MEDICAL UNIVERSITY – PLOVDIV

FACULTY OF PHARMACY

SYLLABUS

IN

ORGANIC CHEMISTRY

Approved by the Department Council on January 29, 2024

Confirmed by the Faculty Council on March 27, 2024

Department of chemical sciences

Syllabus

Discipline	Final exam/ semester	According to the Faculty of Pharmacy curriculum of MU-Plovdiv Academic hours				ECTS	Academic hours in semester			
							III semester		IV semester	
		Auditorium	Lectures	Practices	Non-auditorium		L	P	L	P
Organic chemistry	**IV**	**150**	**60**	**90**	**164**	**10.5**	**30**	**45**	**30**	**45**

DISCIPLINE: Organic Chemistry

TYPE OF DISCIPLINE ACCORDING TO THE UNIFORM STATE REQUIREMENTS: Mandatory

LEVEL OF QUALIFICATION: Master degree

FORMS OF TRAINING: Regular

YEAR OF TRAINING: Second year

DURATION OF TRAINING: Two semesters

ACADEMIC HOURS: 150

TECHNICAL EQUIPMENT APPLIED IN THE TRAINING: Practical training in organic chemistry takes place in a specialized laboratory equipped with nonflammable and chemically-resistant workbenches. The laboratory is equipped with a fume cupboard and a ventilation system. A wide range of glassware and chemicals are used for practical training, as well as some specific analytical instruments: balances, thermostats, heating plates, electromagnetic stirrers, instrument for determining melting temperature, instruments for electronic and infrared spectroscopy, multimedia device. Internet access to large databases of scientific and reference literature (Google Scholar, Science Direct, SciFinder, European Pharmacopeia, etc.) is provided through the university network. The students are provided with electronic resources (copies of lecture presentations, electronic textbooks, etc.) for their preparation for the exam.

FORMS OF EVALUATION: Current control, two colloquiums ("Nomenclature, isomerism and properties of hydrocarbons" – I semester, and "Carboxylic acids and their functional derivatives" – II semester), semestrial exam after completion of the IV semester.

EVALUATION CRITERIA: Q_{final} assessment = 0.1 $Q_{current\ control}$ + 0.1 $Q_{colloquiums}$ + 0.5 $Q_{written\ exam}$ + 0.3 $Q_{oral\ exam}$

ASPECTS OF EVALUATION CRITERIA: If the student fails in the assessment of one of the components, then the final assessment is “Failed”.

SEMESTRIAL EXAM: The semestrial exam has two components: solving a test of ten multiple-choice and 20 open questions, as well as a short theoretical essay; followed by an oral exam on the questions from the written work.

STATE EXAM: No.

LECTURER: The lecture course is conducted by a qualified lecturer who has the required qualification. Up to 30% of the lecture course can be held by a lecturer holding a PhD degree in the field. The practical training is conducted by Assistant Professors who have a master's degree in chemistry and have successfully passed a competition under an approved program for the specialty.

DEPARTMENT: Chemical Sciences

ANNOTATION

Organic chemistry is a mandatory subject according to the Uniform State Requirements for pharmacy students with a minimum horary of 120 hours. According to the approved curriculum for the specialty "Pharmacy", adopted by the AC of MU – Plovdiv with Protocol No. 01/25.01.2024, the horary of the discipline "Organic Chemistry" at MU – Plovdiv is 150, with sixty hours lectures and 90 hours practical training. The discipline is studied during the 3rd and 4th academic semesters and finishes with an exam at the end of the fourth semester. After successfully passing the exam, students receive 10.5 ECTS credits.

The Faculty Council (Protocol No. 3/17.03.2021) determined the successful passing of the exam in organic chemistry as a necessary pre-condition for passing the exam in pharmaceutical chemistry and pharmacognosy. The reason for this decision is the importance of organic chemistry as a basis for pharmacy students’ further education in disciplines such as biochemistry, pharmaceutical chemistry, pharmaceutical analysis, toxicology and pharmacognosy.

BASIC AIMS OF THE DISCIPLINE

The course in organic chemistry uses already acquired knowledge in other basic chemical disciplines: general and inorganic chemistry, analytical chemistry, and physical chemistry. For a better understanding of the teaching material in organic chemistry, it is necessary the students to know in detail the following fundamental topics: types of chemical bonds (covalent, ionic, dative, *van der Waals* interactions), hybridization of carbon atom, factors that affect the state of chemical equilibrium, rate of chemical reactions and influencing factors, *Arrhenius*, *Brønsted – Lowry* and *Lewis* theories of acids and bases, strength of acids and bases expressed by pK_a values, meaning of pH, properties of buffer solutions, determination oxidation state, identification of oxidizing agent and reducing agent, oxidation and reduction, basic principles of thermodynamics and meaning of the related terms.

