ODESSA NATIONAL MEDICAL UNIVERSITY
DEPARTMENT OF DRUGS TECHNOLOGY

APPROVE
Head of Department

_____ (Borisyuk I.Yu.)
signature
«29» August 2022 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty Pharmaceutical

Course Biopharmacy

Topic №1 **«Subject and objectives of biopharmacy. Biopharmaceutical factors and their role in the development of the composition and technology of drugs.»**

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
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signature

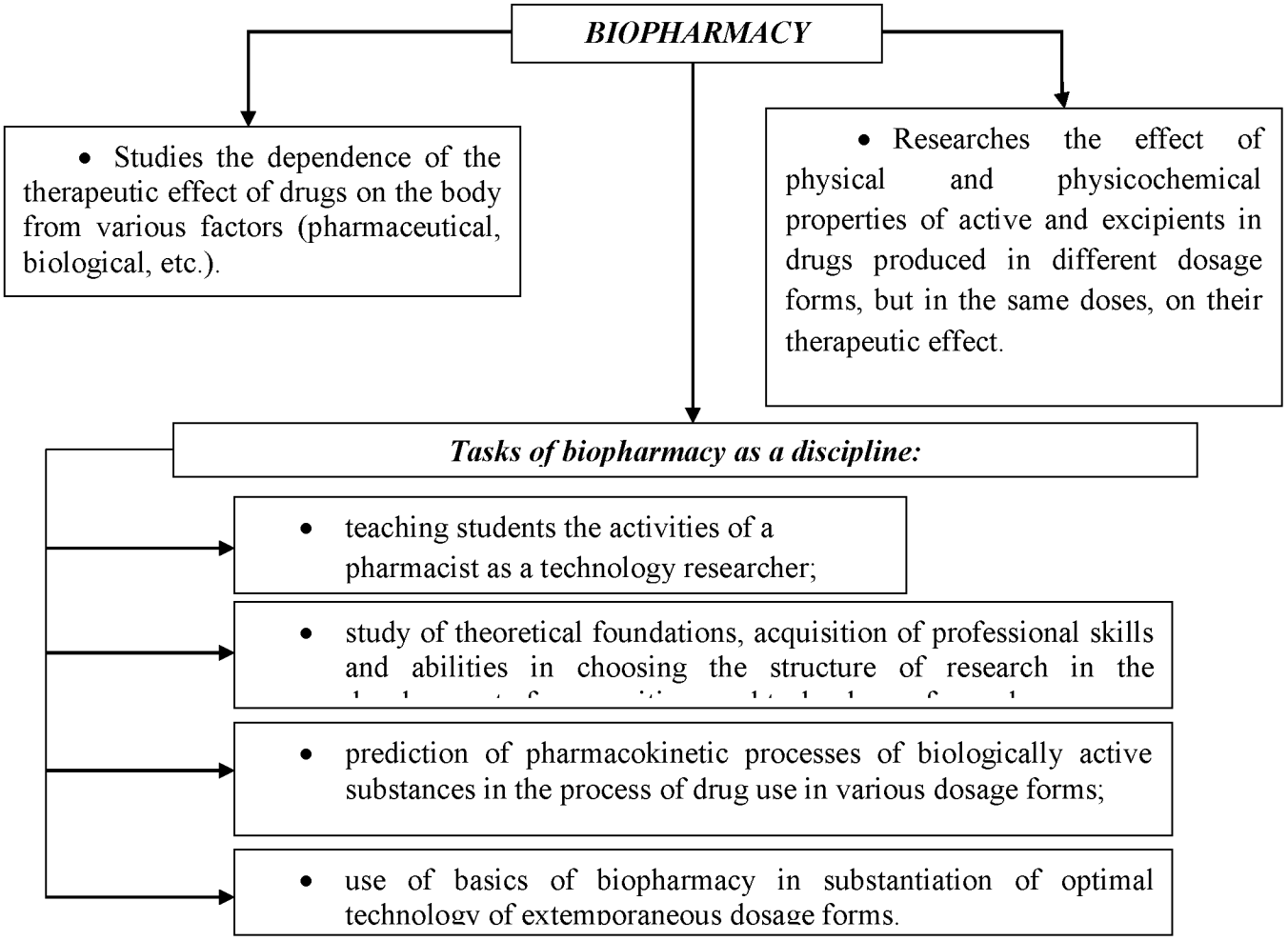
Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» August 2022 y.
Protocol № 1

Odesa - 2022

Subject: Subject and tasks of biopharmacy. Biopharmaceutical factors and their role in the development of the composition and technology of drugs "- 6 hours.
Purpose: Substantiation of the purpose and objectives of biopharmacy, history of its origin, basic terms and concepts, the concept of therapeutic non-equivalence of drugs, purpose and objectives of biopharmacy as a new scientific field, as well as the definition of biopharmaceutical factors and their role in creating new drugs.
Basic concepts: generics, polymorphism of medicinal substances.

Plan

I. Theoretical questions for the lesson:



Questions for self-control

1. Biopharmacy as a scientific discipline and its importance in the development of composition and technology of dosage forms.
2. History of biopharmacy development.
3. Basic concepts and terms of biopharmacy.
4. The main tasks of biopharmacy at the present stage and their role for practical health care.
5. The concept of pharmaceutical factors influencing the therapeutic efficacy of drugs, their classification.

6. The physical state of drugs and excipients in dosage forms and its effect on the rate of release and absorption of drugs.
7. The influence of the physical state of drugs on the pharmacological action.
8. The influence of the degree of dispersion of drugs on the therapeutic effect of drugs.
9. The effect of crystal structure and polymorphism of drugs on the pharmacological activity of drugs.
10. The influence of the nature of the solvent, solubility, degree of viscosity and pH of the medium on the absorption of drugs.
11. The degree of purity of the drug and its effect on pharmacotherapy.
12. Dependence of therapeutic activity of drugs on the type and quality of packaging.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic
2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	**The main tasks**	**Instructions**	**Answers**
1.	Define the science of biopharmacy, what it studies, for what purpose?	See answer	Biopharmacy is the theoretical basis of drug technology, the subject of which is the study of the influence of physical and physicochemical properties of active and excipients in drugs that are manufactured in different dosage forms, but in the same doses and differently affect therapeutic activity. Biopharmacy is a science that studies the dependence of the therapeutic effect of drugs on various variables (exogenous and endogenous).

