



MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
Department of Biotechnology

TECHNOLOGIES OF MICROBIAL SYNTHESIS OF DRUGS

(name of educational component)

**WORK PROGRAM
of educational component**

training for _____ second (master's) level _____
(Higher Educational Level Name)
in specialty _____ «226 Pharmacy, industrial pharmacy» _____
(Code and Specialty Name)
field of knowledge « _____ 22 Health care _____
(Code and Knowledge Field Name)
of educational program _____ «Pharmacy» _____
(Educational Program Name)

Kharkiv - 2023
(year of creation)

The work program of the educational component "Pharmaceutical biotechnology" in specialty 226 Pharmacy, industrial pharmacy of the educational program "Pharmacy" for applicants for higher education 4th year of study.

EDUCATIONAL COURSE TEAM:

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(specify the LAST NAME, first name of the authors, their positions, scientific degrees and academic titles)

Work program has been considered and approved at the Department meeting
Department of biotechnology

Record from « 1 » 09 2023 № 1

Head of the Department  prof. Natalya KHOKHLENKOVA
(sig.) (first name LAST NAME)

Work program has been approved at the meeting of the Methodical Commission of technological educational components

Record from « 1 » 09 2023 № 1

Deputy Head of Methodical Commission  prof. Olena RUBAN
of technological educational components

1. Description of the educational component

Language of instruction: English

Status of the educational component: selective

Prerequisites for studying the educational component: the educational component is based on the study of biology with the basics of genetics, general and inorganic chemistry, organic chemistry, physical and colloidal chemistry, biological chemistry, microbiology with the basics of epidemiology, pharmacognosy with the basics of resource science, and industrial drug technology;

the educational component is the basis for studying the technological aspects of modern biotechnological production, which involves integration with the above educational components.

The subject matter of the educational component "Pharmaceutical Biotechnology" is the main provisions and trends in the development of pharmaceutical biotechnology in the world and in Ukraine; mastering the modern principles of production of active pharmaceutical ingredients and medicines using biotechnology methods - microbial synthesis, cellular technology, genetic engineering methods, familiarization with the main modern types of biotechnology production equipment.

Information content of the educational component. _3_ ECTS credit _90_ hours are assigned to the study of the educational component.

2. Objectives and tasks of the educational component

The purpose of teaching the educational component "Pharmaceutical biotechnology" is the assimilation by students of higher education of the theoretical foundations and practical skills and abilities of carrying out biotechnological processes, cultivation of individual strains of industrial microorganisms, management of processes of cultivation of microorganisms and quality control of the received target products, environmental safety of biotechnology products created on the basis of microorganisms, assimilation of features and familiarization with achievements biotechnologies for the production of pharmaceutical products of the latest generation: vaccines, hormones, immunomodulators, vitamins, enzymes, probiotics, antibiotics and other medical preparations and dietary supplements using producer organisms and other biological objects, which will make it possible to effectively realize the scientific and creative potential of future specialists.

Mastering the theory and practice of manufacturing medicinal products by biotechnological methods is necessary for a specialist to perform the duties of a specialist, which is provided for legal and procedural legislation and the corresponding order of the Ministry of Health of Ukraine.

The main tasks of the educational component "Pharmaceutical biotechnology" is:

- mastering the theoretical foundations of biotechnological processes, means and methods of obtaining biologically active substances using living objects and their enzyme systems;
- the formation of students of higher education in the practical use of biotechnological processes for the industrial production of valuable products of the vital activity of microorganisms and other biotechnological objects, their biomass, the production of useful substances and medicines, as well as preventive and diagnostic tools based on them, which are used in various in the fields of medicine and pharmacy;
- assimilation of the methodology of creation, standardization, evaluation of the quality and safety of medicines obtained by biotechnological methods on the basis of general laws of chemical and biological sciences for the performance of professional tasks of a pharmacy specialist;
- formation of systematized knowledge on handling, storage, transportation, use of information about biotechnological drugs and provision of information on these issues to consumers.