The lecture course aims to give basic knowledge of the methods of obtaining organic compounds, including those used as medications; to outline the basic chemical properties of organic molecules so that students can predict possible drug-drug interactions; to acquaint

students with the main classes of natural compounds and to emphasize the relationship between the steric configuration of organic compounds and their biological activity.

The practical course introduces students to the basic techniques for preparation, isolation, purification, structural characterization, and identification of organic compounds by classical and modern instrumental methods. The practical exercises students' dexterity and ability to work in a team, to know and follow the safety rules for work in chemical laboratories.

EXPECTED RESULTS

At the end of the training in organic chemistry, students in pharmacy are expected to know the belonging of a given drug to a certain class of organic compounds, to be able to predict its main chemical properties (acid-base, reductive, stability to oxidants and in aqueous solution), to know the structure of biologically important compounds such as lipids, carbohydrates, proteins, polynucleotides, vitamins, and natural products such as terpenes, flavonoids, saponins, tannins, etc. To be able to independently perform some chemical operations such as distillation, recrystallization, extraction, and simple syntheses of organic compounds.

LECTURES

1. Introduction. Presentation of organic compounds and organic reactions. Homolytic and heterolytic processes, electrophiles, and nucleophiles. Types of ionic reactions – substitution, addition, elimination, rearrangements (examples).
2. Electronic effects in organic molecules. Localized and delocalized chemical bonds - examples of systems with delocalized bonds. Induction effect. Mesomeric effect. Resonance theory – canonical structures, hybrid structure, resonance energy. Methods for studying the mechanism of organic reactions.
3. Alkanes and cycloalkanes. Basic principles of IUPAC nomenclature for open-chain and cyclic compounds; condensed and spiro compounds. Preparation of alkanes. Halogenation – mechanism of radical substitution reactions (S_R), reactivity and selectivity. Nitration and sulfochlorination. Stability and specific reactions of cycloalkanes. Cracking, petroleum products.
4. Stereochemistry Part I. Conformational isomerism. Perspective and *Newman* projections. Conformation analysis of ethane and butane. Cyclohexane – "chair" and "boat" conformations, equatorial and axial substituents. Conformation analysis of substituted cyclohexanes. Conformations of polycyclic compounds. Conformation and biological activity.
5. Stereochemistry Part II. Enantiomers and σ-diastereomers. Optical activity and chirality of molecules – examples of asymmetry in organic molecules. Absolute and relative configuration. *Fischer* projection formulas, D,L-configuration. *Kang-Ingold-Prelog* system (R, S-nomination system). Enantiomers and biological activity. Sigma -diastereomers.
6. Alkenes and cycloalkenes. π-diastereomeric alkenes. Preparation – mechanism and stereochemistry of β-elimination reactions (E2 and E1). *Zaitsev*'s rule, *Hoffman*'s rule – examples. Addition reactions of alkenes – hydrogenation, halogenation, addition of hydrogen halides, water, etc.; *Markovnikov*'s rule Mechanism and stereochemistry of electrophilic addition (A_E) reactions. Oxidation of alkenes. Polymerization of alkenes – examples.

7. Alkynes and dienes. Preparation and properties of alkynes. *Kucherov* reaction, keto-enol tautomerism. Acidity of alkynes, alkynides as bases and nucleophiles. Preparation of 1,3-dienes. 1,2- and 1,4-addition to conjugated dienes – kinetic and thermodynamic control of the reaction. *Diels-Alder* reaction, diene synthesis (examples).

8. Arenes. Criteria for aromaticity, *Hükkel*'s rule. Benzene and benzene homologues. Chemical properties of benzene and its derivatives – mechanism of electrophilic substitution reactions (S_E), energy diagram. Nitration, sulfonation, halogenation, *Friedel-Crafts*' alkylation and acylation. Radical substitution, oxidation, and reduction of arenes.

9. Effect of substituents on reactivity and orientation in electrophilic aromatic substitution. Activating and deactivating substituents, o-, m- and p-directing substituents. Stability of the corresponding arenium ions (σ-complexes) in o-, m- and p-substitution. Influence of two or more substitutes. Condensed arenes, naphthalene sulfonation.

10. Alcohols, diols, and thioalcohols. Industrial and laboratory methods for preparation. Chemical properties of alcohols – mechanism and stereochemistry (*Walden* inversion, racemization) of the nucleophilic substitution (S_N) reactions; dehydration, etherification, esterification. Laboratory and biological oxidation of alcohols. Periodate oxidation of diols. Properties of thioalcohols.

