MINISTRY OF HEALTH OF THE REPUBLIC OF BELARUS
EDUCATIONAL INSTITUTION
BELARUSIAN STATE MEDICAL UNIVERSITY

Контрольный экземпляр

APPROVED
by First Vice-Rector, Professor
_____I.N. Moroz
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Reg. # UD-1.592/1920 /edu.

PHARMACEUTICAL BIOTECHNOLOGY

Curriculum of higher educational institution in the educational discipline for the specialty:

1-79 01 08 «Pharmacy»

2019

The curriculum is based on the educational program «Pharmaceutical biotechnology», approved 01.12.2016, registration number № УД-L.592/1617уч.

COMPILERS:

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RECOMMENDED FOR APPROVAL:

by the Department of Pharmaceutical Technology of the Educational Institution «Belarusian State Medical University»
(protocol № 3 of 03.10.2019);

by the Scientific Methodical Council of the Educational Institution «Belarusian State Medical University»
(protocol № 3 of 20.11.2019)

EXPLANATORY NOTE

«Pharmaceutical biotechnology» is the educational discipline that contains systematized scientific knowledge about the methods of medicines and pharmaceutical substances production using living systems, as well as methods of quality control.

The teaching and learning purpose of the discipline «Pharmaceutical biotechnology» is to provide students with the scientific knowledge about the pharmaceutical substances and medicines production using biotechnological methods, as well as methods of quality control.

The tasks of teaching and studying the academic discipline are to develop the students' academic, social, personal and professional competencies based on the knowledge and application of:

- biotechnological drugs classification;
- the most important principles of the original biotechnological drugs and biosimilars development;
- methods of using biological processes and objects in pharmaceutical substances and medicines production;
- methods of biotechnological production assessment in accordance with the requirements of Good Manufacturing Practice, environmental safety requirements in relation to the producers used in manufacturing, target products and production waste;
- the principles of standardization of medicines obtained by biotechnological methods.

Teaching and successful learning of the discipline «Pharmaceutical Biotechnology» is carried out on the basis of knowledge and skills acquired by the student in the following sections of academic disciplines:

Biology. Genetic engineering, its goals and objectives. Genetic material obtaining. Insertion of genetic material. Inclusion of new genes in the cellular genetic material.

Microbiology. Bacteria nutrition, sources of carbon, nitrogen and minerals. Bacterial growth factors. Bacterial growth and reproduction. Phases of the bacterial reproduction in liquid and solid growth media. Antibodies (immunoglobulins). Immunoglobulin classes, their main characteristics. Monoclonal antibodies, production methods, their value. Characteristics of modern vaccines: live, killed and chemical vaccines, toxoids, conjugated vaccines, genetically engineered and synthetic vaccines. State quality control of vaccines and immunoglobulins. Immunomodulators (interferons, interleukins).

Pharmaceutical chemistry. Normative legal acts regulating the quality of pharmaceutical substances and medicines. State Pharmacopoeia of the Republic of Belarus, pharmacopoeial monographs. Classification of antibiotics by chemical structure, mechanism and direction of action. Antibiotics production methods. Methods of antibiotics quality assessment.

Industrial technology of medicines. Good Manufacturing Practice. Processes and machines used in industrial technology. Production processes validation of sterile

and non-sterile medicines. The procedure of preparing water for pharmaceutical purposes. Certification of clean rooms, water treatment and air treatment systems.

As a result of studying the discipline «Pharmaceutical biotechnology» the student must

know:

– the basic terms and definitions, objects and methods of biotechnology;

– the stages of industrial production, isolation and purification methods of the most important biotechnological products used in the manufacture of medicines;

– the methodology for the cultivation of isolated cells, tissues and organs of plants and animals, obtaining monoclonal antibodies;

– the requirements of Good Manufacturing Practice for biotechnological production;

be able to:

– use the normative legal acts regulating the production and quality assurance of medicines obtained by biotechnological methods;

– justify the technological and machine design of biotechnological production;

master:

– the methods of growing isolated cells, tissues and organs of plants and animals in culture in order to obtain pharmaceutical substances and medicines;

– the nomenclature of medicines obtained by biotechnological methods.