3. Competencies and planned learning outcomes

The educational component "Pharmaceutical Biotechnology" ensures that students of higher education acquire the following **competencies**:

- *integral*:

ability to solve typical and complex specialized tasks and critically comprehend and solve the practical problems in the professional pharmaceutical and/or research and innovation activity using provisions, theories and methods of the fundamental, chemical, technological, biomedical, socio-economic science; integrate knowledge and solve complex issues, formulate judgments in the presence of

incomplete or limited information, clearly and unambiguously to convey their conclusions and use their knowledge, reasonably substantiating them, to professional and non-professional audience.

- *special (professional, subject):*

PC 1. Ability to conduct sanitary and educational work among the population to prevent common diseases, prevent dangerous infectious, viral and parasitic diseases, as well as to facilitate the timely detection and maintenance of adherence to treatment of these diseases in accordance with their medical and biological characteristics and microbiological characteristics.

PC 15. Ability to organize and participate in the production of medications in the context of pharmaceutical companies, including the selection and justification of the technological process, equipment in accordance with the requirements of Good Manufacturing Practice (GMP) with the appropriate development and design of the necessary documentation. Determine the stability of medications.

Integrative final program learning outcomes (PLO), the formation of which is facilitated by the educational component:

PLO 27. To substantiate the technology and organize the production of medicines at pharmaceutical enterprises and draw up technological documentation for the production of medicines at pharmaceutical enterprises.

As a result of studying the academic discipline, the student of education must

know:

- history and directions of development of pharmaceutical biotechnology;
- main producers and methods of obtaining APIs and medicinal products by biotechnological methods;
- traditional and innovative ways of obtaining biologically active substances by biotechnology methods;
- main stages of the biotechnological process;
- basic regulatory documents on standardization, production, quality control and compliance with environmental safety of medicinal products obtained by biotechnological methods, as well as biological objects - their producers.

be able:

- - to perform various technological operations of the biotechnological process of drug production;
- - to justify the conditions of cultivation of microorganisms, cells and tissues of plants and animals;
- - to carry out certain types of technological control of production and standardization of the obtained drugs (determination of antimicrobial activity of antibiotics, activity of enzyme preparations, concentration of viable cells, viability of microorganisms)
- - choose optimal storage conditions for medicinal products obtained by biotechnological methods;

4.The educational component structure

Names of content modules and topics	The amount of hours					
	Full-time study					
	the whole amount	including				
		L	Sem	Practical lessons	lab	Self study
<i>1</i>	2	3	4	5	6	7
Topic 1. Tasks and features of microbial synthesis. Objects and products of microbial synthesis.	12	1		4		7
Topic 2. Raw materials and nutrient media. The main stages of the process of microbial synthesis.	13	2		4		7

Topic 3. Methods of cultivation of microorganisms for the implementation of microbial synthesis technologies.	10	1		2		7
Topic 4. Technologies of microbial synthesis of amino acids, enzyme preparations..	10	1		2		7
Topic 5. Technologies of microbial synthesis of vitamins.	12	1		4		7
Topic 6. Technologies of microbial synthesis of antibiotics.	10	1		2		7
Topic 7. Technologies for obtaining recombinant cytokine proteins. <i>Control of content module 1.</i>	21	1		4		16
The whole amount of hours for the content module 1	88	8		22		58
Semester credit/semester differential credit from module 1				2		
<i>The whole amount of hours for the course</i>	90	8		24		58

5. Content of the educational component

Content module 1. Objects, methods and technological processes of microbial synthesis of drugs.

Topic 1. Tasks and features of microbial synthesis. Objects and products of microbial synthesis.

Definition and main directions of biotechnology. Color biotechnology. The concept of microbial synthesis. Features and tasks of microbial synthesis. Objects of microbial synthesis. Classification of biological objects by levels of organization. Examples of biological objects and their use. Modern trends in the use of microbial cells. Classification of biological objects by production functions. Requirements for to microorganisms-producers. Products of microbial synthesis.

Topic 2. Raw materials and nutrient media. The main stages of the process of microbial synthesis.

Definition and purpose of the biotechnological process. The main stages of the biotechnological process of microbial synthesis. Preparatory stages (creation of aseptic conditions, preparation of nutrient media, sterilization of nutrient media, preparation and sterilization of gases, preparation of defoamers, preparation of inoculum). Purpose of culture media, requirements for them. Classification and chemical composition of culture media. Methods of sterilization of culture media. Culture passport. Preservation and storage of bioproduct cultures. Scheme of multi-stage preparation of inoculum. Types of fermentation processes. Physical and chemical conditions for cultivation. Classification of fermentation processes. Batch and continuous deep fermentation. Post-fermentation stages: separation of separation of culture liquid and biomass, isolation of biosynthesis products, product purification, product concentration, and final product product concentration, production of finished products.