2.	Indicate biopharmaceutical factors and their role in the development of the composition and technology of drugs	See the textbook	1. Biopharmacy: textbook / edited by: Borisyuk IY, Fizor NS, Akisheva AS Odessa, ONMedU, 2020. - pp. 4-23. 2. Gladyshev VV, Davtyan LL, Drozdov AL, Biryuk IA, Kechin IL Biopharmacy. Textbook for pharmaceutical universities and faculties. 2nd ed. Edited by VV Гладышева. Dnipro: ChMP "Economy". 2018.- p.4-13

II. Practical work (tasks) that will be performed in class:

Write recipes in Latin according to the current orders of the Ministry of Health of Ukraine. Justify the technology and make the appropriate calculations. Write a written control passport.

Take: Anesthesia 2.0
Boric acid 1.5
Tar 5.0
Castor oil 2.5
Ethyl alcohol 96% to 50 ml
Mix. Come on. Mark. Apply to hands.

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs_technology / Tests Step-2 on the following topics:

-Technology of powder preparation. Dosage by weight. Powder quality assessment (ATL)

IV. Individual tasks for students on the topic of the lesson

Prepare a presentation (abstract): Biopharmaceutical factors and their role in the development of the composition and technology of drugs.

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.
3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.

4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p

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«29» August 2022 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty Pharmaceutical

Course Biopharmacy

Topic №2 **«Biopharmaceutical and physicochemical aspects of suspensions and emulsions. Release and bioavailability of drugs from these dosage forms.»**

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
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Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odesa - 2022

Topic: "Biopharmaceutical and physicochemical aspects of suspensions and emulsions. Release and bioavailability of drugs from these dosage forms. " - 6 years

Objective: To deepen knowledge in the method of studying the pharmaceutical availability of drugs from suspensions and emulsions.

Basic concepts: Heterogeneous system, suspension, emulsion.

Plan

I. Theoretical questions for the lesson:

Liquid heterogeneous dispersed systems. Absorption of drugs used in the form of emulsions and suspensions takes place mainly in the upper part of the small intestine, because for absorption from the stomach they do not have sufficient solubility in water. The liquid state of these drugs promotes their rapid penetration into the site of absorption, increases the secretion of the gastrointestinal tract and stimulates peristalsis. The rapid transition from the stomach to the intestine is hindered by the high content of lipids in the emulsions and the increased viscosity of the emulsion and suspension systems. The excipients contained in these dosage forms interact with the intestinal membrane and, as a rule, improve its permeability.

Physico-chemical properties important for the release and transport of the drug substance from emulsions and suspensions are expressed by the following equations.

For the diffusion of soluble drug substance from the conductor is really:

$$Q = 2 \cdot C_0 \sqrt{\frac{Dt}{\pi}}.$$

Diffusion of the suspended drug substance from the conductor proceeds depending on:

$$Q = \sqrt{(2 \cdot C_0 - C_s) \cdot C_s \cdot D \cdot t}.$$

Diffusion of the emulsified drug substance from the conductor can be established by the equation:

$$D \to D_e = \frac{D_1}{V_1 + P \cdot V_2} \left(1 + 3V_2 \frac{P \cdot D_2 - D_1}{P \cdot D_2 - 2D_1}\right).$$

The Stokes-Einstein diffusion constant has the form:

$$D = \frac{R \cdot T}{N_A \cdot 6 \cdot \pi \cdot \eta \cdot r},$$,where

Q - released substance
C_s -solubility
P -distribution coefficient
N_A -Avogadro's number
D, D1, D2 -diffusion coefficient

η — viscosity
r — the radius of the molecule
C_0 — initial concentration
t — time
R — gas constant
V_1, V_2 — phase volume 1.2
T — absolute temperature
D_e — effective ratio

From the above equations it is seen that the absorption of drugs from oral emulsions and suspensions is affected by surface size, viscosity, surface tension, surfactants, which dissolves the ability of the components of the dispersion medium and the formation of complexes.

Viscosity. In emulsions, the viscosity of the oil increases:

- when using a narrower oil;
- when dissolving in it higher fatty alcohols and acids, emulsifier T-2, monoglycerides;
- with increasing molecular weight of the oily medium.

The viscosity of the aqueous medium increases with inclusion

to the composition of oil / water emulsions (m / v) gelling excipients: derivatives of cellulose and alginic acid, various polysaccharides.

The high viscosity of the dispersion medium is considered to be a factor that slows down the diffusion of the drug in the membrane, which is manifested in a slow absorption. The maximum concentration of the drug in the blood in this case reaches the initial value relatively later, and incomplete absorption may occur. A clear decrease in the DB with increasing viscosity was proved by the example of sodium salicylate, nitrofurantoin, salicylic acid, and others. In contrast to these drugs, thiamine and riboflavin from the system with higher viscosity are absorbed as well as from non-viscous solutions, obviously because in the mechanism of their absorption the active element predominates over the diffusion one.

It is not easy to specify the effect of viscosity on the database, because the viscosity affects the peristalsis of the gastrointestinal tract, and, in addition, substances that achieve high viscosity, often change the pH, dielectric characteristics and osmotic pressure of the liquid medium. , forming complexes and precipitates with many substances (especially polysaccharides).

Surfactants. The effect of surfactants on the absorption is manifested in the fact that they change the permeability of the membrane, improve surface wetting, thereby affecting the solubility and dissolution rate.

The best wetting is achieved by a small amount of surfactant, which is sufficient to accelerate the dissolution of many hydrophobic substances. When associated with a surfactant molecule, the active substance approaches the site of absorption, resulting in an increase in this factor. This mechanism is confirmed by the addition of sorbimacrogel Oleat to cholesterol, phenacetin, spironolactone and others.

Surfactants affect the membrane by dissolving and releasing phospholipids (lysolecithin), which changes the structure of the membrane, which becomes extremely permeable.

The effect of surfactants on absorption is manifested not only in increasing the wettability of the surface and changing the absorption properties of membranes, but also in the ability to solubilize hydrophobic substances. As a result of the transition of less soluble substance into solution increases, on the one hand, its DB, and on the other - the substance is fixed in the micelles, which complicates its diffusion to the site of absorption. This phenomenon occurs when the surfactant concentration exceeds the critical micelle concentration (CCM). The micelles form a second, accumulating on the solubilized substance colloidal phase. Absorption is slowed down because the micelles form a kind of accumulation of the active substance, from which, under stationary conditions, it is released by kinetics of pseudo-zero order. This is true, for example, for salicylic acid, but not for ethanol, which is not retained in the micelles.

