MINISTRY OF HEALTH OF UKRAINE
BOGOMOLETS NATIONAL MEDICAL UNIVERSITY

GUIDELINES
to the lectures

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-time

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 N1. Basic modern strategies for finding new medicines. The use of modern technologies in the search for new medicines. Drug design methodology. Dual-, hybrid-, pro-drugs.

Type of lecture: traditional (informational)

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 the systematized foundations of scientific knowledge regarding the main modern strategies for the search for new drugs, the use of modern technologies in the search for new drugs, the methodology of "drug design", dual and hybrid structures, pro-drugs; to provide an approximate basis for further assimilation of educational material in practical classes.

Lecture equipment: laptop, multimedia projector, blackboard.

Tasks of the lecture:

the student should know

basics of organic synthesis;

peculiarities of conduct and devices for laboratory synthesis;

ways of modeling biologically active molecules;

principles of strategy and tactics of organic synthesis of biologically active substances (BAS) and medicinal products (MP);

classification of BAS of organic and inorganic origin;

methods of isolation and purification of chemical substances - products of reactions and methods of their analysis using chemical and physical-chemical methods;

Plan of the Lecture

The name the stage of the lecture	Content of the stages	Educational goal of the stage	Time
Introduction	Announcement of the topic of the lecture, plan o lecture, definition of the purpose of the lecture, a description of the problems proposed to be considered during lecture, a brief description of the literature.	Activation of the previously acqu scientific knowledge of students other disciplines and laying the scien basis for assimilating the le material.	10 min
Main part	1.Elective discipline "Theoretical foundations of synthesis and the relationship betv the structure and action of medicinal produ Purpose and task: to reveal the content, purpose tasks of the elective discipline. 2. Organic synthesis as the main tool for the cre of biologically active substances (BAS) medicines (MP): reveal the basic technique organic synthesis, familiarize yourself with chen utensils and the rules for assembling the device. 3. Strategy and tactics of organic synthesis of BAS and drugs: emphasize the main techniques i development of new biologically active substa list modern strategies and tactics of organic synthe	To acquire knowledge about the sci of creating new biologically a molecules and the relationship betv their chemical structure and biolo activity. To acquire knowledge about metho creating new biologically a molecules, methods of their synth taking into account the relation between their chemical structure biological activity. Get acquainted with the strategy tactics of the organic synthesis of BAS and drugs.	65 min
Final part	Generalization in short formulations of the main i of the lecture, logically concluding it as a com work; direction of further independent work students; laying the scientific basis for the follo lectures.	Learning the actual material of lecture, the main theoretical provis with the help of logical nodes - the questions of the lecture.	15 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. Piir, G.; Sild, S.; Maran, U. Interpretable machine learning for the identification of estrogen receptor agonists, antagonists, and binders. *Chemosphere* **2024**, *347*, 140671. http://dx.doi.org/10.1016/j.chemosphere.2023.140671

3. Kotli, M.; Piir, G.; Maran, U. Data for: Pesticide effect on earthworm lethality via interpretable machine learning. QsarDB repository, QDB.258. **2023**. http://dx.doi.org/10.15152/QDB.258

4. Kotli, M.; Piir, G.; Maran, U. Pesticide effect on earthworm lethality via interpretable machine learning. *Journal of Hazardous Materials*. **2024**. http://dx.doi.org/10.1016/j.jhazmat.2023.132577

5. 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

6. Oja, M.; Sild, S.; Piir, G.; Maran, U. Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. *Pharmaceutics* **2022**, *14*, 2248. http://dx.doi.org/10.3390/pharmaceutics14102248

7. Lowe, C. N.; Charest, N.; Ramsland, C.; Chang, D. T.; Martin, T. M.; Williams, A. J. Transparency in Modeling through Careful Application of OECD's QSAR/QSPR Principles via a Curated Water Solubility Data Set. Chem. Res. Toxicol., **2023**, 36, 465–478. DOI: 10.1021/acs.chemrestox.2c00379

8. Sosnowska, A.; Bulawska, N.; Kowalska, D.; Puzyn, T. Towards Higher Scientific Validity and Regulatory Acceptance of Predictive Models for PFAS. Green Chem., **2023**, 25, 1261–1275. DOI: 10.1039/d2gc04341f

