VOLGOGRAD STATE MEDICAL UNIVERSITY

DEPARTMENT OF PHARMACOLOGY AND BIOINFORMATICS

Methodological recommendations for students for practical classes
«Immunobiological and gene therapy drugs»

Thematic block: **Immunobiological drugs**

Class topic:

History of the use of biological drugs, their place in medicine and pharmaceuticals. Production of biological drugs and pharmacological safety of the country. Biological drugs: classification, use in medicine. Representatives of this group in the lists of drugs for medical use.

Pharmaceutical faculty

1. Class aims:

• learn how to analyze the action of biological drugs based on the totality of their pharmacological properties, mechanisms and localization of action;

• learn the general principles of production of biological drugs and the principles of compliance with the pharmacological safety of the country;

• learn to assess the risks of contamination of raw materials and materials in direct contact with process equipment or products;

• get acquainted with the process of state registration of biological medicinal products and consider the problems of regulation and production of gene and cell products in the Russian Federation;

2.Objectives

- • For groups of biological medicinal products (BMPs), study:
  - classification of biotechnological drugs;
  - composition of biological medicinal products;
  - the main mechanisms of action and application of biopreparations in medicine.
- Study the features of development and production of biological drugs:
  - methods of integrating a gene into the genome of a biomaterial cell (electroporation, viral vector)
- Study the basic terms and definitions used in the process of creating biopreparations:
- Study the general requirements for the production of medicinal products.

3. THE FOLLOWING PRACTICAL SKILLS AND ABILITIES ARE PRACTISED IN THE CLASS

• ability to classify biologically active substances based on the mechanism of action and methods of application;

• ability to analyze the possibilities of using BLS;

• the ability to analyze the risks of contamination of raw materials and materials that directly contact technological equipment or products during the production and use of biologically active drugs.

4. Class timetable:

Venue: classroom of the Department of Pharmacology and Bioinformatics.
Time of event: part 1 –2 AH
Formed competencies: УК-1.1.3, УК-1.2.1, УК-1.2.2, УК-1.2.3., УК-1.3.1, УК-1.3.2., УК-6.1.1., УК-6.2.1, УК-6.2.2, УК-6.3.1, УК-6.3.2, УК-6.3.3, УК-6.3.4, ОПК-1.1.1., ОПК-1.2.1, ОПК-1.2.2., ОПК-1.3.1, ОПК-6.1.1, ОПК-6.2.1, ОПК-6.3.1, ПК-7.1.1, ПК-7.2.1, ПК-7.3.1.

4.1 Technological map of the lesson

Part	№	Class stage	Time
1	1	Checking the students present at the lesson, lesson mode, lesson topic.	5 min
	2	Checking the initial level of students' knowledge (written survey).	10 min
	3	Survey on the topic of the lesson.	45 min
	4	Independent work of students (on prescriptions with analysis of the most complex prescriptions (if any in the topic), analysis of errors in medical prescriptions written by students; work with synonyms).	15 min
	5	Checking independent work	5 min
	6	Summing up the lesson. Assignment for the next lesson.	5 min
	7	Cleaning of workplaces.	5 min

4.2 Demonstrations

1. 1. Demonstration of advertising brochures on this topic during a survey on the topic of the lesson.

4.3 Lesson plan

4.3.1 The lesson begins with an introductory speech by the teacher, a statement of the purpose of the lesson and answers to students' questions.

In the teacher's opening remarks, draw the students' attention to the fact that at the end of the second millennium, drugs of a completely new type appeared – medicines based on biological molecules. Biological drugs (mainly monoclonal antibodies) have proven to be more specific and have made it possible to "target" previously inaccessible targets (due to protein-protein interactions), which has led to the emergence of new successful treatments in rheumatology and oncology. Such advantages have contributed to the wider introduction of biologics, and soon these drugs have gained considerable popularity due to their effectiveness, which has already allowed them to occupy a significant share of the pharmaceutical market. And yet, like small molecules, biological drug molecules also have disadvantages, antibodies, for example, are not able to penetrate cells due to their size, and therefore their therapeutic effect is limited mainly to extracellular proteins, such as hormones, growth factors, other antibodies, cellular receptors, etc. But since science does not stand still, today we see how medicine and drug therapy boldly go beyond traditional pharmaceuticals, and more and more new therapeutic modalities appear in the arena of clinical research, at the forefront of which is the so-called advanced therapy: gene and cell therapy.

The importance of the topic in the system of training and activities of a pharmacist:

- informing the population about the use of BLS;
- draw the attention of pharmacists to the prohibition of dispensing medicinal products by pharmacy organizations (clause 5, 6 of the RF Government Resolution of 22.12.2011 No. 1081 "On licensing pharmaceutical activities")

4.3.2 4.3.2 Checking the initial level of knowledge (written survey).