The solubility of the components of the dispersion medium. To improve the degree of dispersion in liquid heterogeneous systems in most cases for technological reasons add ethanol, sorbitol, glystyrene, propylene glycol, dimexid, etc. These substances accelerate and increase the absorption, first, by dissolving part of the suspended matter , and secondly, due to its high lipophilicity facilitate the passage of drugs across the membrane.

The size of the surface. In suspensions, the surface size depends on the size of the dispersed particles. Properly formulated, in terms of the rate of absorption of drugs, the suspension is between the solution and the tablet, because the substance is not yet dissolved, but the phase of release (decomposition) and wetting is absent.

The particle size of the suspended drug particles is often a decisive factor for dissolution and absorption. By grinding the particles, the solubility of the drug increases slightly, and the dissolution rate increases significantly. Acceleration of dissolution promotes faster absorption, although it proceeds according to the laws of diffusion.

Reducing the particle size has its limits not only in terms of technology, but also in terms of database. For example, when taking trimethoprimsulfamethoxazole with a particle size of 12 and 6 nm, the difference was still determined, while at a value of 5 and 3 nm it was absent. The reason for this was the poor wettability of very small particles of the drug substance.

To ensure a high database, it is not the size of the particles that is crucial, but their effective surface, which depends on the interaction between the particle size and the surface tension of the dispersion medium. This phenomenon also explains why the absorption of drugs containing more mucous substances is slower than from the tablet.

Emulsions are characterized by a large surface area of the dispersing phase. However, this advantage is largely paralyzed by the very slow transport of the drug (diffusion) to the membrane.

The advantage of emulsions is that the drug substance in the internal phase is not exposed to gastric juice. In addition, the oily drug associated with food fat molecules can enter the systemic circulation through the lymph. For example, the absorption of vitamin A from fat systems is explained. Absolute absorption of insulin and macromolecular compounds (IUD) was achieved from water / oil (i / m) systems.

Suspensions. If in the technology of solutions the main issue is the solubility of the drug substance, then in the technology of suspension production - thermodynamic stability. The development of theoretical and practical issues of stabilization of pharmaceutical suspensions is associated primarily with the study of adsorption processes by various methods, which allow to obtain a number of parameters that characterize not only the surface area of the drug, but also its degree of filler, specific surface area and others.

These issues are especially important in the preparation of suspensions with hydrophobic drugs, for which it is advisable to possibly large hydro-phylization of the surface. It is carried out using surfactants, which dramatically reduce the absolute amount of wetting.

1. Biopharmacy: textbook / edited by: Borisyuk IY, Fizor NS, Akisheva AS Odessa, ONMedU, 2020. - pp. 69-72.

Questions for self-control

1. Stabilization of emulsions.
2. Pharmaceutical factors, their importance in drug technology.
3. .Influence of physicochemical state of drug substance on its pharmaceutical and bioavailability.
4. The main tasks of biopharmacy at the present stage and their role for practical health care.
5. Pharmaceutical factors influencing the therapeutic efficacy of drugs.
6. Physical state of medicinal and excipients in dosage forms and their effect
7. on the rate of release and absorption of drugs.
8. The use of different degrees of dispersion of drugs to create drugs with different bioavailability.
9. The concept of polymorphism.
10. The effect of crystal structure and polymorphism of drugs on the therapeutic activity of drugs.
11. Influence of the nature of the solvent, solubility, degree of viscosity and pH of the medium on the absorption of drugs.

12. The degree of purity of the drug and its effect on pharmacotherapy.
13. Dependence of therapeutic activity of drugs on the type and quality of packaging.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic
2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ WITH	The main tasks	Instructions	Answers
1.	What determines the release and resorption of the drug from the suspension.	Give an explanation	The release and resorption of drugs from suspensions is largely determined by the concentration of surfactants. And the principle: the more, the better - does not always justify itself. For example, it has been shown that better release and resorption of norsulfazole are observed from a suspension with 0.001% sucrose mono-laurate than from a suspension with a higher concentration of this surfactant. Therefore, it is of interest to study the creation of methods for selecting the amount of surfactants, in particular, using the value of the surface tension, measuring the absorption coefficient of ultrasound, and others.
2.	The stability of the emulsions that affect it.	Give an explanation	The stability of emulsions depends on the nature of the emulsifier, the dispersion medium and the oil phase, the ratio between oil, water and emulsifier, the method of preparation of the emulsion, the method of introduction of the emulsifier (surfactant, Navy, etc.). Depending on the objectives, emulsions should either promote

			the rapid and complete release of drugs, or provide a prolongation of their action.

II. Practical work (tasks) that will be performed in class:

Task1

To establish the influence of the degree of dispersion of streptocide on the process of its release from ointments by the method of "agar plates".

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs technology / Tests Step-2 on the following topics: Technology of preparation of aqueous and non-aqueous solutions. Evaluation of the quality of solutions

IV. Individual tasks for students on the topic of the lesson

Prepare a presentation (abstract): Features of liquid dosage forms

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.
3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.
4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p

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«29» August 2022 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty Pharmaceutical

Course Biopharmacy

Topic №3 **«Factors affecting the pharmaceutical and bioavailability of drugs from capsules. New solid dosage forms.»**

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
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Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» August 2022 y.
Protocol № 1

