MINISTRY OF HEALTH OF UKRAINE
BOGOMOLETS NATIONAL MEDICAL UNIVERSITY

GUIDELINES
to the practical classes

Discipline of choice "Theoretical foundations of synthesis and the relationship between the structure and action of medicinal products"

Field of knowledge 22 Health care

Specialty 226 "Pharmacy, industrial pharmacy"

Specialization 226.01 "Pharmacy"

Form of study Full-day

Department of medicinal chemistry and toxicology

Approved at the meeting of the department on "30"August 2024, protocol No. 14

Head of the Department of medicinal chemistry and toxicology
Doctor of Medicine, Professor Nizhenkovska I.V.

Considered and approved:
on the meeting of cycle methodical commission of specialty 226 "Pharmacy, industrial pharmacy" dated August 30, 2024, protocol No. 1

Topic N 1. Implementation of the main stages of organic synthesis: delineation of the structure of the target molecule, consideration of possible synthesis schemes, selection of products, conducting chemical reactions, isolation of intermediate and target products, their analysis and purification. Single-reactor synthesis of multifunctional derivatives of biologically active substances (medicines).

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized foundations of scientific knowledge regarding the implementation of the main stages of organic synthesis (one-reactor synthesis): delineation of the structure of the target molecule, consideration of possible synthesis schemes, selection of products, conducting chemical reactions, selection of intermediate and target products, their analysis and purification; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation tasks, situational tasks), a workbook, a calculator, a set of laboratory dishes - devices for distillation and synthesis.

Class plan and organizational structure:

Name of the	Content of the stages	Levels of	Time

stage		assimilation	
Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks of extracurricular independent work	Reproductive	20 min
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.1-2. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. Piir, G.; Sild, S.; Maran, U. Data for: Interpretable machine learning for the identification of estrogen receptor agonists, antagonists, and binders. QsarDB repository, QDB.259. **2023**. http://dx.doi.org/10.15152/QDB.259

2. *Organic Syntheses*: *http://www.orgsyn.org/*.

3. Hartmuth C. Kolb, M. G. Finn, K. Barry Sharpless: Click Chemistry: Diverse

Chemical Function from a Few Good Reactions. In: Angew. Chem. Int. Ed. 2001, Band 40, S. 2004; *DOI:10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.0.CO;2-5.*

4. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. **2022**. http://dx.doi.org/10.15152/QDB.257

Information resources

1.Europian Pharmacopoeia- pheur.edqm.eu
2.The British Pharmacopoeia 2021 - www.pharmacopoeia.com
3.The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com
4.Pharmacopoea USP. www.usp.org.

5.Website of the Department of Medicinal Chemistry and Toxicology of Bogomolets NMU

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

6.Distance learning platform LIKAR_NMU https://likar.nmu.kiev.ua/

7.Official website of the Ministry of Health of Ukraine https://moz.gov.ua/

8.Journal of Medicinal Chemistry (J. Med. Chem.)

9.QSAR & Combinatorial Science (QSAR Comb. Sci.)

10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. Describe organic synthesis. Its purpose and tasks.
2. Single-reactor synthesis. Its advantages.
3. Name the types of reactions by mechanism: radical, electrophilic, nucleophilic. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
4. Addition-detachment reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
5. Condensation reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
6. Cyclization reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
7. Rearrangement reactions. Give examples of such reactions in the synthesis of

biologically active compounds and drugs.
8. Aromatization reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
9. What is the essence of "click" synthesis. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
10. Name the sources of raw materials for organic synthesis. Cyclization reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs and indicate the sources of raw materials.
11. Reagents and solvents in synthesis. Give examples of such reactions in the synthesis of biologically active compounds and drugs and indicate which reagents and solvents are used in these reactions.
12. Electronic effects in a molecule. Give the chemical formulas of biologically active compounds and drugs. Indicate what electronic effects operate in this molecule. How does it affect its reactivity?
13. Functional groups. Give the chemical formulas of biologically active compounds and drugs. Indicate which functional groups are present in this molecule. How do they affect its reactivity?
14. Methods of purification of chemical substances (filtering, recrystallization, extraction, distillation). Describe the methods.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 2. Pharmacophore groups. Variability of molecules based on bioisosteric substitution. Peptide and double bond; aldehyde and imine groups, SH, NH2, CH3, OH-groups, S, NH, CH2O-linkers. QSAR, SAR analysis.