Topic 3. Methods of cultivation of microorganisms for the implementation of microbial synthesis technologies.

The concept of fermentation. Growth curve of microorganisms. Kinetics of formation of metabolic products and biomass in the culture of microorganisms. Methods of cultivation: on the basis of the target product of the process, by the location of the producer on the nutrient medium, by the main phase in which the enzyme process takes place. The main phase in which the fermentation process takes place, or by the condition of the culture medium, in relation to oxygen, by the degree of protection from extraneous microflora, by the number of microorganism species, by the relation to light. Types of fermentation according to the way the process is organized: batch, batch with substrate feeding, negative-top-up, continuous. Chemostats and turbidostats are bioreactors, ideal displacement reactors

Topic 4. Technologies of microbial synthesis of amino acids, enzyme preparations.

The concept of primary and secondary metabolites of microorganisms. Amino acids: the main methods of production. Microbiological synthesis of amino acids. Production of lysine. Chemical and microbiological synthesis of amino acids. Production of tryptophan. Enzymatic synthesis of amino acids. Production of aspartic

acid. The concept of enzymes. Distinctive features. Classification. Production of enzymes by microbial synthesis. Solid-phase surface fermentation in the production of enzymes. Deep fermentation in the production of enzymes.

Topic 5. Technologies of microbial synthesis of vitamins.

The concept of primary and secondary metabolites of microorganisms. Amino acids: the main methods of production. Microbiological synthesis of amino acids. Production of lysine. Chemical and microbiological synthesis of amino acids. Production of tryptophan. Enzymatic synthesis of amino acids. Production of aspartic acid. The concept of enzymes. Distinctive features. Classification. Production of enzymes by microbial synthesis. Solid-phase surface fermentation in the production of enzymes. Deep fermentation in the production of enzymes.

Topic 6. Technologies of microbial synthesis of antibiotics.

Definition of antibiotic substances. Features of antibiotic substances. Specificity of antibiotics. Industrial production of antibiotics. Two-phase development of antibiotic producers: trophophase, idiophase.

Topic 7. Technologies for obtaining recombinant cytokine proteins.

The concept of cytokines. The main subgroups and families of cytokines. General properties of cytokines. Biotechnological approaches to the production of recombinant human cytokines. Strains producing recombinant cytokines. Nutrient media for cultivation of E. coli. Methods of cultivation of E. coli. Isolation and purification of recombinant cytokines. Use of other producers to obtain recombinant cytokine proteins. Open cell-free synthesis systems (OCFS).

Semester control of module 1 is conducted in the form of a semester undifferentiated assessment.

6. Topics of lectures

№	Topic name	The amount of hours
		Full-time study
1	Topic 1. Tasks and features of microbial synthesis. Objects and products of microbial synthesis.	1
2	Topic 2. Raw materials and nutrient media. The main stages of the process of microbial synthesis.	2
3	Topic 3. Methods of cultivation of microorganisms for the implementation of microbial synthesis technologies.	1
4	Topic 4. Technologies of microbial synthesis of amino acids, enzyme preparations.	1
5	Topic 5. Technologies of microbial synthesis of vitamins.	1
6	Topic 6. Technologies of microbial synthesis of antibiotics.	1
7	Topic 7. Technologies for obtaining recombinant cytokine proteins.	1
The whole amount of hours		8

7. Topics of seminars

Not provided for in the working program.

8. Topics of practical lessons

№	Name of topic	The amount of hours
		Full-time study
1	Topic 1. Tasks and features of microbial synthesis. Objects and products of microbial synthesis.	4
2	Topic 2. Raw materials and nutrient media. The main stages of the process of microbial synthesis.	4

3	Topic 3. Methods of cultivation of microorganisms for the implementation of microbial synthesis technologies.	2
4	Topic 4. Technologies of microbial synthesis of amino acids, enzyme preparations.	2
5	Topic 5. Technologies of microbial synthesis of vitamins.	4
6	Topic 6. Technologies of microbial synthesis of antibiotics.	2
7	Topic 7. Technologies for obtaining recombinant cytokine proteins. <i>Control of content module 1.</i>	4
8	Semester control (semester assessment).	2
The whole amount of hours		24

9. Topics of laboratorial lessons

Not provided for in the working program.

