At the level of knowledge and understanding</u>

1. To understand the basis of organic compounds structure. The electronic structure of carbon atom and organogene elements, the electronic structure of chemical bonds interconnecting with the mutual influence of the atoms in the molecule. Electronic effects of the substitutes, conjugation and aromaticity, acidity and basicity of organic compounds, the general mechanisms of chemical reactions.
2. To know the main classes of organic homofunctional compounds, structure, nomenclature, the obtaining methods, general and specific properties, the reaction mechanisms.
3. To understand the structure, the composition and the main properties of heterofunctional organic compounds - traditional specialty of pharmacy.
4. To know the peculiarities of structure, reactivity and the significance of heterocyclic compounds with nitrogen, oxygen and sulfur.
5. To understand the structure and the main properties of biologically active heterofunctional organic compound - participants in the metabolic processes (hydroxy-, amino-, and oxo-acids, nucleosides, nucleotides and biopolymers - peptides and proteins, polysaccharides, nucleic acids).
6. To understand the structure, properties and importance of plant and animal organic compounds - simple and complex lipids, terpenoids, steroids, alkaloids and their synthetic analogues.
7. To know the informational possibilities of physico-chemical methods of analysis (IR spectroscopy, UV-Vis, NMR, MS) and the identification of organic compounds.

8. To know the main procedures of organic chemistry laboratory (purification, elimination, extraction, recrystallization, melting temperature determination, simple and fractional distillation in vacuum and with vapor). The accident prevention in the chemical laboratory.

- At the level of application

1. To determine the class and group of organic compounds according to the classification rules. The structural formulas according to systematic nomenclature.
2. To represent graphically the structural, stereochemical and conformational formulas of organic compounds, types of stereoisomers.
3. To determine the acidic and basic sites and to appreciate and compare the acidity of organic compounds.
4. To determine and describe the mechanisms of organic reactions to forecast the direction and outcome of organic transformations.
5. To apply the qualitative analysis identification reactions of organic combinations.
6. To carry out the synthesis of a given organic compound from the documentation to the obtaining of a pure compound and its characteristic.

- At the level of integration

1. To appreciate the importance of organic chemistry in content of integration in profile disciplines (pharmaceutical chemistry, toxicological chemistry, drugs technology, pharmacology etc.);
2. To know the identification reactions of different pharmaceutical organic compounds classes;
3. To be able to perform the synthesis of organic molecules that are used frequently in pharmaceutical practice;
4. To explain the pharmacological properties of organic molecules depending on their chemical structure.

III. Provisional terms and conditions

The Organic chemistry is one of the fundamental disciplines for students of Faculty of Pharmacy and is the basic one in studying the most subjects in the field (pharmaceutical chemistry, toxicological chemistry, medicinal technology, pharmacognosia, pharmacology, etc.).

To obtain a better understanding of Organic Chemistry course, fundamental knowledge from pre-university institutions in chemistry is required: electronic structure of bio elements, structural theory of organic compounds, structural isomerism, types of chemical bonds in organic compounds, basic nomenclature and classification of organic compounds.

IV. Main theme of the course

A. Lectures:

№	Theme	Hours
	III-*rd* semester	
1.	Introduction. Chemical bonds and reciprocal influence of atoms in organic molecules. Types of chemical bonds in organic compounds. The inductiv	2