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized bases of scientific knowledge regarding the main concepts of the topic – pharmacophore groupings, variability of molecules based on bioisosteric substitution (peptide and double bond; aldehyde and imine groups, SH, NH2, CH3, OH-groups, S, NH, CH2O-linkers), computer prediction of chemical and biological properties of BAS and drugs using QSAR, SAR analysis; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, computer programs.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time

Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks of extracurricular independent work	Reproductive	20 min
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.1-25. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. *Organic Syntheses*: *http://www.orgsyn.org/.*

2. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. **2022**. http://dx.doi.org/10.15152/QDB.257

Information resources

1.Europian Pharmacopoeia- pheur.edqm.eu

2.The British Pharmacopoeia 2021 - www.pharmacopoeia.com
3.The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com
4.Pharmacopoea USP. www.usp.org.

5.Website of the Department of Medicinal Chemistry and Toxicology of Bogomolets NMU

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

6. Distance learning platform LIKAR_NMU https://likar.nmu.kiev.ua/

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8.Journal of Medicinal Chemistry (J. Med. Chem.)

9.QSAR & Combinatorial Science (QSAR Comb. Sci.)

10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. What is CADD? What are the positive features of automated drug design?
2. QSAR, SAR analysis and their role in predicting BAR activity.
3. What methods of "drug design" are relevant today?
4. Describe the concept of "molecular docking".
5. Pharmacophores. Give a description. Specify the pharmacophores in the structures of the molecules - active substances of sulfonamides, benzodiazepines, barbiturates. Phenanthren isoquinolines, etc.
6. Scaffolds. Give examples of scaffolds in molecules of active substances - representatives of drug classes.
7. Task of bioisosteric substitution.
8. Linkers. Give examples of linkers: peptide and double bond; aldehyde and imine groups, SH, NH2, CH3, OH-groups, S, NH, CH2O-linkers in the molecules of active substances - representatives of drug classes.
9. Design de novo. Main tasks.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 3. Ways to improve ADME/Tox parameters of biologically active compounds: modifications by hydroxy-, mercapto-, carboxy-, caralkyloxy-, carbonyl, amino groups.

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form a systematized basis of scientific knowledge regarding the main methods of improving ADME/Tox parameters of biologically active compounds: modifications by hydroxy-, mercapto-, carboxy-, carbalkyloxy, carbonyl, amino groups; to form systematized bases of scientific knowledge regarding basic synthetic methods of obtaining double-, double-, hybrid-molecules as biologically active compounds, methods of synthesis of pro-drugs and protective groups in organic synthesis; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, computer programs.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the	Familiarization	5 min

	presence of students)		
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks of extracurricular independent work	Reproductive	20 min
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-55. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. *Organic Syntheses*: *http://www.orgsyn.org/.*

2. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. 2022. http://dx.doi.org/10.15152/QDB.257

Information resources

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5.Website of the Department of Medicinal Chemistry and Toxicology of Bogomolets NMU

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

6. Distance learning platform LIKAR_NMU https://likar.nmu.kiev.ua/

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10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. ADME, role and tasks.
2. Describe the processes: absorption, distribution, metabolism, excretion.
3. Name the ways of excretion of substances.
4. SwissADME and protox-II programs and their purpose.
5. How does the chemical structure of substances affect ADME parameters?
6. What methods and reactions are used to modify the hydroxy group? Give examples. Write the reaction schemes.
7. What methods and reactions are used to modify the mercapto group? Give examples. Write the reaction schemes.
8. What methods and reactions are used to modify the carboxyl group? Give examples. Write the reaction schemes.
9. What methods and reactions are used to modify the carbolic group? Give examples. Write the reaction schemes.
10. What methods and reactions are used to modify the carbonyl (aldehyde and keto) group? Give examples. Write the reaction schemes.
11. What methods and reactions are used to modify the amino group? Give examples. Write the reaction schemes.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 4. Synthetic methods of obtaining double-, hybrid-molecules as biologically active compounds, methods of synthesis of pro-drugs. Protective groups in organic synthesis. *Control work 1.*