10. Self-study work

№	Topic name	The amount of hours
		Full-time study
1	Topic 1. Tasks and features of microbial synthesis. Objects and products of microbial synthesis. The structure of the global biotechnology market. The most developed companies and their areas of specialization in terms of medicinal products and their areas of application. Dependence of the degree of complexity of biotechnology production processes on the nature of the biological object, the target product, its purpose and dosage form.	7
2	Topic 2. Raw materials and nutrient media. The main stages of the process of microbial synthesis. Variety and characteristics of culture media for the cultivation of producers. Principles of compilation, preparation and preparation of nutrient media for the cultivation of microorganisms-producers of BAS. Equipment for carrying out the stages of the microbial synthesis process. Methods of equipment sterilization.	7
3	Topic 3. Methods of cultivation of microorganisms for the implementation of microbial synthesis technologies. Principles of choosing a cultivation method for the microbial synthesis of various classes of biologically active substances. One-, two- and multi-stage processes of microbial synthesis.	7
4	Topic 4. Technologies of microbial synthesis of amino acids, enzyme preparations. The biological role of amino acids and their use in the pharmaceutical industry and as medicines. Creation of amino acid superfoods. Distinctive features of enzymes from other BAS. Structure of enzymes. Features of solid-phase and suspension cultivation in the production of enzymes. Areas of application of enzymes in medicine.	7
5	Topic 5. Technologies of microbial synthesis of vitamins. Biological role of vitamins. Classification of vitamins. The advantages of obtaining vitamins by microbial synthesis over traditional methods of obtaining (isolation from natural sources and chemical synthesis).	7
8	Topic 6. Technologies of microbial synthesis of antibiotics.	7

	Classification of antibiotics. Classification of antibiotics by the nature of their action on the bacterial cell. Methods of obtaining active strains of producers. Types of culture media and requirements for them.	
9	Topic 7. Technologies for obtaining recombinant cytokine proteins. Types of recombinant drugs obtained with the help of microbial cells. The use of cytokines in therapeutic and diagnostic practice. Biotechnological approaches to the production of recombinant human cytokines in bacterial expression systems. <i>Preparation for control of content module 1.</i>	16
The whole amount of hours		58

Tasks for self-study work

1. Study of lecture material and preparation for practical classes.
2. Mastering the rules of work in a biotechnology laboratory.
3. Mastering the rules of working with biological objects (microorganisms-producers and their enzyme systems).
4. Familiarization with the basic methods of experimental research in biotechnology.
5. Learning how to create aseptic conditions when working with biological objects (preparation of air, premises, equipment, personnel).
6. Familiarization with the mechanisms of intensification of processes of obtaining cellular metabolism products.
7. Familiarization with the history of the discovery of antibiotics and the contribution of modern scientists to the development of biotechnological methods of antibiotic production.
8. Acquaintance with innovative technologies in the production of biologically active substances by biotechnological methods using microorganisms-producers.

11. Criteria and evaluation order of educational outcomes

The criteria for evaluating the knowledge and skills of higher education students from the educational component "Fundamentals of research in biotechnology" were developed in accordance with the "Regulations on the procedure for evaluating the results of higher education students at the National Pharmaceutical University A2.2-25-031-B".

The evaluation of the success of higher education applicants in the educational component is a rating, presented on a one-point scale and defined according to the ECTS system and the traditional scale adopted in Ukraine.

Assessments (in points) are reflected in the calendar-thematic plans of practical and seminar classes.

Criteria for evaluating the knowledge and skills of students of higher education in correspondence form of education in laboratory and seminar classes

Assessment of current educational activities (held during each lesson) – control of theoretical knowledge, practical skills and abilities. When mastering each topic of the content modules for the current educational activity, higher education applicants are awarded points for all types of activities, which are added up at the end of studying the content module.