9. Gousiadou, C.; Doganis, P.; Sarimveis, H. Development of Artificial Neural Network Models to Predict the PAMPA Effective Permeability of New, Orally Administered Drugs Active against the Coronavirus SARS-CoV-2. Netw. Model. Anal. Health Inform. Bioinform., **2023**, 12. DOI: 10.1007/s13721-023-00410-9

10. Király, P.; Kiss, R.; Kovács, D.; Ballaj, A.; Tóth, G. The Relevance of Goodness-of-fit, Robustness and Prediction Validation Categories of OECD-QSAR Principles with Respect to Sample Size and Model Type. Mol. Inform., **2022**, 41, 2200072. DOI: 10.1002/minf.202200072

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 lecture:

1. Organic synthesis as the main tool for the practical creation of BASs and pharmaceuticals.
2. Methods of cleaning chemicals.
3. Laboratory utensils and devices for the synthesis of organic substances.
4. What is the task of subtle organic synthesis?
5. The essence of "green" chemistry.
6. Computer (calculated) screening. Its purpose and tasks. The concept of "descriptors" in computer prediction of the structure and properties of BAS and pharmaceuticals.
7. QSAR-analysis, SAR-analysis programs. Purpose and tasks.
8. The main principles of the strategy and tactics of creating BAS and pharmaceuticals.
9. The principle of "copying known pharmacological active substances".
10. The principle of "chemical modification of the structure of known synthetic and natural BASs and pharmaceuticals."
11. The principle of "pharmacophore introduction and modification".
12. Pro-medicine strategy.
13. The concept of "antagonists of natural metabolites".

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

Topic N2. Studying patterns of structure-activity dependence of barbituric acid derivatives as drugs and biologically active compounds at different stages of research. Synthetic approaches to obtaining barbiturates from classical to modern methods of synthesis.

Type of lecture: traditional (informational)

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 the systematized foundations of scientific knowledge regarding the main modern strategies for searching and studying patterns of structure-activity dependence of barbituric acid derivatives as drugs and biologically active compounds at various stages of research, synthetic approaches to obtaining barbiturates from classical to modern methods of synthesis; to provide an approximate basis for further assimilation of educational material in practical classes.

Lecture equipment: laptop, multimedia projector, blackboard.

Tasks of the lecture:

the student should know

basics of organic synthesis of barbituric acid derivatives;

patterns of structure-activity dependence of barbituric acid derivatives as drugs and biologically active compounds, based on the features of the chemical structure;

ways of modifying molecules of barbituric acid derivatives;
the strategy of pro-drugs in a number of synthesized barbiturates;
classical and modern methods of synthesis of barbituric acid derivatives;

Plan of the Lecture

The name the stage of the lecture	Content of the stages	Educational goal of the stage	Time
Introduction	Announcement of the topic of the lecture, of the lecture, definition of the purpose o lecture, a brief description of the problems proposed to be considered during lecture, a brief description of the literature.	Activation of the previously acqu scientific knowledge of students other disciplines and laying scientific basis for assimilating lecture material.	10 min
Main part	1. Peculiarities of the chemical structur barbituric acid derivatives as representative the class of pyrimidine drugs: to reveal peculiarities of the chemical structure pyrimidines.	To acquire knowledge about peculiarities of the chemical stru of pyrimidines and the possibilitie modifying their chemical structur consider the peculiarities of relationship between their chen structure and biological activity.	65 min
	2. Studying the regularities of the "struc biological activity" dependence of barbi acid derivatives: to reveal the peculiaritie the relationship "structure-biological acti of barbiturates as pyrimidine derivatives.	To acquire knowledge about peculiarities of the chemical stru of barbituric acid and its derivat the possibilities of modifying chemical structure, to consider peculiarities of the relation between their chemical structure biological activity.	
	3. Synthetic approaches to obtaining deriva of barbituric acid: consider classic and modern methods of synthesis of barbiturate	Get acquainted with the strategy tactics of the organic synthesis of derivatives of barbituric acid pyrimidines.	
Final part	Generalization in short formulations of the ideas of the lecture, logically concluding it complete work; direction of further indepen work of students; laying the scientific basi the following lectures.	Learning the actual material of lecture, the main theoretical provis with the help of logical nodes - main questions of the lecture.	15 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.1-6. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