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form a systematized basis of scientific knowledge regarding the main methods of improving ADME/Tox parameters of biologically active compounds: modifications by hydroxy-, mercapto-, carboxy-, carbalkyloxy, carbonyl, amino groups; to form systematized bases of scientific knowledge regarding basic synthetic methods of obtaining double-, double-, hybrid-molecules as biologically active compounds, methods of synthesis of pro-drugs and protective groups in organic synthesis; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, computer programs.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the	Familiarization	5 min

	presence of students)		
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks of extracurricular independent work	Reproductive	20 min
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-55. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. *Organic Syntheses*: *http://www.orgsyn.org/.*

2. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. 2022. http://dx.doi.org/10.15152/QDB.257

Information resources

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2.The British Pharmacopoeia 2021 - www.pharmacopoeia.com

3.The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com
4.Pharmacopoea USP. www.usp.org.

5.Website of the Department of Medicinal Chemistry and Toxicology of Bogomolets NMU

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

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10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. The concept of multistage syntheses. Give examples of multistage synthesis of a medicinal product.
2. Concept of target molecule (TM).
3. "Powerful reactions" of synthesis and their examples.
4. Building block. Give examples of a building block in the synthesis of a medicinal product.
5. Main types of strategic relationships.
6.Principles of Carbon-Carbon Bond Construction. Give examples of the construction of a C-C bond during the synthesis of a medicinal product.

Control work No. 1 - on questions of topics 1-4.

List of questions for control work No. 1.

1. Describe organic synthesis. Its purpose and tasks.
2. Single-reactor synthesis. Its advantages.
3. Name the types of reactions by mechanism: radical, electrophilic, nucleophilic. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
4. Addition-detachment reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
5. Condensation reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.
6. Cyclization reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.

7. Rearrangement reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.

8. Aromatization reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs.

9. What is the essence of "click" synthesis. Give examples of such reactions in the synthesis of biologically active compounds and drugs.

10. Name the sources of raw materials for organic synthesis. Cyclization reactions. Give examples of such reactions in the synthesis of biologically active compounds and drugs and indicate the sources of raw materials.

11. Reagents and solvents in synthesis. Give examples of such reactions in the synthesis of biologically active compounds and drugs and indicate which reagents and solvents are used in these reactions.

12. Electronic effects in the molecule. Give the chemical formulas of biologically active compounds and drugs. Indicate what electronic effects operate in this molecule. How does it affect her reactivity.

13. Functional groups. Give the chemical formulas of biologically active compounds and drugs. Indicate which functional groups are present in this molecule. How do they affect her reactivity.

14. Methods of purification of chemical substances (filtering, recrystallization, extraction, distillation). Describe the methods.

15. What is CADD? What are the positive features of automated drug design?

16. QSAR, SAR analysis and their role in predicting BAS activity.

17. What methods of "drug design" are relevant today?

18. Describe the concept of "molecular docking".

19. Pharmacophores. Give a description. Specify the pharmacophores in the structures of the molecules - the active substances of sulfonamides, benzodiazepines, barbiturates, phenanthrenisoquinolines, etc.

20. Scaffolds. Give examples of scaffolds in molecules of active substances - representatives of drug classes.

21. The task of bioisosteric substitution.

22. Linkers. Give examples of linkers: peptide and double bond; aldehyde and imine groups, SH, NH_2, CH_3, OH-groups, S, NH, CH_2O-linkers in the molecules of active substances - representatives of drug classes.