Evaluation criteria	Scores
1	2
<ul style="list-style-type: none"> ➤ showed a comprehensive and deep knowledge of theoretical material on the topic of the class, which is set out in the texts of lectures, compulsory and additional literature, gave comprehensive answers to theoretical questions of the teacher ➤ answered 90%-100% of the test tasks correctly; ➤ has studied the methodological recommendations for the practical lesson and mastered the methodology of practical work; ➤ correctly completed the practical task; 	7.0

<ul style="list-style-type: none"> ➤ correctly formulated conclusions based on the results of the work performed. 	
<ul style="list-style-type: none"> ➤ showed full knowledge of the theoretical material on the topic of the class, which is set out in the texts of lectures, compulsory and additional literature, and answered theoretical questions of the teacher with minor deficiencies; ➤ correctly answered 74%-89% of the test tasks; ➤ has worked out the methodological recommendations for the practical lesson, but has not fully mastered the methodology of practical work; ➤ correctly completed the practical task, but made minor mistakes that do not affect the quality of the result; ➤ formulated conclusions based on the results of the work performed with minor inaccuracies. 	6.0
<ul style="list-style-type: none"> ➤ showed knowledge of theoretical material on the topic of the lesson to the extent that is considered necessary and sufficient to apply knowledge in standard situations; ➤ answered theoretical questions with errors that were corrected with the help of the teacher; ➤ correctly answered 60%-73% of the test tasks; ➤ did not work out the methodological recommendations for the practical lesson in full, made gross mistakes in teaching the methodology of practical work; ➤ correctly completed the practical task, but with the help of the teacher, needs to rely on the sample; ➤ made mistakes in formulating conclusions based on the results of the work performed. 	5.0
<ul style="list-style-type: none"> ➤ did not familiarize himself with the theoretical material on the topic of the class, which is set out in the texts of lectures, compulsory and additional literature; ➤ did not answer theoretical questions of the teacher; ➤ answered less than 60% of the test tasks correctly; ➤ performed certain methodological actions incorrectly, performed the task not independently (following the instructor's instructions) or not in full; ➤ did not formulate conclusions based on the results of the work performed. 	0-4.0

The independent work of a higher education student is monitored during each practical lesson, during the control of the content module.

In the event that the applicant comes to class unprepared, he or she must be present at the class. After working with the recommended literature and / or electronic sources on the topic of the lesson and an individual conversation with the teacher on the topic of the lesson, the higher education applicant is allowed to practice.

The sum of the points of the current control is the sum of the points received by the higher education applicant during the study of all topics of the module and the control of the content module on the educational component.

Criteria for evaluating the knowledge and skills of higher education applicants on the control of the content module

Candidates of higher education who have completed all types of work provided for in the curriculum and have scored at least the minimum number of points while studying the topics of the content module are admitted to the control of the content module (CCM). CCM is carried out in the last lesson of the content module and is evaluated in points.

Evaluation criteria	Scores
<p><i>theoretical task:</i></p> <ul style="list-style-type: none"> ➤ gave a comprehensive answer to the theoretical question; <p><i>practical task:</i></p> <ul style="list-style-type: none"> ➤ answered 90-100% of the test questions; 	43-51
<p><i>theoretical task:</i></p> <ul style="list-style-type: none"> ➤ gave a correct but incomplete answer to a theoretical question; <p><i>practical task:</i></p> <ul style="list-style-type: none"> ➤ answered 74-89% of test questions; 	34-42
<p><i>theoretical task:</i></p>	25-33

➤ gave answers to theoretical questions with errors or not at all; practical task: ➤ answered 60-73% of test questions;	
theoretical task: ➤ did not answer the theoretical question; practical task: ➤ answered less than 60% of the test questions.	0-24

For those applicants who want to improve their performance in the educational component on the ECTS scale and increase the rating of the module, this is possible at the last session of the module during the semester assessment.

Scheme of accrual and distribution of points

Current control and independent work								
Content module 1								
T1	T2	T3	T4	T5	T6	T7	T7	Sem. con.
PL1	PL2	PL3		PL4	PL5		PL6 CCM1	PL7
4-7	4-7	4-7	4-7	12-18	4-7	4-7	24-40	
60.0-100.0								

T1, T2 ... T7 – topics of the module.