The structure of the curriculum in the discipline «Pharmaceutical biotechnology» consists of three sections: «General issues of pharmaceutical biotechnology», «Cellular biotechnology», «Microbial biotechnology».

The total number of hours for the study of the discipline is 114 academic hours. Classroom hours according to the types of studies: lectures – 16 hours, practical classes – 36 hours, student independent work (self-study) – 62 hours.

Current assessment is carried out in accordance with the curriculum for the specialty in the form of an exam (8th semester).

Form of education is full-time.

ALLOCATION OF EDUCATIONAL TIME BY SEMESTERS

Code, Name of specialty	Semester	The number of academic hours					Form of current assessment
		total	in-class	including		out-of-class self-studies	
				lectures	practical classes		
1-79 01 08 «Pharmacy»	**8**	114	52	16	36	62	exam
Total hours		114	52	16	36	62	

THEMATIC PLAN

Name of the section (topics)	Number of hours for classes	
	lectures	practical classes
1. General issues of pharmaceutical biotechnology	**6**	**9**
1.1. Introduction to the discipline «Pharmaceutical biotechnology». Objects and methods of pharmaceutical biotechnology. Biological and environmental safety of biotechnological drugs. The main stages of the original biotechnological drugs and biosimilars development	2	6
1.2. Technological process organization in biotechnological production. Industrial cultivation of microorganisms. Methods of biotechnological products isolation and purification	4	3
2. Cellular biotechnology	**6**	**15**
2.1. Genetic engineering in biotechnology. The cultivation of isolated animal and human cells. Quality control methods for medicines obtained from animal and human cells	2	6
2.2. Production technology and standardization of medicines based on cytokines (interferons). Vaccines and sera production technology and standardization	2	3
2.3. Production technology and standardization of medicines based on monoclonal antibodies. Cultivation of plant cells and tissues. Obtaining biologically active compounds using plant cell cultures	2	6
3. Microbial biotechnology	**4**	**12**
3.1. Production technology and standardization of probiotics and prebiotics, vitamins B_2, B_{12}, D_2, amino acids, organic acids, alcohols, thrombolytic medicines and anticoagulants	2	6
3.2. Production technology and standardization of steroid hormones, insulin, enzymes, antibiotics	2	6
Total hours	**16**	**36**

CONTENT OF EDUCATIONAL MATERIAL

1. General issues of pharmaceutical biotechnology

1.1. Introduction to the discipline «Pharmaceutical biotechnology». Objects and methods of pharmaceutical biotechnology. Biological and environmental safety of biotechnological drugs. The main stages of the original biotechnological drugs and biosimilars development

Subject and content of the discipline «Pharmaceutical biotechnology». Objects and methods of pharmaceutical biotechnology. Integration of pharmaceutical biotechnology with other sciences. The main pharmaceutical biotechnology directions. Historical stages in the biotechnology development. The most important groups of medicines and pharmaceutical substances obtained using biotechnological methods. The concept of biological and environmental safety of medicines.

Organizations of the Republic of Belarus that develop biological medicines. Research and development (R&D) departments at pharmaceutical enterprises. The main stages of the biotechnological drugs creation. The concept of biosimilar. Requirements for the volume of preclinical, clinical and post-registration trials of biotechnological drugs. Registration dossier for biotechnological drug. Evaluation of registration dossier documents on biotechnological drugs quality, efficiency and safety.

1.2. Technological process organization in biotechnological production. Industrial cultivation of microorganisms. Methods of biotechnological products isolation and purification

Good Manufacturing Practice (GMP) requirements for biotechnological production. Flowchart of biotechnological production. Preparatory operations of biotechnological production: preparation of air, water, growth media; preparation of fermenters; microbiological culture growing. Obtaining and composition of growth media used in biotechnological processes. Sources of carbon, nitrogen, macro- and microelements. Production process: biosynthesis (fermentation); products unloading; purification and concentration, prepackaging and packaging of products. Bioreactors. Preparation of bioreactors for work. Biomass utilization and biodegradation. Environmental protection and compliance with environmental requirements in biotechnological production.