	effect. Aromaticity. The mesomeric effect. Electron donor ED and withdrawn EW substitutes.	
2.	The spatial structure of organic compounds. Configuration. Stereochemical formulas. Stereoisomerism and enantiomerism. Absolute and relative configuration. D, L and R, S series. Racemic mixture. Energetic characteristics of open and cyclic chain conformations.	2
3.	Acidity and basicity of organic compounds. The Bronsted theory. Types of acids. Factors that influence the acidity and basicity. Classification of reagents and organic reactions. General mechanisms of radical, electrophile and nucleophile reactions.	2
4.	The reactivity of unsaturated hydrocarbons. Alkenes, π-diastereomeria. The mechanism of electrophile addition (A_E – reactions): the addition of halides, halogenated acids, hydration reaction. The Markovnikov`s rule. Oxidation reactions. Dependencies of oxidation products and the reaction conditions. Polymerization reactions. Natural and synthetic. Alkines. Reactionary ability. Qualitative reactions of alkenes and alkines.	2
5.	The reactivity of monocyclic arenes. Aromaticity. Electrophile substitution reactions, S_E mechanism. Halogenation, nitration, sulphonation, alkylation and acylation of arenes. The substitution rules at benzene ring. I-st and II-nd order functional groups. The coordinating and non-coordinating orientation.	2
6.	The reactivity of condensed arenes. The naphthalene group. Obtaining. Electrophile substitution reactions. Substitution orientation in naphthalene ring. Oxidation and reduction. Anthracene, phenanthrene and their reactivity. The polinuclear condensate arenes.	2
7.	Alkylhalydes. Mono and bimolecular nucleophile substitution reactions. The alkylhalydes in the organic chemistry synthesis. Elimination reactions. The alkenhalydes, alyl- and vinyl. Halogenoarenes.	2
8.	The reactivity of hydroxyl derivatives of hydrocarbons and their sulfur analogues. Nucleophilic substitution and elimination reactions. Alcohols and thiols oxidation. Applying these reactions for aldehydes, ketones, carboxylic acids synthesis and for primary, secondary and tertiary alcohols identification.	2
9.	The reactivity of ethers and thioethers. Nomenclature. The most important representatives. Phenols, structural particularities and chemical reactivity. Extending the synthesis possibilities by carboxylation, hydroxylation and formylation reactions. Mono- and dihydroxy phenol oxidation. Qualitative reactions of phenols.	2
10.	Carbonyl compounds. Synthesis methods. Structure and reactivity of carbonyl group. The nucleophilic addition reactions and their mechanism. Role of acid catalysis in A_E reactions. The addition of Grignar reagent. The polymerization reactions.	2
11.	The reactivity of aldehydes and ketones. The addition-elimination reactions. Reactions with CH acid site. The holoformic reaction. Oxidation and reduction.	2
12.	The reactivity of carboxyl compounds. Classification of carboxylic acids. The structure of carboxyl group and carboxyl anion. Nucleophilic substitution reactions, mechanism. Role of catalyst. Nucleophilic	2

	substitution reactions in synthesis of halide anhydrides, anhydrides, esters, amides, hydrazine functional derivatives.	
13.	Saturated and unsaturated dicarboxylic acids. Their chemical reactivity. CH acidity of ethylacetate and malonic esters. The condensation reaction of ethylacetate and malonic ester synthesis.	2
14.	Carbonic acid derivatives. The carbaminic acid and its esters. The urea, its synthesis and chemical reactivity. Urea acids and acids ureides. The biuret obtaining and biuret test. Guanidine and its propreties.	2
15.	The reactivity of amines. Classification of amines. Methods of obtaining. Base and nuleophile propreties. The amines reaction with nitrous acid. The benzene cycle influence by amino group. S_E reactions (halogenation, nitration, sulphonation).	2
16.	The reactivity of diazocombinations. Diazotation reactions. The structure of diazonium salts. Diazotation agents. The diazonium salts reactions with nitrogen elimination. The reactions of azocombination. The azo colorants (methyl orange, congo red) and their proprieties. The colour theory.	2
17.	The reactivity of heterofunctional carboxylic acids. Halogen acids. Classification, obtaining and propreties. Hydroxiacids. Classification, obtaining, heterofunctional properties and characteristic reactions. Lactides. Lactones. Aminoacids. Classification, obtaining and characteristic reactions. Diketopyperazines and lactams.	2
IV-*th* semester		
18.	Heterofunctional carboxylic acids. Oxo acids. Classification and their obtaining. The main metabolites: pyroracemic, acetylacetic, oxalylacetic and cetoglutaric. The keto-enol tautomeria. The acetylacetic ester synthesis.	2
19.	Phenolic acids. The salicylic acid. Preparation. Chemical particularities. Functional derivatives: aspirin, salol, methyl salicylate. The PABA (p-aminobenzoic acid) and its derivatives: benzocaine and novocain. Aminophenol and its derivatives: phenacetin, phenatidine and paracetamol.	2
20.	α-Aminoacids, peptides and proteins. Protein aminoacids. Structure, classification, nomenclature. The acid-basic properties and the bipolar structure of α-aminoacids. Chemical properties of α-aminoacids as heterofunctional compounds. Biological important chemical reactions of α-aminoacids: transamination, deamination, hydroxylation and decarboxylation. Peptides. Determination of peptides primary structure. The determination of N α-aminoacids sequence by Edman method. Strategy of peptides synthesis.	2
21.	Monosaccharides. Classification, stereoisomerism and cyclo-oxo tautomerism. The Haworth formulas. Conformations. Chemical reactivity capability. Qualitative chemical reactions. The most important representatives. Vitamin C.	2
22.	Oligo- and polysaccharides. Disaccharides. Classification. The structure of non-reducing and reducing disaccharides. Nomenclature, cyclo-oxo tautomerism and chemical properties. Polysaccharides. Starch (amylose, amylopectin). Structure and chemical properties. Glycogen. Dextran. Cellulose, its structure and derivatives. The notion of heteropolysaccharides.	2
23.	Five-membered heterocycles with one heteroatom. Definition, structure and	2