Odessa – 2022

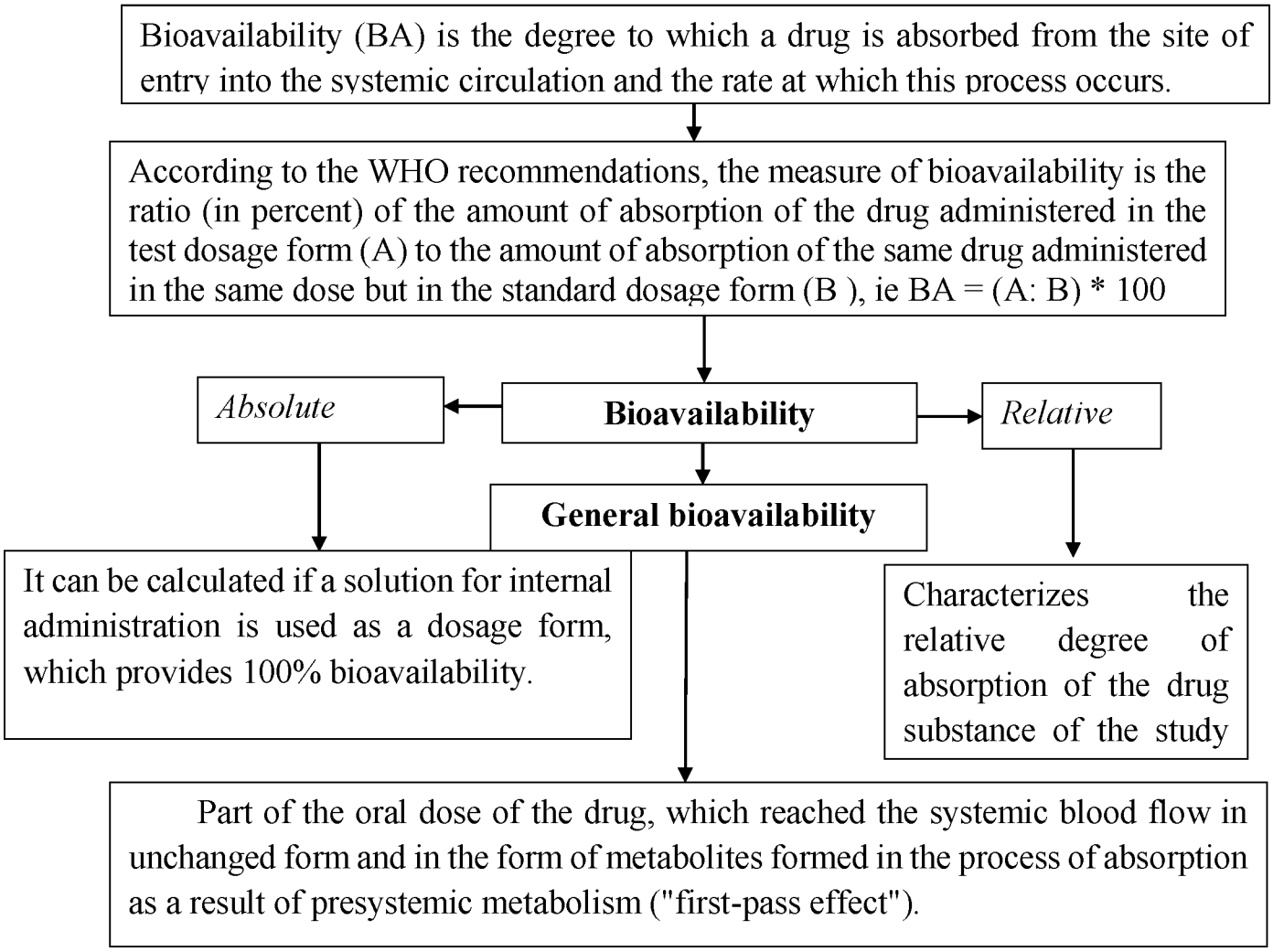
Topic: "Factors affecting the pharmaceutical and bioavailability of drugs from capsules. New solid dosage forms "- 6 hours.

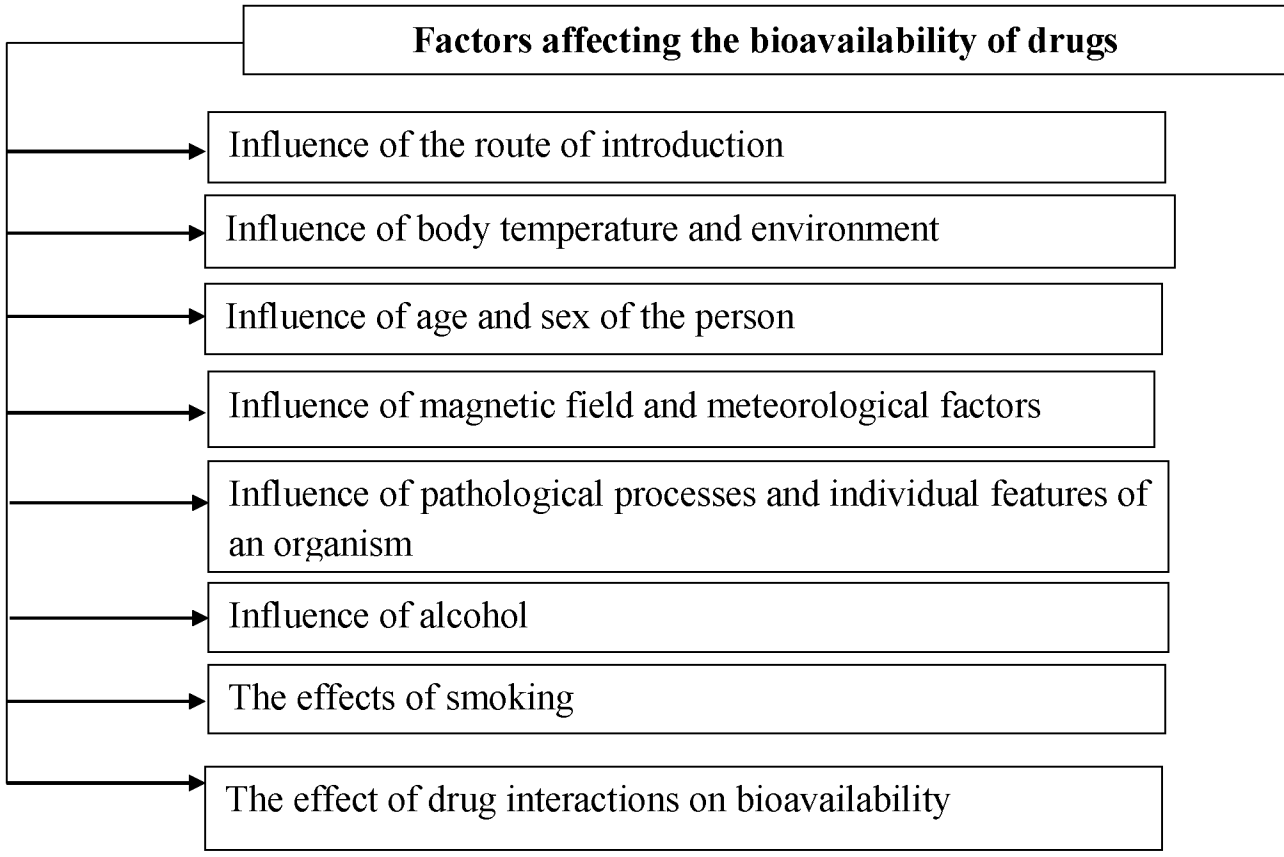
Objective: To deepen knowledge in considering the factors that affect the pharmaceutical and bioavailability of drugs from capsules. New solid dosage forms.