4.3.3 Analysis of theoretical material

Plan for analyzing theoretical material

1. **Biological drugs**
   - *Biological drugs classification.*
   - *General characteristics of biotechnological and gene therapy drugs. Differences in application.*

- *Biological drugs composition.*
- *Features of biological drugs.*
- *Biological drugs mechanism of action.*
- *Methods of integrating a gene into the genome of a cell of a biomaterial.*

2. Basic terms and definitions used in the process of creating biopreparations:

- *adjuvant;*
- *antigen/antibody;*
- *cell bank, master cell bank, cell stock, cell culture. host cells; working cell bank, cell stock, plasmid;*
- *biological pharmaceutical substance, excipients;*
- *vector/viral vector;*
- *passage, gene transfer;*
- *producer strain;*
- *pure culture, expression construct*
- *biohazard level.*

3 General requirements for the production of biological drugs

✓ *cell culture or extraction of material from living organisms*

✓ *variability of biological processes, inconstancy of the spectrum and nature of accompanying products*

✓ *safety of biological medicinal products. Strict control of starting materials, assessment of risks of contamination of starting materials and starting materials (special attention is paid to the risk associated with contamination by pathogens of animal spongiform encephalopathy (OFS "Reducing the risk of transmission of pathogens of animal spongiform encephalopathy when using medicinal products") and latent viruses (OFS "Viral safety").*

✓ *prevention of undesirable changes in properties that may occur as a result of multiple reseedings or a large number of generations, the production of biological pharmaceutical substances and medicinal products obtained from microorganism cultures, cell cultures or reproduction in embryos, tissues and organs of animals should be based on a system of main and working seed cultures and (or) cell banks.*

✓ *the number of generations (doubles, passages) between the seed culture or cell bank and the biological pharmaceutical substance or medicinal product must comply with the specifications in the registration dossier or clinical trial protocol. Seed cultures and cell banks must be created, stored and used in such a way that the risk of their contamination or change is minimal (e.g. stored in sealed containers in liquid nitrogen). The creation of seed culture systems and cell banks, including master and working seed cultures, must be part of the life cycle management of the biological medicinal product and carried out under appropriate conditions.*

✓ *cells and materials of biological origin used in the production process must be characterized and meet the requirements of microbiological and viral safety in accordance with the General Pharmacopoeia Monograph "Requirements for cell cultures-substrates for the production of biological medicinal products".*

4 *Conditions for ensuring the quality of biological medicinal products.*

✓ *only studied, genetically stable production strains of microbes are used in production, characterized and deposited in official collections, annually monitored for all biological properties, in accordance with regulated requirements; in this case, the genetic stability of the production strain is a criterion limiting the number of passages of the microbe*

✓ *use adequate nutrient media with high growth properties (raw materials, reagents and reactants used in the production of nutrient media must have certificates confirming their quality);*

✓ *use cell cultures in accordance with WHO recommendations, deposited in official collections and approved for use in production (when culturing cells, the use of native hu-*

man blood serum, as well as antibiotics of the penicillin group, is not permitted)

- ✓ *animals and birds, chicken embryos used for the production of biologically active medicinal products are obtained from farms that are free from bacterial, viral, prion and other diseases dangerous to humans, which is confirmed by veterinary certificates and certificates from a veterinary laboratory on the sanitary condition of the livestock, including microbiological and biochemical controls (OFS "Immunoglobulins and serums (antibodies) heterologous");*
- ✓ *when producing medicinal products from human blood plasma and cells and organs, the requirements imposed on the donor's health status must be met (OFS "Medicinal products from human blood plasma");*
- ✓ *Biological drugs that include donor tissues or cells must comply with the requirements of the legislation of the Russian Federation in terms of traceability, notification of the authorized federal executive body about adverse reactions and clinical cases during therapy, as well as in terms of technical requirements for the identification, processing, protection, storage and transportation of donor tissues and cells.*

5 Stages of Biological drugs research

- ✓ *Preclinical. Both in vitro and in vivo tests are conducted. The drug's activity, toxicity, minimum toxic doses, manifestations of toxicity over time, and receptor binding are assessed.*
- ✓ *Clinical. Conducted with the participation of large groups of people. The effectiveness of use, side and unwanted effects are assessed.*

* *The registration scheme for a biopreparation is similar to that of a drug obtained through chemical synthesis. Only after a comprehensive dossier has been compiled is the drug allowed for registration.*

6 The process of state registration of biological medicinal products

- ✓ *consider the problems of regulation and production of gene and cell products in the Russian Federation.*

4.3.4 Independent work:

1. Conduct a search and write out new terms and definitions. They are entered into students' workbooks. The list is given in the appendix 1.
2. Working with advertising brochures of medicines on this topic.

4.3.5 Checking the completion of independent work.

4.3.6 Summing up the lesson. Answers to questions.

4.3.7 Concluding remarks by the teacher.

Compiled by,
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