11. Phenols. Acidity of phenols, influence of substitutes in aromatic ring. Natural sources of phenols, industrial production of phenols. Electrophilic substitution in the benzene ring. Competitive acylation and alkylation reactions in the benzene ring and the phenol group. Laboratory and biological oxidation of phenols. Concept of polyphenols.

12. Aldehydes and ketones. Classification and nomenclature. Industrial and laboratory synthetic methods – ozonolysis of alkenes, hydration of alkynes, oxidation of alcohols. *Gattermann–Koch* and *Reimer–Tiemann* reaction. *Friedel-Crafts* acylation of aromatic compounds. Chemical properties of carbonyl compounds – mechanism of nucleophilic addition (A_N) and addition – elimination (A_N + E) reactions. Reactions with *Grignard* reagents. Aldol condensation and crotonylation (mechanisms of the reactions). *Cannizzaro* reaction. Oxidation and reduction of carbonyl compounds. Quinones.

13. Carboxylic acids. Classification and nomenclature. Methods for synthesis of carboxylic acid, *Perkin*'s reaction (mechanism). Acidity of carboxylic acids; substituents and acid strength. More important representatives of mono-, di- and polycarboxylic acids. Salts of carboxylic acid. Preparation of halogenated acids – *Hell-Volhard-Zelinsky* reaction.

14. Functional derivatives of carboxylic acids. Esters, acyl halides, anhydrides, amides, hydroxamic acids, nitriles – structure, the most important methods of preparation, reactivity, and properties.

15. Acetoacetic and malonic esters. Synthesis (mechanism of *Claisen* condensation). Applications of acetoacetate and malonic ester in organic synthesis – alkylation, *Knoevenagel* and *Michael* reactions (mechanism). Halogenated acids – *Reformatsky*'s reaction.

16. Oxy and oxo acids. Important representatives. Stereoisomerism in oxy acids (lactic acid, malic acid, tartaric acid). Synthesis of salicylic acid. Decarbonylation and decarboxylation, lactides, lactones and polyesters.

17. Natural esters. Waxes, fats, and phospholipids – structure, properties, and biological role. Concept of prostaglandins. Surface-active substances (surfactants) – classification.

18. Terpenes. Classification, biosynthesis, isoprene rule. Examples of mono-, di- and tetraterpenes (carotenoids). Steroids – cholesterol, vitamin D, bile acids, corticosteroids, and sex hormones.

19. Monosaccharides. Classification, nomenclature, and representatives of trioses, tetroses, pentoses and hexoses. Cyclic forms of monosaccharides – *Haworth* projections. Stereoisomerism – anomers, epimers, mutarotation. Chemical properties – glycoside formation, reaction with amino compounds, oxidation and reduction, chain extension and shortening.

20. Disaccharides and polysaccharides. Reducing and non-reducing disaccharides. Polysaccharides – structure and biological role of cellulose, starch, and glycogen. Cellulose derivatives with practical application. Polysaccharides containing uronic acids and amino sugars.

21. Aliphatic and aromatic amines. Classification and structure. Methods of preparation (from ammonia and amines, by reduction, by molecular rearrangements, etc.). Link between structure and basicity (pK_b). Salt formation, N-alkylation and N-acylation. *Mannich* reaction (mechanism), *Hofmann* and *Cope* elimination. Diazonium salts – production and chemical properties (*Sandmeyer* reaction and coupling).

22. Amino alcohols, amino phenols, and amino acids. More important representatives – aminoethanol, choline, acetylcholine, ephedrine, adrenaline, and noradrenaline. Drugs derived from 3-amino-1,2-propanediol (β-blockers). Proteinogenic amino acids – classification and representatives. Formation of 2,5-dioxopiperazines, lactams, and polyamides.

23. Peptides and proteins. Methods for studying primary structure of proteins. Strategies of protein synthesis. Secondary, tertiary, and quaternary structure of proteins, biological importance.

24. Heterocyclic compound – classification, principles of *Hantzsch-Widman* and IUPAC nomenclature for naming heterocyclic compounds.

25. Five-membered aromatic heterocyclic compounds. Pyrrole, furan and thiophene. *Knorr* synthesis of pyrrole ring. Structure and reactivity – comparison of chemical properties. Indole – *Fischer* synthesis, indole derivatives of biological significance.