23. De novo design. Main tasks.

24. What does the abbreviation ADME stand for?

25. Describe the processes: absorption, distribution, metabolism, excretion.

26. Name the ways of excretion of substances.

27. SwissADME and protox-II programs and their purpose.

28. How does the chemical structure of substances affect ADME parameters?

29. What methods and reactions are used to modify the hydroxy group? Give examples. Write the reaction schemes.

30. What methods and reactions are used to modify the mercapto group? Give examples. Write the reaction schemes.

31. What methods and reactions are used to modify the carboxyl group? Give examples. Write the reaction schemes.

32. What methods and reactions are used to modify the carbonyl (aldehyde and keto) group? Give examples. Write the reaction schemes.

33. What methods and reactions are used to modify the amino group? Give examples. Write the reaction schemes.

34. The concept of multistage syntheses. Give examples of multistage synthesis of a medicinal product.

35. Concept of target molecule (TM).

36. "Powerful reactions" of synthesis and their examples.

37. Building block. Give examples of a building block in the synthesis of a medicinal product.

38. Main types of strategic relationships.

39. Principles of Carbon-Carbon Bond Construction. Give examples of the construction of a C-C bond during the synthesis of a medicinal product.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 5. Derivatives of phenyl(heteryl)ethylamines as biogenic amines and drugs, methods of synthesis/modification. Structure-activity relationship.

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized foundations of scientific knowledge regarding the main methods of synthesis and modification of molecules of derivatives of phenyl(heteryl)ethylamines, as biogenic amines and drugs, and their structure-activity relationship; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, computer programs.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min

	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks of extracurricular independent work	Reproductive	20 min
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-55. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. *Organic Syntheses*: *http://www.orgsyn.org/.*

2. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. **2022**. http://dx.doi.org/10.15152/QDB.257

Information resources

1.Europian Pharmacopoeia- pheur.edqm.eu
2.The British Pharmacopoeia 2021 - www.pharmacopoeia.com
3.The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com
4.Pharmacopoea USP. www.usp.org.

5.Website of the Department of Medicinal Chemistry and Toxicology of Bogomolets NMU

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

6. Distance learning platform LIKAR_NMU https://likar.nmu.kiev.ua/

7.Official website of the Ministry of Health of Ukraine https://moz.gov.ua/

8.Journal of Medicinal Chemistry (J. Med. Chem.)

9.QSAR & Combinatorial Science (QSAR Comb. Sci.)

10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. Methods of synthesis of phenyl(heteryl)ethylamine derivatives.
2. Peculiarities of the chemical structure of molecules of active substances of local anesthetic agents.
3. Classifications of local anesthetic agents.
4. Mechanism of action of local anesthetic agents.
5. Influence of the chemical structure of molecules on the solubility of local anesthetics.
6. Functional groups in the composition of molecules of active substances of local anesthetic agents.
7. Relationship between the structure and activity of the molecules of active substances of local anesthetic agents.
8. Structure-activity dependence of drugs affecting the serotonergic system.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 6. Local anesthetic agents, methods of synthesis/modifications. Structure activity relationship. Establishment of pharmacophore grouping.

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized bases of scientific knowledge regarding local anesthetic agents and sulfonamides, methods of their synthesis and modification, structure-activity relationship, establishment of pharmacophore grouping; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, calculator, program for computer prediction of BAS properties.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks	Reproductive	20 min

	of extracurricular independent work		
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-55. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. Piir, G.; Sild, S.; Maran, U. Data for: Interpretable machine learning for the identification of estrogen receptor agonists, antagonists, and binders. QsarDB repository, QDB.259. **2023**. http://dx.doi.org/10.15152/QDB.259

2. *Organic Syntheses*: *http://www.orgsyn.org/.*

3. Hartmuth C. Kolb, M. G. Finn, K. Barry Sharpless: Click Chemistry: Diverse Chemical Function from a Few Good Reactions. In: Angew. Chem. Int. Ed. 2001, Band 40, S. 2004; *DOI:10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.0.CO;2-5.*

4. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB

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Information resources

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http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

6. Distance learning platform LIKAR_NMU https://likar.nmu.kiev.ua/

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10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. Describe the features of the chemical structure of molecules of active substances of local anesthetic agents: lipophilic and hydrophilic parts, intermediate chain.
2. Describe the "structure-activity" relationship in the Articaine molecule.
3. Articaine. Peculiarities of metabolism. What active metabolites are formed? What features of the chemical structure do active metabolites have?
4. Describe the "structure-activity" relationship in the Bupivacaine molecule.
5. Bupivacaine. Peculiarities of metabolism. What active metabolites are formed? What features of the chemical structure do active metabolites have?
6. Describe the "structure-activity" relationship in the Lidocaine molecule.
7. Lidocaine. Peculiarities of metabolism. What active metabolites are formed? What features of the chemical structure do active metabolites have?
8. Describe the main regularities of the influence of "structure-activity" of local anesthetic agents - Aminoesters.
9. Describe the main regularities of the "structure-activity" effect of local anesthetic agents - Aminoamides.
10. Describe the main regularities of the "structure-activity" effect of local

anesthetic agents - Aminoethers.
11. Describe the main regularities of the "structure-activity" influence of local anesthetic agents - Aminoketones.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 7. Sulfanilamides, methods of synthesis/modifications. Structure-activity relationship.

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized bases of scientific knowledge regarding sulfonamides, methods of their synthesis and modification, structure-activity relationship, establishment of pharmacophore grouping; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, calculator, program for computer prediction of BAS properties.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks	Reproductive	20 min

	of extracurricular independent work		
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-55. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. Piir, G.; Sild, S.; Maran, U. Data for: Interpretable machine learning for the identification of estrogen receptor agonists, antagonists, and binders. QsarDB repository, QDB.259. **2023**. http://dx.doi.org/10.15152/QDB.259

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3. Hartmuth C. Kolb, M. G. Finn, K. Barry Sharpless: Click Chemistry: Diverse Chemical Function from a Few Good Reactions. In: Angew. Chem. Int. Ed. 2001, Band 40, S. 2004; *DOI:10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.0.CO;2-5.*

4. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. 2022. http://dx.doi.org/10.15152/QDB.257

5. Peng Wu, Joachim Demaerel, Deshen Kong, Ding Ma, Carsten Bolm. Copper-

Catalyzed, Aerobic Synthesis of NH-Sulfonimidamides from Primary Sulfinamides and Secondary Amines. *Organic Letters* 2022, *24* (38), 6988-6992. https://doi.org/10.1021/acs.orglett.2c02804

6.Matthew A. Sguazzin, Jarrod W. Johnson, Jakob Magolan. Hexafluoroisopropyl Sulfamate: A Useful Reagent for the Synthesis of Sulfamates and Sulfamides. *Organic Letters* 2021, *23* (9), 3373-3378. https://doi.org/10.1021/acs.orglett.1c00855

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Information resources

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3.The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com
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10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. Peculiarities of the chemical structure of sulfonamide molecules.
2. Classifications of sulfonamide drugs.
3. Mechanism of action, pharmacokinetics, indications, side effects.
4. Chemical formulas of sulfonamides and features of synthesis/modification of their molecules, bioisosteric substitutions, scaffold.
5. Sulfacetamide, Sulfacil sodium. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
6. Sulfamethoxazole. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
7. Phthalazole. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
8. The main regularities of the interaction of the chemical structure and biological activity of sulfonamides.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 8. The pyridine cycle as an example of «preferred structures», methods of synthesis/modifications of pyridine derivatives. Structure-activity relationship.