2.Marianne H. Paulsen, Magnus Engqvist, Dominik Ausbacher, Trude Anderssen, et al. Amphipathic Barbiturates as Mimics of Antimicrobial Peptides and the Marine Natural Products Eusynstyelamides with Activity against Multi-resistant Clinical Isolates. *J. Med. Chem.* 2021, 64, 15, 11395–11417. Publication Date:July 27, 2021 https://doi.org/10.1021/acs.jmedchem.1c00734

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. Kotli, M.; Piir, G.; Maran, U. Data for: Pesticide effect on earthworm lethality via interpretable machine learning. QsarDB repository, QDB.258. **2023**. http://dx.doi.org/10.15152/QDB.258

4. Kotli, M.; Piir, G.; Maran, U. Pesticide effect on earthworm lethality via interpretable machine learning. *Journal of Hazardous Materials*. **2024**. http://dx.doi.org/10.1016/j.jhazmat.2023.132577

5. 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

6. Oja, M.; Sild, S.; Piir, G.; Maran, U. Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. *Pharmaceutics* **2022**, *14*, 2248. http://dx.doi.org/10.3390/pharmaceutics14102248

7. Lowe, C. N.; Charest, N.; Ramsland, C.; Chang, D. T.; Martin, T. M.; Williams, A. J. Transparency in Modeling through Careful Application of OECD's QSAR/QSPR Principles via a Curated Water Solubility Data Set. Chem. Res. Toxicol., **2023**, 36, 465–478. DOI: 10.1021/acs.chemrestox.2c00379

8. Sosnowska, A.; Bulawska, N.; Kowalska, D.; Puzyn, T. Towards Higher Scientific Validity and Regulatory Acceptance of Predictive Models for PFAS. Green Chem., **2023**, 25, 1261–1275. DOI: 10.1039/d2gc04341f

9. Gousiadou, C.; Doganis, P.; Sarimveis, H. Development of Artificial Neural Network Models to Predict the PAMPA Effective Permeability of New, Orally Administered Drugs Active against the Coronavirus SARS-CoV-2. Netw. Model. Anal. Health Inform. Bioinform., **2023**, 12. DOI: 10.1007/s13721-023-00410-9

10. Király, P.; Kiss, R.; Kovács, D.; Ballaj, A.; Tóth, G. The Relevance of Goodness-of-fit, Robustness and Prediction Validation Categories of OECD-QSAR Principles with Respect to Sample Size and Model Type. Mol. Inform., **2022**, 41, 2200072. DOI: 10.1002/minf.202200072

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 lecture:

1. Organic synthesis as the main tool for the synthesis of barbituric acid derivatives.
2. Patterns of structure-activity dependence of barbituric acid derivatives as drugs and biologically active compounds based on the features of the chemical structure.
3. Modifications of molecules of barbituric acid derivatives.

4. Pro-drugs in a number of synthesized barbiturates.
5. Methods of synthesis of barbituric acid derivatives.
6. The principle of "copying known pharmacological active substances" in the synthesis of barbituric acid derivatives.
7. The principle of "pharmacophore introduction and modification" in the synthesis of barbituric acid derivatives.
8. Prodrug strategy in the synthesis of barbituric acid derivatives.

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

Topic N3. Pyridine derivatives as an example of "privileged structures" in the synthesis of new drugs. The study of patterns of structure-activity dependence of pyridine derivatives and related heterocyclic systems.

Type of lecture: traditional (informational)

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 the systematized foundations of scientific knowledge regarding the main modern strategies for the search of new pyridine derivatives as an example of "privileged structures" in the synthesis of new drugs, the study of patterns of structure-activity dependence of pyridine derivatives and related heterocyclic systems; to provide an approximate basis for further assimilation of educational material in practical classes.

Lecture equipment: laptop, multimedia projector, blackboard.

Tasks of the lecture:

the student should know

basics of organic synthesis of pyridine derivatives;

patterns of structure-activity dependence of pyridine derivatives as drugs and biologically active compounds, based on the peculiarities of the chemical structure;

ways of modifying molecules of pyridine derivatives;

prodrug strategy in a number of synthesized pyridine derivatives;
classical and modern methods of synthesis of pyridine derivatives;