Basic concepts: Bioavailability, capsules.

Plan

I. Theoretical questions for the lesson:





Biopharmacy: textbook / edited by: Borisyuk IY, Fizor NS, Akisheva AS Odessa, ONMedU, 2020. - p29-50, 73-77.

Questions for self-control

1. Methods of obtaining tablets. The influence of pharmaceutical factors on the therapeutic efficacy of tablets.
2. Gelatin capsules, preparation and methods of filling. Influence of pharmaceutical factors on their therapeutic activity.
3. Classification of solid therapeutic systems.
4. The concept of solubility of drugs. Pharmacopoeial test to determine solubility.
5. The influence of the dosage form on the rate of absorption of the drug, its concentration in biological fluids and the stability of drugs.
6. The concept of pharmacodynamics and pharmacokinetics of drugs.
7. Types of bioavailability of drugs. Determination of absolute and relative bioavailability of drugs.
8. Calculation of the area under the pharmacokinetic curve. Absorption and elimination constants.
9. Distinctive features in the reactivity of different species of animals to the introduction of biologically active substances.
10. Correlation of methods "in vitro" and "in vivo" in determining the release and bioavailability of drugs.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic
2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	The main tasks	Instructions	Answers
1.	The concept of a capsule	Open the question See the textbook	Biopharmacy: Textbook. for students. pharmacy. universities and faculties. / AITikhonov, TG Yarnykh, IA Zupanets, OS Dankevich, EE Bogutskaya; Ed. AI Тихонова. - H .: Published by NUPh; Golden Pages, 2003.- - 169 p
2.	New solid dosage forms of prolonged action	Open the question See answer	Solid dosage forms of prolonged action are diverse, created on the basis of different technological principles, as well as with the use of a wide range of new excipients. Solid dosage forms of prolonged action include the following: multilayer tablets and pills, tablets with insoluble skeleton; tablets with resins; "Drilled" tablets and pills; tablets based on the principle of hydrodynamic balance and "osmotic
			pump "; long-acting coated tablets; tablets, granules and pills, the action of which is determined by the matrix or filler; implanted tablets with controlled release of the drug and others.

II. Practical work (tasks) that will be performed in class:

Task № 3

To establish the influence of the nature of the ointment base on the rate of absorption of medicinal substances from ointments into the blood of animals by the "in vivo" method.

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs technology / Tests Step-2 on the following topics:

-Technology of preparation of suspensions, emulsions, infusions and decoctions. Quality assessment (ATL).

-Industrial production of capsules. Quality assessment (PTLZ).

IV. Individual tasks for students on the topic of the lesson

Methods of studying the bioavailability of drugs.

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.
3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.
4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p

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METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty Pharmaceutical

Course Biopharmacy

Topic №4 «**Biopharmaceutical aspects of ophthalmic dosage forms, therapeutic systems such as "Ocusert". Factors that affect the quality and bioavailability of ophthalmic dosage forms**.»

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
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Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odessa - 2022

Topic: Biopharmaceutical aspects of ophthalmic dosage forms, therapeutic systems such as "Ocusert". Factors that affect the quality and bioavailability of ophthalmic dosage forms. " - 6 years

Objective: To deepen knowledge in the consideration of biopharmaceutical aspects of ophthalmic dosage forms, therapeutic systems such as "Ocusert". Factors affecting the quality and bioavailability of ophthalmic dosage forms.

Basic concepts: "Ocusert" type systems

Plan

I. Theoretical questions for the lesson:

Ophthalmic therapeutic systems

It is known that the volume of tear fluid under normal conditions is 0.0007 cm ^{3}. At the moment when this volume exceeds 0.03 cm ^{3}, a tear flows from the eye. When injected into the eye drops with LR, it is seen that the volume of 1 drop is equal to 0.05 cm ^{3}. This means that 80% of HR is displayed immediately, that lost, but that left the - elk, released the following 7-10hv. Thus, the efficiency of eye drops is low. This defect is eliminated by ocular therapeutic systems (OTC), which are placed under the eyelid.

OTC is the latest technological advancement in the development of long-acting drugs used in the treatment of various eye diseases.

Data from scientific sources indicate that the following film-forming substances are used as biosoluble polymers for the manufacture of ophthalmic films (OCP):

- natural substances of animal and vegetable origin (gelatin, collagen, chitin, pectin, tragacanth, agar-agar, gums, etc.);
- starch-containing derivatives (acetyl starch, oxyethyl starch, oxypropyl starch);
- cellulose derivatives (MC, NaKM4, oxyethyl- and oxypropylmethylcellulose);
- acrylic acid derivatives, polyvinyl derivatives, polymers of oxyethylene and its derivatives.

The release of LR occurs according to the kinetics of the zero-order equation and operates on the principle of diffusion.

Major efforts are applied to create systems with con - rolovanym LR release for use in ophthalmology. An example of such a system is the TTC "Ocusert" from "Alza" (USA), which contains pilocarpine (Fig. 26.3) and has the following advantages:

- dosing accuracy that changes over time ± 20%;
- exclusion ability DR with eyes that usually make up the wat - which drops;
- pH stability of lacrimal fluid;
- ensuring long-term action in time;
- reducing the number of injections to once a week instead of the proceedings before Cho - tyryrazovyh installations;

- reducing the consumption of substances. The release of LR in this system takes place
through a membrane which regulates speed of process depending on the surface and thickness. Media pilocarpine -ovalna plate with acid - lots of alginic, and the membrane is kopoli Mayor of ethylene and vinyl acetate. The energy release process gives HR the difference between the pressure re - zervuari in tears.

But this system is much more expensive than tradi - tional medicines (ointments, drops), and with its introduction there has been some discomfort.