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized bases of scientific knowledge regarding pyridine compounds as an example of "privileged structures", methods of synthesis and modification of pyridine derivatives, structure-activity relationship; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, calculator, program for computer prediction of BAS properties.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey,	Reproductive	20 min

	verification of the performance of tasks of extracurricular independent work		
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-70. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

Auxiliary

1. Islam MB, Islam MI, Nath N, Emran TB, Rahman MR, Sharma R, Matin MM. Recent Advances in Pyridine Scaffold: Focus on Chemistry, Synthesis, and Antibacterial Activities. Biomed Res Int. 2023 May 18; 2023: 9967591. doi: 10.1155/2023/9967591. PMID: 37250749; PMCID: PMC10212683.

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3. *Organic Syntheses*: *http://www.orgsyn.org/*.

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Information resources

1.Europian Pharmacopoeia- pheur.edqm.eu
2.The British Pharmacopoeia 2021 - www.pharmacopoeia.com
3.The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com
4.Pharmacopoea USP. www.usp.org.

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9.QSAR & Combinatorial Science (QSAR Comb. Sci.)

10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1.Write the chemical formulas of pyridine derivatives, which are biologically active substances of natural and synthetic origin.
2. What structure acts as a scaffold in the creation of new molecules of biologically active pyridine derivatives?
3. Name the vitamins that contain pyridine derivatives.
4. What is the difference between the chemical structure of Pyridoxine, Pyridoxal and Pyridoxamine? For what purpose are these compounds used in pharmaceutical and medical practices?
5. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Ftivazid. What active metabolites are formed?
6. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Nicotinic acid and Nicotinamide.

7. Give a description of the "structure-activity" relationship and the features of Cordiamine's metabolism.
8. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Pyriditol.
9. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Isoniazid.
10. Describe the "structure-activity" relationship and the peculiarities of Mexidol's metabolism.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 9. Derivatives of pyrimidine (barbiturates) as drugs and biological active compounds, methods of synthesis/modification. Structure-activity relationship. *Control work N2.*

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized bases of scientific knowledge regarding the features of the structure, methods of synthesis and modification of pyrimidine derivatives (barbiturates), structure-activity relationship; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, calculator, program for computer prediction of BAS properties.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks	Reproductive	20 min

	of extracurricular independent work		
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (control work - auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-70. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

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Auxiliary

1. *Organic Syntheses*: *http://www.orgsyn.org/.*

2. Hartmuth C. Kolb, M. G. Finn, K. Barry Sharpless: Click Chemistry: Diverse Chemical Function from a Few Good Reactions. In: Angew. Chem. Int. Ed. 2001, Band 40, S. 2004; *DOI:10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.0.CO;2-5.*

3. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. **2022**. http://dx.doi.org/10.15152/QDB.257

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6. Distance learning platform LIKAR_NMU https://likar.nmu.kiev.ua/

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9.QSAR & Combinatorial Science (QSAR Comb. Sci.)

10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. Describe the features of the chemical structure of barbituric acid.
2. How does the presence of basic centers in the barbituric acid molecule and the phenomenon of tautomerism affect its chemical properties? Give examples of reactions.
3. What biologically active pyrimidine derivatives are used in medical and pharmaceutical practices? Give their structural formulas.
4. What types of tautomerism are characteristic of barbiturates? Give schemes of tautomeric conversion using Phenobarbital as an example.
5. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Barbital. Describe the "structure-activity" relationship and the peculiarities of Phenobarbital metabolism.
6. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Benzonal.
7. Give a description of the "structure-activity" relationship and the features of Ethaminal-sodium metabolism.
8. Describe the "structure-activity" relationship and the features of Thiopental-sodium metabolism.
9. How does the toxicity of a number of barbituric acid derivatives depend on modifications of their structure?

Control work No. 2 - on questions of topics 5-9.

List of questions for control work No. 2.