26. Six-membered heterocyclic compounds. *Hantzsch* synthesis of pyridine ring. Chemical properties – basicity, salt formation, nucleophilic substitution reactions (*Chichibabin* reaction). Tautomerism – pyridones. Pyridine derivatives of biological significance – nicotinamide, nicotine, vitamin B_6.

27. Heterocyclic compounds fused with benzene. *Skraup* synthesis of quinoline and *Bischler-Napieralski* synthesis of isoquinoline. Quinoline and isoquinoline alkaloids – examples. Acridine, benzazepines.

28. Five-membered heterocyclic compounds with two heteroatoms. Oxazoles, thiazoles and diazols – nomenclature and general characterization. Representatives with biological activity. Pyrazolone derivatives, synthesis of antipyrine.

29. Six-membered heterocyclic compounds with two heteroatoms. Oxazines, thiazines and diazines – nomenclature and general characteristic. Lactam-lactim tautomerism in pyrimidine hydroxyl derivatives. Representatives with biological activity – barbiturates, pyrimidine bases, nucleosides, and nucleotides.

30. Fused heterocyclic compounds. Purines and pteridines – nomenclature and general characteristic. Purine nucleic acid bases, DNA and RNA structure, purine alkaloids. Derivatives of biological activity – folic and folinic acid, alloxazine and isoaloxazine, riboflavin.

PRACTICAL TRAINING

1. Safety rules for work in organic chemistry laboratory. Laboratory equipment. Basic laboratory techniques. Methods for purification of solids.

2. Methods for separation and purification of liquids. Types of distillation. Extraction and drying.

3. Chromatographic methods for separation, purification, and identification of organic compounds.

4. Seminar "Nomenclature of organic compounds. Conformational and Optical Isomerism". Theoretical, practical and percentage yield of reaction products. Preparation of butyl acetate.

5. Seminar "Preparation and properties of alkenes and alkynes". Preparation of 2-chlorobutane.

6. Colloquium "Nomenclature and isomerism of organic compounds. Properties of Hydrocarbons". Electrophilic substitution reactions. Iodination of salicylamide.

7. Seminar "Preparation and properties of alcohols, diols, thioalcohols and phenols". Elimination and oxidation reactions of alcohols. Preparation of cyclohexene and cyclohexanol.

8. Seminar: Properties of alcohols and phenols. Nucleophilic substitution reactions. Preparation of phenoxyacetic acid.

9. Seminar: Nucleophilic addition and condensation reactions of aldehydes and ketones. Synthesis of cinnamic acid.

10. Seminar: Preparation and chemical properties of carboxylic acids. Esterification – synthesis of benzocaine.

11. Seminar: Functional derivatives of carboxylic acids. Syntheses of aspirin and paracetamol.

12. Colloquium "Carboxylic acids and their derivatives". Seminar: Preparation and chemical properties of aliphatic and aromatic amines. Preparation of diazoaminobenzene.

13. Seminar: Classification and properties of heterocyclic compounds. *Fischer* indole ring synthesis.

14. Alkaloids. Isolation of organic substances from natural products – isolation of caffeine from tea.

15. Synthesis of medicinal substances; obtaining antipyrine and diphenin.

BIBLIOGRAPHY

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2. John McMurry. Organic Chemistry, 9th edition. Cengage Learning, 2016.
3. Leroy G. Wade. Organic Chemisty. 8th edition. Prentice Hall; 2012.
4. Paul Dewick. Essentials of organic chemistry for students of pharmacy, medicinal chemistry and biological chemistry. John Wiley & Sons, 2009.

CONSPECTUS

1. Basic concepts in organic chemistry
2. Electronic effects in organic molecules.
3. Alkanes and cycloalkanes.
4. Conformational isomerism
5. Optical isomerism
6. Alkenes and cycloalkenes.
7. Alkynes and dienes.
8. Arenes.
9. Alcohols, diols, and thioalcohols.
10. Phenols.
11. Aldehydes and ketones.
12. Carboxylic acids.
13. Functional derivatives of carboxylic acids.
14. Acetoacetate and malonic ester.
15. Oxy and oxo acids.
16. Natural esters.
17. Terpenes and steroids.
18. Monosaccharides.
19. Disaccharides and polysaccharides.
20. Aliphatic and aromatic amines.
21. Amino alcohols, amino phenols, and amino acids.
22. Peptides and proteins.
23. Five-membered aromatic heterocyclic compounds.
24. Six-membered heterocyclic compounds.
25. Six-membered heterocyclic compounds fused with benzene.
26. Five-membered heterocyclic compounds with two heteroatoms.
27. Six-membered heterocyclic compounds with two heteroatoms.
28. Heterocyclic compounds with fused rings.

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