The release rate of pilocarpine is P20 = 20 μg / h, P40 = 40 μg / h. A steady state of release is observed for 7 days. OTC action can be compared with a 2% solution pilokarpi - well, in the eye, which entered 4 times a day, which is 28mh and the treatment of OTC-3 - 66mh.

Membrane TS have been used in dental prac - purposes, the form of so-called dental drives. In such systems - max shell copolymer is oksietylmetakrylatu and methyl - methacrylate in the ratio 30: 70abo 50: 50.Systema releases sodium fluoride in 0,021mh daily for 30-180dniv.

Questions for self-control

1. Excipients in the production of ophthalmic drugs in Ukraine (bases, solvents, etc.).
2. Methods of obtaining tablets. The influence of pharmaceutical factors on the therapeutic efficacy of tablets.
3. Gelatin capsules, preparation and methods of filling. Influence of pharmaceutical factors on their therapeutic activity.
4. The concept of solubility of drugs. Pharmacopoeial test to determine solubility.
5. The influence of the dosage form on the rate of absorption of the drug, its concentration in biological fluids and the stability of drugs.
6. The concept of pharmacodynamics and pharmacokinetics of drugs.
7. Types of bioavailability of drugs. Determination of absolute and relative bioavailability of drugs.
8. Calculation of the area under the pharmacokinetic curve. Absorption and elimination constants.
9. Distinctive features in the reactivity of different species of animals to the introduction of biologically active substances.
10. Correlation of methods "in vitro" and "in vivo" in determining the release and bioavailability of drugs.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic

2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	**The main tasks**	**Instructions**	**Answers**
1.	Actions are needed to slow the absorption of drugs from ophthalmic dosage forms.	Define the term	lacrimal ducts. The same effect can be achieved by another method - the introduction of microcrystalline suspensions with a reduced rate of absorption. The use of oil solutions for this purpose, despite their gentle effect on the conjunctiva and high resistance to the microflora, has not become widespread due to the fact that a thin layer of oil, covering the cornea, significantly impairs vision.
2.	Isotonicity of ophthalmic solutions.	Define the term	***Isotonicity of ophthalmic solutions*** is a necessary condition for their preparation, as the solutions are not identical to tear fluid in composition, pH and other indicators. It is known that hypertonic and hypotonic solutions are poorly tolerated by patients. This is due to the fact that when instilling a hypertonic solution (more than 7.4 atm) due to the difference in osmotic pressure, the liquid comes out of the cells that come into contact with the solution, which leads to their shrinkage. Introduction of solutions with low OSMO - cal pressure causes swelling of cells and as a result - break the cell membrane. In both cases, these phenomena are accompanied by pain. For isotoning of ophthalmic solutions in accordance with the recommendations of the SF of Ukraine use sodium chloride, sodium nitrate, sodium sulfite, boric acid, glucose, sorbitol and other excipients, which must be compatible with the drugs contained in the solution. The amount of

			isotoning agent should be 0.9 + 0.2% in terms of sodium chloride.

II. Practical work (tasks) that will be performed in class

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs_technology_/_Tests_Step-2 on the following topics:

-Technology of preparation of ointments and suppositories in pharmacy practice. Quality assessment

-Preparation of drugs in aseptic conditions (Solutions for injections, ophthalmic dosage forms). Quality assessment

-Industrial production of ophthalmic dosage forms. Organ preparations. Quality assessment

IV. Individual tasks for students on the topic of the lesson

The effect of the dosage form of the substance on the bioavailability of drugs

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.
3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.
4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p

ODESSA NATIONAL MEDICAL UNIVERSITY
DEPARTMENT OF DRUGS TECHNOLOGY

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Head of Department

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«29» august 2022 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty Pharmaceutical

Course Biopharmacy

Topic №5 «**Influence of physiological and pharmaceutical factors on the pharmaceutical availability and absorption kinetics of drugs administered rectally and vaginally.»**

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
_____ (Fisor N.S.)
signature

Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» August 2022 y.
Protocol № 1

Odessa - 2022

Topic: "The influence of physiological and pharmaceutical factors on the pharmaceutical availability and absorption kinetics of drugs administered rectally and vaginally" - 4 hours.

Objective: To deepen knowledge in considering the influence of physiological and pharmaceutical factors on the pharmaceutical availability and absorption kinetics of drugs administered rectally and vaginally.

Basic concepts: Physiological factors, pharmaceutical factors.

Plan

I. Theoretical questions for the lesson:

1. Biopharmacy: textbook / edited by: Borisyuk IY, Fizor NS, Akisheva AS Odessa, ONMedU, 2020. - pp. 77-79.

Questions for self-control

1. Methods for determining the release of drugs from soft dosage forms
2. Methods for determining the release of drugs from suppositories.
3. The concept of simple chemical modification of drugs and its impact on the bioavailability and stability of drugs.
4. Ways of introduction of drugs into an organism and their influence on therapeutic activity.
5. The main biological factors affecting the absorption of drugs.
6. The influence of the patient's physiological state on the pharmacodynamics and pharmacokinetics of drugs.
7. Variable biochemical factors. Drug metabolism.
8. Influence of exogenous factors on pharmacotherapy.
9. Interaction of drugs with food.
10. Modern methods of analysis of drugs in biological fluids.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic
2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	The main tasks	Instructions	Answers
1.	Features of rectal absorption and what it depends on.	Give an explanation	Rectal absorption is in the nature of penetration, which proceeds according to the laws of diffusion, and therefore absorption through the membrane depends on the concentration of the drug in the

			rectal fluid. The higher this concentration, the faster and more significant its absorption. Because the membrane is lipoid in nature, substances pass through it in non-ionized form. The release of the suspended drug substance from the base is faster the smaller the particle size.
	What pharmaceutical factors affect the process of absorption of drugs administered rectally	Give an explanation	• solubility of substances and their dispersion; • nature and properties of the carrier (melting point, solubility, rheological properties, etc.); • the presence of absorption activators in the drug system (dimethyl sulfoxide , hyaluronidase, etc.). Surfactants can both accelerate and slow down absorption, which depends on the formation of complex compounds with certain physicochemical properties; • the presence of thickeners, such as aerosil, which slows the diffusion of drugs from the drug system to the absorption surface; • type of dosage form.

II. Practical work (tasks) that will be performed in class:

Task1

Task № 3

Calculate the area under the pharmacokinetic curve, the elimination constant and the absorption constant of streptocide in the blood from ointments and suppositories.