1. Methods of synthesis of phenyl(heteryl)ethylamine derivatives.
2. Peculiarities of the chemical structure of molecules of active active substances of local anesthetics.
3. Classifications of local anesthetics.
4. Mechanism of action of local anesthetics.
5. Influence of the chemical structure of molecules on the solubility of local anesthetics.
6. Functional groups in the composition of molecules of active active substances of local anesthetics.
7. Relationship between the structure and activity of the molecules of active active substances of local anesthetics.
8. Features of the chemical structure of molecules of active substances of local anesthetic agents: lipophilic and hydrophilic parts, intermediate chain.
9. Articaine. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
10. Bupivacaine. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
11. Lidocaine. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
12. Aminoesters. Characteristics of the "structure-activity" relationship.
13. Aminoamides. Characteristics of the "structure-activity" relationship.
14. Amino ethers. Characteristics of the "structure-activity" relationship.
15. Aminoketones. Characteristics of the "structure-activity" relationship.
16. Peculiarities of the chemical structure of sulfonamide molecules.
17. Classifications of sulfonamide drugs.
18. Mechanism of action, pharmacokinetics, indications, side effects.
19. Chemical formulas of sulfonamides and features of synthesis/modification of their molecules, bioisosteric substitutions, scaffold.
20. Sulfacetamide, Sulfacil sodium. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
21. Sulfamethoxazole. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
22. Phthalazole. Characteristics of the "structure-activity" relationship. Peculiarities of metabolism.
23. The main regularities of the interaction of the chemical structure and biological activity of sulfonamides.
24. Peculiarities of the chemical structure of the pyridine molecule and its derivatives.
25. Methods of synthesis of pyridine and its derivatives.
26. Substances of natural origin - pyridine derivatives. Alkaloids.
27. Toxicity of pyridine.

28. Metabolism of pyridine.
29. Chemical modifications of the pyridine molecule.
30. Medicinal products that contain a scaffold - a pyridine cycle.
31. Medicinal products are pyridine derivatives. Synthesis, features of the chemical structure and biological activity.
32. The main regularities of the interaction of the chemical structure and biological activity of pyridine derivatives.
33. Features of the chemical structure of barbituric acid molecules and its derivatives.
34. Methods of synthesis of barbituric acid and its derivatives and their chemical modifications. Scaffold.
35. Toxicity of barbituric acid and its derivatives.
36. Metabolism of barbituric acid and its derivatives.
37. Medicinal products containing a pyrimidine cycle scaffold.
38. Medicinal products are derivatives of barbituric acid. Peculiarities of the chemical structure and biological activity.
39. The main regularities of the interaction of the chemical structure and biological activity of barbiturates.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V., as. professor, PhD Golovchenko O.I.

Topic N 10. Purine derivatives as drugs and biologically active compounds, methods of synthesis/modification. Structure-activity relationship. ***Differentiated credit.***

Competencies:

integral: the ability to solve tasks of a research and/or innovative nature in the field of pharmacy and in the field of industrial production of medicinal products.

general:

GC01. Ability to abstract thinking, analysis and synthesis.

GC02. Knowledge and understanding of the subject area; understanding of professional activity.

GC03. Ability to communicate in the national language both orally and in writing.

GC05. Ability to evaluate and ensure the quality of the work performed.

GC06. Ability to work in a team.

GC09. Ability to use information and communication technologies

GC10. Ability to make decisions and act in accordance with the principle of inadmissibility of corruption and any other manifestations of dishonesty.

professionals:

PC02. Ability to collect, interpret and apply data necessary for professional activity, research and implementation of innovative projects in the field of pharmacy.

PC03. Ability to solve pharmacy problems in new or unfamiliar environments in the presence of incomplete or limited information, taking into account aspects of social and ethical responsibility.

PC04. Ability to clearly and unambiguously convey one's own knowledge, conclusions and arguments in the field of pharmacy to specialists and non-specialists, in particular to people who are studying.

Purpose: to form systematized bases of scientific knowledge regarding the peculiarities of the chemical structure of purine derivatives, methods of their synthesis and modification, structure-activity relationship; to provide an approximate basis for further assimilation of educational material in practical classes.

Equipment: practical tasks (tests, calculation problems, situational problems), workbook, calculator, program for computer prediction of BAS properties.