The composition of growth media for the microorganism's cultivation. Superficial and deep cultivation of producer cells. Technological and machine design of the deep cultivation process: continuous and batch.

Methodological approaches to the isolation and purification of biologically active substances (BAS). The main groups of methods for the biologically active substances isolation and purification: precipitation (sedimentation, centrifugation, filtration, ultrafiltration), extraction, chromatography (ion exchange chromatography, affinity chromatography, gel chromatography), electrophoresis, crystallization, evaporation.

2. Cellular Biotechnology

2.1. Genetic engineering in biotechnology. The cultivation of isolated animal and human cells. Quality control methods for medicines obtained from animal and human cells

The main stages of the transgenic organism's creation. Genetic engineering of prokaryotes, plants and animals. Molecular foundations of genetic engineering: structure and functions of DNA, RNA; enzymes used in the construction of recombinant DNA. Obtaining medicines by genetic engineering. Potential hazards when working with recombinant and transgenic organisms. Monitoring of trials in genetic engineering.

Features of animal cells cultivation. Requirements for producers, growth media and culturing conditions of animal and human cells.

Specific tests for medicines obtained using biotechnological methods. Conducting standardized tests «Sterility», «Pyrogenicity», «Toxicity», «Bacterial endotoxins» according to the State Pharmacopoeia of the Republic of Belarus. Determination of the specific activity of vaccines, sera and medicines based on monoclonal antibodies in vivo and in vitro. Calculation of effective doses of medicines obtained from human animal cells.

2.2. Production technology and standardization of medicines based on cytokines (interferons). Vaccines and sera production technology and standardization

Definition, general properties and classification of cytokines.

The main types, species-specificity and pharmacological action of interferons. Synthesis of various human interferons classes in genetically engineered microbiological cells. Quality control of drugs based on cytokines (interferons). The use of cytokines in medicine.

Definition, general properties and classification of vaccines. Vaccine technology. Ways to increase the immunogenicity of vaccines. Vaccine standardization. Sera production and standardization. The use of vaccines and sera in medicine.

2.3. Production technology and standardization of medicines based on monoclonal antibodies. Cultivation of plant cells and tissues. Obtaining biologically active compounds using plant cell cultures

Definition, structure and classification of monoclonal antibodies by pharmacological action. Monoclonal antibody production using hybridoma technology. Standardization of medicines based on monoclonal antibodies. The use of drugs based on monoclonal antibodies in medicine.

Advantages and features of isolated cells and plant tissues cultivation compared with traditional plant materials. Factors affecting the growth of plant cell culture and the accumulation of secondary metabolites. The genotype of the mother plant. Heterogeneity of cultured cells. Chemical and physical cultivation factors. Callus and suspension plant cells cultures. Clonal microreproduction of plants and its

practical application. Plant biomass production in order to isolate biologically active substances using the callus culture of ginseng cells as an example.

3. Microbial biotechnology

3.1. Production technology and standardization of probiotics and prebiotics, vitamins B_2, B_{12}, D_2, amino acids, organic acids, alcohols, thrombolytic medicines and anticoagulants

Normal microflora of the human intestine and its functions. Causes of dysbiosis. Nomenclature of medicines for the restoration of normal microflora. Characteristics of the main probiotics. Probiotics technology on the example of lactobactein. Quality control of medicines based on probiotics. Biochemical processes that occur during the cultivation of lactic acid bacteria. Mono-preparations and preparations based on mixed cultures of bacteria. Classification of the main prebiotics. The use of probiotics and prebiotics in medicine.

Vitamin classification. Vitamins obtained by microbiological synthesis methods. Features of the microbiological synthesis of vitamins by the example of vitamin B_{12}. Technology of isolation, purification, quality control of vitamin B_{12}. Obtaining, purification and quality control of vitamin B_2. Obtaining, purification and quality control of ergosterol and vitamins of group D. Nomenclature of vitamin medicines and biologically active additives produced in Republic of Belarus. The use of vitamins in medicine.