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs_technology_/_Tests_Step-2 on the following topics:

-Industrial production of tablets (Tablets by method: direct compression, with preliminary granulation, trituration tablets. Shells. Granules. Dragees). Quality assessment

IV. Individual tasks for students on the topic of the lesson

-Rectal route of administration. Features of bioavailability.

-Vaginal route of administration. Features of bioavailability.

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.
3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.
4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p

ODESSA NATIONAL MEDICAL UNIVERSITY
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«29» August 2022 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty Pharmaceutical

Course Biopharmacy

Topic №6 **«Bioequivalence of drugs - as a criterion for their quality.»**

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
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signature

Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» August 2022 y.
Protocol № 1

Odessa - 2022

Topic: "Bioequivalence of drugs - as a criterion for their quality" - 4 hours.
Objective: To deepen knowledge in the consideration of bioequivalence of drugs - as a criterion for their quality ..
Basic concepts: Bioequivalence.

Plan

I. Theoretical questions for the lesson:

The concept of bioequivalence is closely related to the concept of bioequivalence. Two drugs are considered bioequivalent if they provide the same bioavailability of the drug substance after administration in the same dose and the same dosage form. According to the WHO regulations (1994, 1996) and the EU (1992), the differences in pharmacokinetic parameters for the bioequivalence of drugs should not exceed 20%.

Currently, the study of bioequivalence is the main type of medical and biological quality control of generic drugs. The introduction of the definition of bioequivalence as a method allows to make a reasonable conclusion about the quality, efficacy and safety of comparable drugs on the basis of less primary information and in a shorter time than in clinical trials.

To date, there are regulations for studying the bioequivalence of the WHO (1996), the EU (1992). They set out the main rationale for the need for bioequivalence studies. These studies must be performed if there is a risk of lack of bioequivalence or a risk of reduced pharmacotherapeutic action and clinical safety of the drug.

For example, drugs for the treatment of conditions that require a guaranteed therapeutic effect must be evaluated; drugs with a small therapeutic breadth; drugs whose pharmacokinetics are complicated by a decrease in absorption of less than 70% or with high elimination (more than 79%); drugs with unsatisfactory physicochemical properties (low solubility, instability, polymorphism); drugs with documented evidence of a bioavailability problem.

Bioequivalence studies (pharmacokinetic equivalence) should in no way be considered as an alternative to pharmaceutical equivalence testing - the equivalence of generic drugs in terms of qualitative and quantitative composition of drugs assessed by pharmacopoeial tests, as pharmaceutical equivalence does not guarantee equivalence. However, bioequivalence studies suggest that the bioequivalence of the original generic drugs provide the same efficacy and safety of pharmacotherapy, ie are therapeutic equivalents.

Assessment of bioequivalence is based on the results of studying the relative bioavailability of the drug in the compared drugs. In essence, the study of bioequivalence is a special type of pharmacokinetic study. First of all, it should be emphasized that the study of bioequivalence is a clinical trial where the subject of the study is a person. Therefore, such studies are subject to all the official requirements and regulations that apply to all other clinical trials. A team of specialists in various fields should plan and conduct research to determine bioequivalence: clinical pharmacologists, clinicians, biochemists, chemists-

analysts. The study of bioequivalence should be conducted in full compliance with the principles of "Good Clinical Practice" (GLP) in order to guarantee the quality of data presented and protect the rights, health and well-being of subjects.

Animal bioequivalence studies have not been widely accepted and are practically not used. They are used only at the stage of preclinical studies or in the case of the study of drugs intended for use in veterinary medicine. Typically, the term "bioequivalence" in this case is replaced by the term "pharmacokinetic equivalence".

In determining the equivalence of antimicrobial drugs, it is possible to use in vitro methods, however, in this case, the term "bioequivalence" is preferred not to use.

Currently in Ukraine there is a sufficient material and technical base, highly effective methods are used to determine pharmacokinetic parameters, specialists are trained in the field of bioequivalence research, which allows to solve the urgent problem of assessing the effectiveness and safety of domestic and foreign generic drugs.

1. Biopharmacy: textbook / edited by: Borisyuk IY, Fizor NS, Akisheva AS Odessa, ONMedU, 2020. - pp. 58-60.

Questions for self-control

1. Generic drugs. Quality control.
2 .Bioequivalence of drugs.
3. The concept of chemical, biological, therapeutic equivalence of drugs.
4. Modern methods for determining the effectiveness of drugs.
5. Methods "in vitro" (direct diffusion through the membrane, "agar plates", chromatographic, solubility test, etc.).
6. Methods "in vivo", which are carried out on laboratory animals, healthy people, volunteers, isolated organs with single and multiple injections.
7. Modern methods for determining the concentration of drugs in biological fluids (blood, urine, excretion).
8. Microbiological and acanthosis tests.
9. Graphic method of calculating the area of the pharmacokinetic curve and the degree of absorption of drugs. Determination of absorption and elimination constants.
10. Radioisotope method.
11. Correlation of methods "in vitro" and "in vivo" in determining the bioavailability of drugs.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic

2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	The main tasks	Instructions	Answers
1.	Which drugs are considered bioequivalent?	Open the question	Drugs are considered bioequivalent if the 90% confidence interval for the geometric mean, calculated for individual relationships of logarithmically converted values of each of these pharmacokinetic parameters (except Stach), for the study drug to those for the comparison drug, is within 0.80 .. .1 , 25. For Stach, the corresponding limits are 0.70 ... 1.43. The limits of the above confidence interval are calculated using two one-way tests (mainly by the method of Schuirmann) after logarithmic conversion of pharmacokinetic parameters. If the specified confidence interval in the case of AUCt or AUC ∝ παραμετερσ□exceeds the established limits, the drugs are considered non-bioequivalent.

II. Practical work (tasks) that will be performed in class:

Task1

To establish the effect of polymorphic modifications of insulin preparations on the rate of its release by the "in vivo" method.

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs technology / Tests Step-2 on the following topics: Industrial production of soft dosage forms. Quality assessment

IV. Individual tasks for students on the topic of the lesson

Therapeutic equivalence.

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.