	nomenclature. The aromatic character. Acid-base properties. Furan, pyrrole, thiophene, acidophobe properties. Electrophilic substitution reactions. The substituents orientation. Furfurol, furacin. porphin, hemoglobin. Corrin cycle. The indole group.	
24.	Five-membered heterocycles with two heteroatoms. Pyrazole, imidazole, oxazole, thiazole. The pyrazole and imidazole tautomeria. The formation of associations. Acid-basic proprieties, S_E reactions. Pyrazole-5-one and derivatives: antipyrine, amidopyrine, analgine, butadione and their synthesis. Thiazolidine. The notions of penicillins and their structures.	2
25.	Six-membered heterocycles. Groups of pyridine, quinoline and pyran. The reactivity and the importance of their derivatives in medicine and pharmacy. Pyrimidine, pyazine, pyperazine. The pyrimidine derivatives: barbituric acid, barbital, phenobarbital, vitamine B_1. Oxazine, phenoxazine.	2
26.	Condensed heterocycles. Purine. Hypoxanthine. Xanthine. Methylated xanthines: theopylline, theobromine, caffeine. Uric acid, acidic and neutral urates. The murexide reaction. Pteridine. Folic acid, riboflavin.	2
27.	Alkaloids. Chemical classification. Qualitative reactions. Chemical properties. Pyridine and piperidine groups of alkaloids: nicotine, coniine, anabasine. The quinoline group of alkoloids: quinine. The isoquinoline and isoquinoline phenantrene groups of alkoloids: papaverine, morphine, codeine. The tropane alkoloid group: atropine, cocaine. The indole alkoloid group: reserpine, lisergic acid and its amide.	2
28.	Nucleic acids. Nucleic bases. Nucleosides. Structure, nomenclature and hydrolysis characteristics. ADN, ARN. Primary structure. Secondary structure notions.	2
29.	Nucleic acids. The nulcleoside mono- and poli- phosphates. The nucleotide coenzymes: ATP, NAD^+, $NADP^+$, FAD. Their structure and importance. The role of nucleic acids in protein biosynthesis.	2
30.	Hydrolysable lipids (neutral). Natural fats as a mixture of triacylglycerols. Fatty acids, components of lipids. Structure, nomenclature and their conformation. The reactivity characteristic of lipids (acid and base hydrolysis, hydrogenation, addition and oxidation reactions) that are used for determination of fats quality. Vaxes, tvines and their pharmaceutical importance.	2
31.	Complex lipids. Phosphatidic acids. Phospholipids: phosphoacylglycerins (phosphatidylcolamine – kephalins, phosphatidylcholine – lecithins). Sfingolipids: sfingomieline and glycolipids (cerebroside and ganglioside). Structure, hydrolysis and biological importance. Biological oxidation. The notion of prostaglandins.	2
32.	Non-hydrolyzable lipids. Structural particularities of terpenoids, carotenoids and steroids as a isoprenoid derivatives. Terpenoids, classification, the isoprenic rule. Monoterpenoids – biologic important molecules, drugs (ether oils, pinene, menthol, camphor etc.). The diterpenoids: vitamin A, retinal. Triterpenoids – squalene and tetraterpenoids – carotene.	2
33.	Steroids. The structure of sterane. Nomenclature, stereoisomeria, 5α and 5β representatives. Main groups of steroids: sterines, biliary acid, sexual androgen and estrogen hormones, aglicans of cardiotonic glycosides,	2

	corticosteroids – main representatives and their characteristic.	
34.	Evaluation lecture. The chemical reactivity of the principal classes of organic compounds as a base for elaboration of synthesis methods and analysis of drugs molecules, prognosis of their metabolism in the organism.	2