Plan of the Lecture

The name the stage of the lecture	Content of the stages	Educational goal of the stage	Time
Introduction	Announcement of the topic of the lecture, of the lecture, definition of the purpose o lecture, a brief description of the problems proposed to be considered during lecture, a brief description of the literature.	Activation of the previously acqu scientific knowledge of students other disciplines and laying scientific basis for assimilating lecture material.	10 min
Main part	1.Peculiarities of the chemical structur pyridine derivatives of "privileged" structures in the synthesis of medi substances: to reveal the peculiarities of chemical structure of pyridines.	To acquire knowledge about peculiarities of the chemical stru of pyridine and its derivatives, possibilities of modifying chemical structure, to consider peculiarities of the relation between their chemical structure biological activity.	65 min
	2. Study of patterns of "structure-biolo activity" dependence of pyridine derivatives to reveal the peculiarities of the relation "structure - biological activity" of pyridine derivatives - LZ and BAS.	To acquire knowledge about peculiarities of the chemical stru of pyridine derivatives - MP, possibilities of modifying chemical structure, to consider peculiarities of the relation between their chemical structure biological activity.	
	3. Synthetic approaches to obtaining pyri derivatives: consider classical and mo methods of synthesis of biologically a pyridine derivatives.	Get acquainted with the strategy tactics of the organic synthesis of pyridine derivatives.	
Final part	Generalization in short formulations of the ideas of the lecture, logically concluding it complete work; direction of further indepen work of students; laying the scientific basi the following lectures.	Learning the actual material of lecture, the main theoretical provis with the help of logical nodes - main questions of the lecture.	15 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.1-6. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

2.Xi-Jie Dai, Paul Krolikowski, James I. Murray, Carolyn S. Wei et al. Synthesis of Substituted Pyridines via Formal (3+3) Cycloaddition of Enamines with Unsaturated Aldehydes and Ketones.*J. Org. Chem.* 2022, 87, 13, 8437–8444. Publication Date:June 9, 2022 https://doi.org/10.1021/acs.joc.2c00576

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.

2. Piir, G.; Sild, S.; Maran, U. Interpretable machine learning for the identification of estrogen receptor agonists, antagonists, and binders. *Chemosphere* **2024**, *347*, 140671. http://dx.doi.org/10.1016/j.chemosphere.2023.140671

3. Kotli, M.; Piir, G.; Maran, U. Data for: Pesticide effect on earthworm lethality via interpretable machine learning. QsarDB repository, QDB.258. **2023**. http://dx.doi.org/10.15152/QDB.258

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5. 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

6. Oja, M.; Sild, S.; Piir, G.; Maran, U. Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. *Pharmaceutics* **2022**, *14*, 2248. http://dx.doi.org/10.3390/pharmaceutics14102248

7. Lowe, C. N.; Charest, N.; Ramsland, C.; Chang, D. T.; Martin, T. M.; Williams, A. J. Transparency in Modeling through Careful Application of OECD's QSAR/QSPR Principles via a Curated Water Solubility Data Set. Chem. Res. Toxicol., **2023**, 36, 465–478. DOI: 10.1021/acs.chemrestox.2c00379

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Administered Drugs Active against the Coronavirus SARS-CoV-2. Netw. Model. Anal. Health Inform. Bioinform., **2023**, 12. DOI: 10.1007/s13721-023-00410-9

10. Király, P.; Kiss, R.; Kovács, D.; Ballaj, A.; Tóth, G. The Relevance of Goodness-of-fit, Robustness and Prediction Validation Categories of OECD-QSAR Principles with Respect to Sample Size and Model Type. Mol. Inform., **2022**, 41, 2200072. DOI: 10.1002/minf.202200072

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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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 lecture:

1. Organic synthesis as the main tool for the synthesis of pyridine derivatives.
2. Patterns of structure-activity dependence of pyridine derivatives as drugs and biologically active compounds based on the features of the chemical structure.
3. Modifications of molecules of pyridine derivatives.
4. Pro-drugs in a number of synthesized pyridine.
5. Methods of synthesis of pyridine derivatives.
6. The principle of "copying known pharmacological active substances" in the synthesis of pyridine derivatives.
7. The principle of "pharmacophore introduction and modification" in the synthesis of pyridine derivatives.
8. Pro-drug strategy in the synthesis of pyridine derivatives.

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

Topic N4. The use of a sulfonamide scaffold in the synthesis of biologically active compounds. Study of structure-activity dependence of compounds containing a sulfonamide fragment (antimicrobial sulfonamides, anti-inflammatory agents, diuretics, etc.).