General characteristics of amino acids. Essential amino acids. Methods of amino acids industrial production, their advantages and disadvantages. Microbiological synthesis of lysine, tryptophan. Obtaining organic acids with a biotechnological method using citric acid as an example. Obtaining and quality control of ethanol. The use of amino acids, organic acids and alcohols in medicine.

The main properties of thrombolytic medicines. Thrombolytic therapy and generations of thrombolytics. Obtaining and quality control of anticoagulants. The use of anticoagulants in medicine.

3.2. Production technology and standardization of steroid hormones, insulin, enzymes, antibiotics

General characteristics and classification of hormones. Insulin: structure, mechanism of action, classification of insulin medicines. Production and quality control of human insulin. Steroid hormones, classification and traditional sources of their production. Microbiological synthesis of hydrocortisone and prednisolone preparation from it with bioconversion. Obtaining androgens and their analogues. Quality control of steroid hormones and their analogues. The use of steroid hormones and insulin in medicine.

The main properties of enzymes. Nomenclature of medicines based on enzymes. Biotechnological production of enzymes. Methods of enzymes isolation and purification. Methods of enzyme activity assessment. Methods of enzyme immobilization. The use of enzymes in medicine.

Classification of antibiotics depending on the chemical structure and production methods. Producers screening methods. Biological role of antibiotics as

secondary metabolites. Antibiotics production technology using microorganisms' fermentation cultures as example. Growth media preparation and optimization of the fermentation process conditions. Special antibiotic technology. Carbon skeleton assembly in beta-lactam antibiotics, aminoglycosides, tetracyclines and macrolides. Ways to create highly active producers. Quality control and standardization of antibiotics using biological and physico-chemical methods. Determination of antimicrobial activity of antibiotics by diffusion and turbidimetry.

CURRICULAR CHART OF THE EDUCATIONAL DISCIPLINE «PHARMACEUTICAL BIOTECHNOLOGY»

Section number, topic	Section title, topic	Amount of in-class hours		students' independent out-of-class work	Form of knowledge assessment
		lectures	practical classes		
1.	**General issues of pharmaceutical biotechnology**	**6**	**9**	**18**	
1.1.	Introduction to the discipline «Pharmaceutical biotechnology». Objects and methods of pharmaceutical biotechnology. Biological and environmental safety of biotechnological drugs. The main stages of the original biotechnological drugs and biosimilars development.	2	6	9	Test, interview, written reports on laboratory work, laboratory work using visual materials
1.2.	Technological process organization in biotechnological production. Industrial cultivation of microorganisms. Methods of biotechnological products isolation and purification.	4	3	9	Test, colloquium, modular rating assessment
2.	**Cellular biotechnology**	**6**	**15**	**27**	
2.1.	Genetic engineering in biotechnology. The cultivation of isolated animal and human cells. Quality control methods for medicines obtained from animal and human cells.	2	6	9	Test, interview, written reports on laboratory work, laboratory work using visual materials
2.2.	Production technology and standardization of medicines based on cytokines (interferons). Vaccines and sera production technology and standardization.	2	3	9	Test, interview, written reports on laboratory work, laboratory work using visual materials
2.3.	Production technology and standardization of medicines based on monoclonal antibodies. Cultivation of plant cells and tissues. Obtaining biologically active compounds using plant cell cultures.	2	6	9	Test, interview, written reports on laboratory work, laboratory work using visual materials

Section number, topic	Section title, topic	Amount of in-class hours		students' independent out-of-class work	Form of knowledge assessment
		lectures	practical classes		
3.	**Microbial biotechnology**	**4**	**12**	**17**	
3.1.	Production technology and standardization of probiotics and prebiotics, vitamins B_2, B_{12}, D_2, amino acids, organic acids, alcohols, thrombolytic medicines and anticoagulants.	2	6	8	Test, interview, written reports on laboratory work, laboratory work using visual materials
3.2.	Production technology and standardization of steroid hormones, insulin, enzymes, antibiotics.	2	6	9	Test, interview, written reports on laboratory work; exam
	Total hours	**16**	**36**	**62**	

INFORMATION AND INSTRUCTIONAL UNIT

LITERATURE

Basic:

1. Pharmaceutical Biotechnology: Fundamentals and Applications / V. Adams, R.R. Alloway, J.M. Beals [et al.]; edited by Daan J.A. Crommelin, R.D. Sindelar, B. Meibohm. – New York: Springer, 2013. – 551 p.