PL1 ...PL7 - numbers of seminar classes.

CCM.. – control of the content module.

Semester control - semester control.

12.Forms of progress and semester supervision of academic achievements

Current control is conducted during each laboratory and seminar session in accordance with specific goals and during the individual work of the teacher with students of higher education. The independent work of students of higher education is also monitored during each practical or seminar session.

After mastering each topic of the module for the current educational activity, higher education applicants are awarded points for all types of activities, which are added up at the end of studying the module.

Content module control is held in the last lesson of the content module. The control is carried out in order to check the level of assimilation of theoretical material, acquisition of practical skills and skills from the educational component.

Semester control is held at the last lesson of the module.

The evaluation of the success of a higher education student in the educational component is a rating, presented on a one-point scale and defined according to the ECTS system and the traditional scale adopted in Ukraine. Applicants of higher education who want to improve their performance in the educational component on the ECTS scale have the opportunity to do so at the last lesson of the module during the semester assessment.

Form of control- semester credit

13.Methodological support

1. Educational work program of the educational component.
2. Work program of the educational component.
3. Syllabus of the educational component.
4. Calendar plan of lectures and practical classes.
5. Lectures in multimedia format.
6. Videos on topics.
7. Interactive teaching methods (transfer of information, discussion, learning about processes, problem solving, simulation and non-simulation technologies, etc.)
8. Methodological recommendations on the topics of practical classes.
9. Test tasks for current knowledge control.

10. Tasks for independent work.
11. Questions for preparation for the control of content modules.
12. Training equipment, technical means of training.

15. Reading suggestions

The main reading suggestions

1. Pharmaceutical Biotechnology in Drug Development / Muhammad Sajid Hamid Akash. – Academic press, 2023.

Supplementary reading suggestions

1. S. Spada. G. Walsh Directory of Approved Biopharmaceutical Products 1st Edition . – CRC Press, 2019. – 336 p.
2. Roque-Borda C.A., Pavan F.R., Meneguín A.B. Pharmaceutical Biotechnology. Life (Basel). 2022 Aug 16;12(8):1240. doi: 10.3390/life12081240.
3. Roque-Borda CA, Pavan FR, Meneguín AB. Pharmaceutical Biotechnology. Life (Basel). 2022 Aug 16;12(8):1240. doi: 10.3390/life12081240.
4. Harcum S.W., Kiss R.D. Editorial overview: Pharmaceutical biotechnology: the pandemic years - new modality development and biomanufacturing innovations in a maturing field. Curr Opin Biotechnol. 2022 Dec;78:102846. doi: 10.1016/j.copbio.2022.102846.
5. Zuba-Surma EK, Józkwicz A, Dulak J. Stem cells in pharmaceutical biotechnology. Curr Pharm Biotechnol. 2011 Nov;12(11):1760-73. doi: 10.2174/138920111798377120.
6. Khavari F, Saidijam M, Taheri M, Nouri F. Microalgae: therapeutic potentials and applications. Mol Biol Rep. 2021 May;48(5):4757-4765. doi: 10.1007/s11033-021-06422-w.
7. Boulay JL, Miot S. Chemical biotechnology pharmaceutical biotechnology. Web alert. Curr Opin Biotechnol. 2000 Dec;11(6):515. doi: 10.1016/s0958-1669(00)00138-5.
8. Bhatia, Saurabh, Tanveer Naved, and Satish Sardana. Introduction to Pharmaceutical Biotechnology, Volume 3; Animal tissue culture and biopharmaceuticals. 2019.

16 Electronic resources, including the Internet

1. European pharmacopeia [Electronic resource]: official website. - Access mode <https://pheur.edqm.eu/home>.
2. National Pharmaceutical University [Electronic resource]: Scientific library of the National Pharmaceutical University. - Access mode :<http://lib.nuph.edu.ua>(date of application 09/26/20).
3. National Pharmaceutical University. Department of Biotechnology [Electronic resource]: website of the Department of Biotechnology. – Access mode: <http://biotech.nuph.edu.ua>
4. Electronic archive of the NUPh library. <http://lib.nuph.edu.ua>; e-mail library@nuph.edu.ua
5. Educational portal <http://pharmel.kharkiv.edu> - center of distance technologies of NUPh