Type of lecture: traditional (informational)

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 modern strategies for finding new sulfonamides, the use of sulfonamide scaffolds in the synthesis of biologically active compounds, studying the structure-activity relationship of compounds containing a sulfonamide fragment; to provide an approximate basis for further assimilation of educational material in practical classes.

Lecture equipment: laptop, multimedia projector, blackboard.

Tasks of the lecture:

the student should know

basics of organic synthesis of sulfonamides;

patterns of structure-activity dependence of sulfonamides as drugs and biologically active compounds, based on the peculiarities of the chemical structure;

ways of modifying sulfonamide molecules;

strategy of pro-drugs in a number of synthesized sulfonamides;
classical and modern methods of synthesizing sulfonamides.

Plan of the Lecture

The name the stage of the lecture	Content of the stages	Educational goal of the stage	Time
Introduction	Announcement of the topic of the lecture, of the lecture, definition of the purpose o lecture, a brief description of the problems proposed to be considered during lecture, a brief description of the literature.	Activation of the previously acqu scientific knowledge of students other disciplines and laying scientific basis for assimilating lecture material.	10 min
Main part	1.Peculiarities of the scaffold oriented synthesis of biologically a compounds - sulfonamides: to reveal peculiarities of the chemical structure sulfonamides.	To acquire knowledge about peculiarities of the chemical stru of sulfanilic acid and its derivat the possibilities of sca modification, to consider peculiarities of the relation between its chemical structure biological activity.	65 min
	2. Studying the patterns of depend "chemical structure - biological activity sulfonamides: to reveal the peculiarities o relationship "structure - biological activity sulfonamides - MP and BAS.	To acquire knowledge about peculiarities of the chemical stru of derivatives of sulfanilic acid - MP, the possibilities of modif their chemical structure, to conside peculiarities of the relation between their chemical structure biological activity.	
	3. Synthetic approaches to obtaining sulfanilic acid amide derivatives: consider classic and modern methods synthesis of biologically active sulfanilic derivatives.	Get acquainted with the strategy tactics of the organic synthesis of sulfanilic acid derivatives.	
Final part	Generalization in short formulations of the ideas of the lecture, logically concluding it complete work; direction of further indepen work of students; laying the scientific basi the following lectures.	Learning the actual material of lecture, the main theoretical provis with the help of logical nodes - main questions of the lecture.	15 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.1-6. (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. Piir, G.; Sild, S.; Maran, U. Interpretable machine learning for the identification of estrogen receptor agonists, antagonists, and binders. *Chemosphere* **2024**, *347*, 140671. http://dx.doi.org/10.1016/j.chemosphere.2023.140671

3. Kotli, M.; Piir, G.; Maran, U. Data for: Pesticide effect on earthworm lethality via interpretable machine learning. QsarDB repository, QDB.258. **2023**. http://dx.doi.org/10.15152/QDB.258

4. Kotli, M.; Piir, G.; Maran, U. Pesticide effect on earthworm lethality via interpretable machine learning. *Journal of Hazardous Materials*. **2024**. http://dx.doi.org/10.1016/j.jhazmat.2023.132577

5. 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

6. Oja, M.; Sild, S.; Piir, G.; Maran, U. Intrinsic aqueous solubility: mechanistically transparent data-driven modeling of drug substances. *Pharmaceutics* **2022**, *14*, 2248. http://dx.doi.org/10.3390/pharmaceutics14102248

7. Lowe, C. N.; Charest, N.; Ramsland, C.; Chang, D. T.; Martin, T. M.; Williams, A. J. Transparency in Modeling through Careful Application of OECD's QSAR/QSPR Principles via a Curated Water Solubility Data Set. Chem. Res. Toxicol., **2023**, 36, 465–478. DOI: 10.1021/acs.chemrestox.2c00379

8. Sosnowska, A.; Bulawska, N.; Kowalska, D.; Puzyn, T. Towards Higher Scientific Validity and Regulatory Acceptance of Predictive Models for PFAS. Green Chem., **2023**, 25, 1261–1275. DOI: 10.1039/d2gc04341f

9. Gousiadou, C.; Doganis, P.; Sarimveis, H. Development of Artificial Neural Network Models to Predict the PAMPA Effective Permeability of New, Orally Administered Drugs Active against the Coronavirus SARS-CoV-2. Netw. Model. Anal. Health Inform. Bioinform., **2023**, 12. DOI: 10.1007/s13721-023-00410-9

10. Király, P.; Kiss, R.; Kovács, D.; Ballaj, A.; Tóth, G. The Relevance of Goodness-of-fit, Robustness and Prediction Validation Categories of OECD-QSAR Principles with Respect to Sample Size and Model Type. Mol. Inform., **2022**, 41, 2200072. DOI: 10.1002/minf.202200072

11. Ovung A, Bhattacharyya J. Sulfonamide drugs: structure, antibacterial property, toxicity, and biophysical interactions. Biophys Rev. 2021 Mar 29;13(2):259-272. doi: 10.1007/s12551-021-00795-9. PMID: 33936318; PMCID: PMC8046889.