B. Practical lessons:

№	Theme	Hours
III-*rd* semester		
1.	The classification, nomenclature and structural isomerism of organic compounds. The rules to work in an organic chemistry chemical laboratory.	3
2.	Chemical bonds and mutual influence of atoms in organic molecules. Organic synthesis. The laboratory glassware.	3
3.	The spatial structure of organic compounds. Configuration and conformation. Organic synthesis. Extraction and recrystallization.	3
4.	The acidity and basicity of organic compounds. Classification of reagents and organic reactions. Organic synthesis: The determination on melting temperature.	3
5.	Test 1: “The basis of organic compounds structure” Organic synthesis: Simple distillation.	3
6.	The qualitative analysis of organic molecules, micropracticum. Organic synthesis: Fractional distillation.	3
7.	Electronic and IR spectroscopy of organic compounds. NMR and mass spectroscopy of organic compounds. Organic synthesis: Steam distillation.	3
8.	Alkenes, dienes and alkynes. Electrophile addition reactions. Qualitative analysis. Organic synthesis: The chromatography analysis.	3
9.	Arenes. Electrophile substitution reactions. Qualitative analysis. Organic synthesis: The safety rules in the chemical laboratory.	3
10.	Hydrocarbon halogen derivatives. The nucleophile substitution and elimination reactions. Qualitative analysis.	3
11.	Hydroxyl organic compounds. Chemical reactivity of alcohols, phenols, ethers and their sulfur derivatives. Qualitative analysis. Test 2.	3
12.	Carbonyl compounds. The nucleophile addition reactions. Qualitative analysis.	3
13.	Carboxylic compounds and derivatives. The nucleophile substitution reactions. Qualitative analysis.	3
14.	Amines. Qualitative analysis. Organic synthesis: Acylation.	3
15.	Diazocombinations. Qualitative analysis. Organic synthesis: Acylation.	3
16.	Test 3: “Carbonyl and carboxyl compounds, amines azo- and diazocombinations.”	3
17.	Final assessment. Colloquium.	3
IV-*th* semester		

18.	Organic synthesis: Sulfonation.	4
19.	Organic synthesis: Sulfonation.	4
20.	Heterofunctional carboxylic acids. Qualitative analysis. Organic synthesis: Nitration.	4
21.	α-Aminoacids, peptides and proteins. Qualitative analysis. Organic synthesis: Nitration.	4
22.	Monosaccharides. Qualitative analysis. Organic synthesis: Halogenation.	4
23.	Oligo- and polysaccharides. Qualitative analysis. Organic synthesis: Halogenation.	4
24.	Test 1: "Heterofunctional acids, α-aminoacids and carbohydrates" Organic synthesis: Nitrosation.	4
25.	Five-membered heterocycles. Qualitative analysis. Organic synthesis: Nitrosation.	4
26.	Six-membered heterocycles. Qualitative analysis. Organic synthesis: Diazotization and azo-combitation.	4
27.	Organic synthesis: Diazotization and azo-combitation.	4
28.	Condensed heterocycles. Alkaloids. Qualitative analysis. Organic synthesis: Oxidation.	4
29.	Test 2: "Heterocycle compounds" Organic synthesis: Oxidation.	4
30.	Nucleic acids. Organic synthesis: Acylation.	4
31.	Hydrolysable lipids. Qualitative analysis. Organic synthesis: Acylation.	4
32.	Non-hydrolyzable lipids. Terpenoids. Qualitative analysis. Organic synthesis: Condensation.	4
33.	Test 3: "Nucleic acids, lipids, terpenoids and steroids." Organic synthesis: Condensation.	4
34.	Assessment of practical skills. Exam.	4

V. Recommended literature:

J *A. compulsory:*

1. N.Barbă, G.Dragalina, P.Vlad. Chimie organică. Chişinău. "Ştiinţa", 1997.
2. N.Tiukavkina, I.Baukov, V.Rucikin. Chimia bioorganică. Chişinău: "Lumina", 1992.
3. Mirca Iovu. Chimie organică. Bucureşti: "Editura didactică şi pedagogică", 1999.
4. C.Cheptănaru, I.Santevoi. Compendiu de lucrări practice si de laborator la chimia organică pentru studentii facultătii Farmacie. Chişinău, CEP "Medicina", 2009.

J *B. additional:*

1. C.D.Neniţescu. Chimie organică. Bucureşti: "Editura didactică şi pedagogică", 1984.
2. В.Л.Белобородов, С.Э.Зарубян, А.П.Лузин, Н.А.Тюкавкина, Органическая химия, в двух книгах. Москва, „Дрофа", 2008.
3. Н.Тюкавкина, Ю.Бауков. Биоорганическая химия. Москва. "Медицина", 1991, 2011.
4. А.И.Рево, В,В,Зеленкова. Малый практикум по органической химии. М., 1980.

5. О.Я.Нейланд. Органическая химия. Москва: “Высшая школа”, 1990.
6. Р. Моррисон, Р.Бойд. Органическая химия (Пер. с англ.). Москва: “Мир”, 1984.
7. Гауптман, Ю.Грефе, Х.Ремане. Органическая химия. (Пер. с нем), Москва. „Химия”, 1979.