Additional:

1. Plotkin's Vaccines / S.A. Plotkin, W.A. Orenstein, P.A. Offit [et al.] – Philadelphia: Elsevier, 2018. – 2331 p.

2. Brown, T.A. Gene Cloning and DNA Analysis: An Introduction / T.A. Brown. – Hodoken: Wiley-Blackwell, 2016. – 376 p.

3. Pharmaceutical Biotechnology: Drug Discovery and Clinical Applications / S. Ahmad, M. Balls, D. Barh [et al.]; edited by O. Kayser, H. Warzecha. – Weinheim: Wiley-Blackwell, 2012. – 676 p.

LIST OF AVAILABLE DIAGNOSTIC TOOLS

Oral form:

- interview.

Written form:

- test;
- colloquium;
- written reports on laboratory work.

Oral and written form:

- exam;
- modular rating assessment.

Technical form:

- laboratory work using visual materials.

LIST OF PRACTICAL SKILLS

– the use of normative legal acts for production management and quality assurance of medicines obtained by biotechnological methods;

– development of technological and machine schemes for biotechnological production;

– the use of basic methods of growing isolated bacterial cells, plants' and animals' cells, tissues and organs in culture.

LIST OF LECTURES
8th SEMESTER

1. Introduction to the discipline «Pharmaceutical biotechnology». Objects and methods of pharmaceutical biotechnology. Biological and environmental safety of biotechnological drugs. The main stages of the original biotechnological drugs and biosimilars development.

2. Technological process organization in biotechnological production. Industrial cultivation of microorganisms.

3. Technological process organization in biotechnological production. Methods of biotechnological products isolation and purification.

4. Genetic engineering in biotechnology. The cultivation of isolated animal and human cells. Quality control methods for medicines obtained from animal and human cells.

5. Production technology and standardization of medicines based on cytokines (interferons). Vaccines and sera production technology and standardization.

6. Production technology and standardization of medicines based on monoclonal antibodies. Cultivation of plant cells and tissues. Obtaining biologically active compounds using plant cell cultures.

7. Production technology and standardization of probiotics and prebiotics, vitamins B_2, B_{12}, D_2, amino acids, organic acids, alcohols, thrombolytic medicines and anticoagulants.

8. Production technology and standardization of steroid hormones, insulin, enzymes, antibiotics.

LIST OF PRACTICAL LESSONS
8th SEMESTER

1. Introduction to the discipline «Pharmaceutical biotechnology». Objects and methods of pharmaceutical biotechnology. Biological and environmental safety of biotechnological drugs. The main stages of the original biotechnological drugs and biosimilars development.

2. Technological process organization in biotechnological production. Industrial cultivation of microorganisms. Methods of biotechnological products obtained from microorganisms isolation and purification.

3. Methods of biotechnological products isolation and purification.

4. Genetic engineering in biotechnology. The cultivation of isolated animal and human cells.

5. Quality control methods for medicines obtained from animal and human cells.

6. Production technology and standardization of medicines based on cytokines (interferons).

7. Vaccines and sera production technology and standardization.

8. Production technology and standardization of medicines based on monoclonal antibodies.

9. Cultivation of plant cells and tissues. Obtaining biologically active compounds using plant cell cultures.

10. Production technology and standardization of probiotics and prebiotics, vitamins B_2, B_{12}, D_2.

11. Production technology and standardization of amino acids, organic acids, alcohols, thrombolytic medicines and anticoagulants.

12. Production technology and standardization of steroid hormones, insulin, enzymes, antibiotics.

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Curriculum content, composition and accompanying documents comply with established requirements.

Dean of the Medical Faculty of International Students of the Educational Institution «Belarusian State Medical University» — O.S.Ishutin

21. 11. 2020

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21. 11. 2020

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