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 lecture:

1. Organic synthesis as the main tool for synthesizing sulfonamides.
2. Patterns of structure-activity dependence of sulfonamides as drugs and biologically active compounds based on the features of the chemical structure.
3. Modifications of sulfonamide molecules.
4. Pro-drugs in a number of synthesized sulfonamides.
5. Methods of synthesizing sulfonamides.
6. The principle of "copying known pharmacological active substances" in the synthesis of sulfonamides.
7. The principle of "pharmacophore introduction and modification" in the synthesis of sulfonamides.
8. Pro-drug strategy in the synthesis 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 N5. Studying patterns of structure-activity dependence of purine derivatives as drugs and biologically active compounds at various stages of research. Synthetic approaches to obtaining and modifying xanthines and related heterocyclic compounds.

Type of lecture: traditional (informational)

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 modern strategies for searching and studying patterns of structure-activity dependence of purine derivatives as drugs and biologically active compounds at various stages of research, synthetic approaches to obtaining and modifying xanthines and related heterocyclic compounds; to provide an approximate basis for further assimilation of educational material in practical classes.

Lecture equipment: laptop, multimedia projector, blackboard.

Tasks of the lecture:

the student should know

basics of organic synthesis of purine derivatives;

regularities of structure-activity dependence of purine derivatives as drugs and biologically active compounds, based on the peculiarities of the chemical structure;

ways of modifying molecules of purine derivatives;

prodrug strategy in a number of synthesized purine derivatives;
classical and modern methods of synthesis of purine derivatives.

Plan of the Lecture

The name the stage of the lecture	Content of the stages	Educational goal of the stage	Time
Introduction	Announcement of the topic of the lecture, of the lecture, definition of the purpose o lecture, a brief description of the problems proposed to be considered during lecture, a brief description of the literature.	Activation of the previously acqu scientific knowledge of students other disciplines and laying scientific basis for assimilating lecture material.	10 min
Main part	1. Peculiarities of the chemical structur purine and its biologically active derivative reveal the peculiarities of the chemical stru of purine and its derivatives.	To acquire knowledge about features of the chemical structur purine and its derivatives, possibilities of scaffold modification, to consider the features of the relationship betwee chemical structure and biological activity.	65 min
	2. Patterns of dependence "chemical struct biological activity" of purine derivative drugs (MP) and biologically active substa (BAS): to reveal the peculiarities of relationship "structure - biological activity" of purine derivatives - MP and BAS.	To acquire knowledge about peculiarities of the chemical stru of purine derivatives - MP, possibilities of modifying chemical structure, to consider peculiarities of the relationship between their chen structure and biological activity.	
	3. Synthetic approaches to obtaining modifying xanthines and related heteroc compounds: consider classical and modern methods of synthesis of biologi active purine derivatives and related heterocycles.	Get acquainted with the strategy tactics of the organic synthesis of biologically active purine deriva and related heterocycles**.**	
Final part	Generalization in short formulations of the ideas of the lecture, logically concluding it complete work; direction of further indepen work of students; laying the scientific basi the following lectures.	Learning the actual material of lecture, the main theoretical provis with the help of logical nodes - main questions of the lecture.	15 min

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activity relationship models. iScience 24, 103052, 2021, p.1-6. (Review Article). http://creativecommons.org/licenses/by-nc-nd/4.0/

2.Huang, Z., Xie, N., Illes, P. *et al.* From purines to purinergic signalling: molecular functions and human diseases. *Sig Transduct Target Ther* **6**, 162 (2021). https://doi.org/10.1038/s41392-021-00553-z

Auxiliary

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Principles with Respect to Sample Size and Model Type. Mol. Inform., **2022**, 41, 2200072. DOI: 10.1002/minf.202200072

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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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/

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