VI. Teaching and learning methods:

The Organic Chemistry discipline is taught in a classical manner: with lectures, practical and laboratory works. The lectures include theoretical information and are delivered by senior lectures of the department. During practical and laboratory lessons students extend, develop and confirm theoretical knowledge, learn about accessible principles and methods for organic qualitative and quantitative analysis, write reports to laboratory works. The Department reserves the right to place some practical work in interactive way.

VII. Suggestions for individual activity:

In order to obtain good results in organic chemistry the student should work actively during lectures and laboratory hours, as well as independently. This means:

1. Read the original material attentively, not formally, take notes. Try to elucidate the major moments of the text. Study the diagrams and figures from the lecture notebook and book. Solve the tests set termed in the guidebook and compendium.
2. Attend the courses and practical lessons, but not just to make attendance! If you do so, unlikely that you will obtain the expected results. Write your lecture notebook carefully. Reflect the information through yourself and question yourself: am I agree with the Professor? Do I understand what it is all about? Does the lecture information correspond to the guidebook one?
3. Ask questions to teacher, each other, to yourself. The fact that you put questions means that you are trying to understand and process the taught material and this can only be a welcomed. We organize special hours for tutorials. Don't hesitate to come to them.
4. Organize groups of 2-3 students to meet regularly for discussions about lectures and studying for practical lessons and for midterm exams. As a rule, in small working groups the understanding is much wider and clearer than working individually. In addition the ability to explain to colleagues the assimilated material will be very helpful for the future.
5. Use your time wisely. The Organic Chemistry discipline sets high requirements. Disciplines taught during this year of study submit the same requirements. Therefore, you have to manage your time and find a rational "gold" balance of effort to obtain knowledge, other responsibilities and personal life. In accordance with the requirements in force for each working hour in direct contact with the teacher, the student must work individually 1-2 hours. In other words, for a sufficient understanding of organic chemistry individually each student should work at least 7 hours weekly.
6. Individual studying of Organic Chemistry includes also the analysis of solved exercises and finding solutions for problems proposed in the guidebook.
7. Finding the answers to the tests in the guidebook is another way of assimilation the theoretical and practical material.

VIII. Methods of assessment:

The evaluation during the year of study of Organic Chemistry discipline contains 6 tests:

- Test 1: Theoretical bases of the organic compounds structure;
- Test 2: Chemical reactivity of hydrocarbon and their halogen, hydroxyl derivatives and their sulfur homology;
- Test 3: Carbonyl and carboxyl compounds, amines azo- and diazocombinations.;
- Test 4: Heterofunctional acids and carbohydrates;
- Test 5: Heterocycle compounds, five-, six- membered and condensed rings. Alkaloids;
- Test 6: Nucleic acids, hydrolysable lipids, terpenoids and steroids.

So, the current assessment is made up of 6 midterm exams. Each exam consists of theoretical questions, situational problems and tests. Each part of the exam is assessed from 0 to 10 and can be recovered 2 times during the semester, plus once in the last week of the semester (attestation week). The annual mark represents the average of points obtained during the year of study.

During the year of study the student carries out laboratory work to qualitative analysis of organic compounds and 8 organic syntheses. At the end of each laboratory work the student shows the report made according to a specific template to the teacher for approval.

Promotional examinations within the discipline of Organic Chemistry (final assessment) combines grid-test and oral part.

The grid-test part consists of a minimum of 20 questions (simple and multiple choice) and is appreciated with grades from 0 up to 10.

The oral part consists of an examination card with 2 – 3 theoretical questions and one problem. The student must explain the essence of the questioned material, solve the problem and respond orally to questions provided by the teacher. The student has 40 minutes to prepare the answer. The oral part is assessed with grades from 0 to 10.

The exam topics are approved at the meeting of the Chair council and shall be announced to students with at least one month before the session.

The final grade consists of three components: an annual average (coefficient 0.5); oral part (coefficient 0.3), grid-test part (coefficient 0,2).

Knowledge is assessed with grades from 10 to 1, as follows:

Methods of mark rounding

The average of current and final marks	Final mark
5	**5**
5,1-5,5	**5,5**
5,6-6,0	**6**
6,1-6,5	**6,5**
6,6-7,0	**7**
7,1-7,5	**7,5**
7,6-8,0	**8**
8,1-8,5	**8,5**

8,6-9,0	**9**
9,1-9,5	**9,5**
9,6-10	**10**

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

IX. Language of study:

The organic chemistry is taught in Romanian, Russian and English languages.