Class plan and organizational structure:

Name of the stage	Content of the stages	Levels of assimilation	Time
Preparatory	Organizational issues (checking the presence of students)	Familiarization	5 min
	Formation of motivation, activation of cognitive activity	Perception	5 min
	Control of the initial level of training: test control and/or individual survey, verification of the performance of tasks	Reproductive	20 min

	of extracurricular independent work		
Basic	Debate and discussion of theoretical issues according to the subject of the class	Comprehension Understanding	15 min
	Solving calculation and situational problems	Application in practice Search creative activity	25 min
	Independent work of the student under the supervision of the teacher (auditory work of the student)	Application in practice Search creative activity	20 min
	Generalization of knowledge	Fixing	10 min
Final	Control of the final level of training (solving calculation and situational problems)	Playback	20 min
	General evaluation of the student's educational activity	Familiarization	10 min
	Informing students about the topic of the next lesson and tasks for independent work	Familiarization	5 min

Recommended literature:

Basic

1.Jiashun Mao, Javed Akhtar, Xiao Zhang, Liang Sun, Shenghui Guan, Xinyu Li et al. Comprehensive strategies of machine-learning-based quantitative structure-activity relationship models. iScience 24, 103052, 2021, p.30-70. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

2.M. V. Tarasca, C. J. Tomlinson, P. Gris, G. K. Murphy. *One-Step, Gram-Scale Synthesis of Caffeine-d_9 from Xanthine and CD_3I*. *Synthesis* **2022**, DOI: 10.1055/a-1972-3819

Auxiliary

1. Piir, G.; Sild, S.; Maran, U. Data for: Interpretable machine learning for the identification of estrogen receptor agonists, antagonists, and binders. QsarDB repository, QDB.259. **2023**. http://dx.doi.org/10.15152/QDB.259

2. *Organic Syntheses*: *http://www.orgsyn.org/*.

3. Hartmuth C. Kolb, M. G. Finn, K. Barry Sharpless: Click Chemistry: Diverse Chemical Function from a Few Good Reactions. In: Angew. Chem. Int. Ed. 2001,

Band 40, S. 2004; *DOI:10.1002/1521-3773(20010601)40:11<2004::AID-ANIE2004>3.0.CO;2-5.*
4. Oja, M.; Sild, S.; Piir, G.; Maran, U. Data for: Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. QsarDB repository, QDB.257. **2022**. http://dx.doi.org/10.15152/QDB.257

Information resources

1.Europian Pharmacopoeia- pheur.edqm.eu
2.The British Pharmacopoeia 2021 - www.pharmacopoeia.com
3.The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com
4.Pharmacopoea USP. www.usp.org.

5.Website of the Department of Medicinal Chemistry and Toxicology of Bogomolets NMU

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

6. Distance learning platform LIKAR_NMU https://likar.nmu.kiev.ua/

7.Official website of the Ministry of Health of Ukraine https://moz.gov.ua/

8.Journal of Medicinal Chemistry (J. Med. Chem.)

9.QSAR & Combinatorial Science (QSAR Comb. Sci.)

10.Quantitative Structure-Activity Relationships (Quant. Struct.-Act. Relat.)

11.Journal of Chemometrics (J. Chemom.)

12.Journal of Chemical Information and Modeling (J. Chem. Inf. Model.)

13.QSAR Research Unit of the University of Insubria

Questions for student self-preparation for the class:

1. How are purine derivatives classified?
2. Describe the features of the chemical structure of methylated purines - xanthines. Prove the amphoteric properties of xanthines using chemical equations.
3. What alkaloids - purine derivatives are used in medical and pharmaceutical practices? Give their structural formulas.
4. Describe the features of the chemical structure of Caffeine, Theophylline and Theobromine. How are their molecules different?
5. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Acyclovir.
6. Give a description of the "structure-activity" relationship and the features of the metabolism of Adenosine triphosphoric acid (ATP).

7. Describe the "structure-activity" relationship and the features of Riboxin's metabolism.
8. Give a description of the "structure-activity" relationship and the peculiarities of the metabolism of Diprofilin.
9. How does the toxicity of a number of purine derivatives depend on modifications of their structure?

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