3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.
4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p

ODESSA NATIONAL MEDICAL UNIVERSITY
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«29» August 2022 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty of Pharmaceutical

Course Biopharmacy

Topic №7 «**Procedure for preclinical study of drugs, requirements for the conditions of preclinical studies.»**

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
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signature

Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» August 2022 y.
Protocol № 1

Odessa - 2022

Topic: "The procedure for preclinical studies of drugs, requirements for the conditions of preclinical studies." - 4 years

Objective: To deepen knowledge in considering the procedure for conducting preclinical studies of drugs, the requirements for the conditions of preclinical studies.

Basic concepts: Preclinical studies.

Plan

I. Theoretical questions for the lesson:

ORDER

conducting preclinical studies of drugs, requirements for the conditions of individual studies

The procedure for conducting preclinical studies of medicinal products, requirements for the conditions of certain studies have been developed in accordance with Article 6 of the Law of Ukraine "On Medicinal Products".

1. TERMS

1. Preclinical study of drugs involves chemical, physical, biological, microbiological, pharmacological, toxicological and other scientific studies to study their specific activity and safety.

2. Preclinical study of drugs involves the implementation of chemical, physical, biological, microbiological, pharmacological, toxicological and other scientific studies to establish specific and general pharmacological activity, as well as harmlessness to the body of active substances and finished drugs.

3. Preclinical study is an integral part of the drug development process. The characteristics of specific pharmacological activity and safety during use and in relation to its possible long-term consequences established by the results of preclinical study are fundamental factors that determine the possibility of transferring the drug to commercial release and the feasibility of its medical use.

Regulating and control functions on the organization and conduct and to identify the necessary volumes preclinical studied - tion medicines performs Pharmacological Committee of Ministry of Health of Ukraine.

1.4. Clinical trial conducted special purpose - vanymy research databases (institutions, organizations and businesses - we are), the list of which is determined based on certification of the norms applied in international practice.

1.5. Certification of databases of preclinical study of drugs and control over their activities in order to facilitate compliance with the requirements for planning and conducting research, the order of registration of results obtained by the Pharmacological Committee of the Ministry of Health of Ukraine through the Center for Preclinical Study of Medicines and relevant expert groups.

1.6. Control of materials (report) of preclinical study of a medicinal product on observance of methodical requirements, necessary volumes and reliability is carried out by specialized expert commissions of the Pharmacological Committee of the Ministry of Health of Ukraine. In the case of pre-clinical study of drugs for non-certified research databases or subject to preclinical studies specialized agencies -

we have other countries that are not certified by the standards of OR obtained D - from entrepreneurs to be controlled by the Center preclinical study drugs Pharmacological Committee of the Ministry of Health of Ukraine on their compliance with the requirements .

1.7. Preclinical studies of drugs can be performed on a contractual basis. Copyright, property and non-property rights related to the pre-clinical study of medicines are regulated by law.

2. PROCEDURE FOR PRECLINICAL STUDIES OF MEDICINES

1. The order of preclinical studies is determined according to the rubrication of drugs in the following groups:

I. Medicines from new pharmacological substances.

II. Known drugs with a new route of administration.

III. Known drugs with fundamentally new approaches to dosing.

IV. Drugs with altered technology for obtaining known pharmacological substances without changing the type and composition of the dosage form.

V. Medicines based on resynthesized pharmacological substances (by known technology).

VI. Combined drugs that contain two or more known pharmacological substances.

VII. Drugs are combined, which, along with the known ones, contain new pharmacological substances.

VIII. Drugs with a change in the composition of subsidiary Pharmaceuti - these substances on the basis of known pharmacological substances in a certain dosage form.

IX. Medicines recommended for new indications without changing the type, composition of the dosage form and mode of administration.

X. Medicines registered in the former USSR before 01.12.91, NTD for which are developed in Ukraine.

XI. Drugs produced by domestic technology with Viko - ristaniya imported pharmaceutical substances and (or) import headlights - matsevtychnyh substances suitable dosage forms which are registered in Ukraine if the former Soviet Union.

XII. Drugs manufactured by the licensed technology using pharmacological and pharmaceutical substances, the doctor - schimi shape for registration in Ukraine or of the former - it is the Soviet Union.

XIII. Homeopathic medicines.

XIV. Drugs manufactured by the new technology of Use - Tanna import tabletmasy, granules, appropriate dosage forms which are registered in Ukraine if the former Soviet Union.

XV. Medicinal products manufactured using a new technology using imported pharmacological substances and (or) imported pharmaceutical substances, the relevant dosage forms of which are registered in Ukraine or in the former USSR.

XVI. Medicines made from "in bulk" (packaging of the finished dosage form), registered in the form "in bulk".

2. The volume of preclinical studies that must be conducted to submit materials to the Pharmacological Committee of the Ministry of Health of Ukraine for further examination is determined according to these I-XVI groups of drugs and is the same for domestic and foreign drugs (studies are conducted as needed).

1. Medicines from new pharmacological substances: *Harmlessness*
   1. Acute toxicity to three species of animals;
   2. Subacute toxicity;
   3. Chronic toxicity;
   4. Local irritant and (or) ulcerogenic action;
   5. Possible cumulative effect;
   6. Possible allergenic properties;
   7. Toxic effect on the immune system;
   8. Teratogenicity; embryolethality; fetotoxicity; gonadotoxicity;
   9. Possible mutagenic properties;
   10. Possible carcinogenic effect;
   11. Drug dependence: if necessary; necessarily - for fundamentally new drugs;
   12. Treatment of poisoning in case of overdose in the experiment.

   Pharmacological activity
   1. Specific activity according to several criteria;
   2. General pharmacology.

   Pharmacokinetics

   2.2.2. Known drugs with a new route of administration: *Harmless*
   1. Acute toxicity in one species of animal;
   2. Subacute toxicity;
   3. Local irritant and (or) ulcerogenic action.

   Pharmacological activity

1. Specific activity according to several criteria. *Pharmacokinetics*

   3. Known drugs with fundamentally new approaches to dosing:

   Harmlessness
   1. Acute toxicity to three species of animals;
   2. Subacute toxicity;
   3. Chronic toxicity;
   4. Local irritant and (or) ulcerogenic action;
   5. Possible cumulative effect;
   6. Possible allergenic properties;
   7. Toxic effect on the immune system;
   8. Teratogenicity; embryolethality; fetotoxicity; gonadotoxicity;
   9. Possible mutagenic properties;
   10. Drug dependence.

   Pharmacological activity
   1. Specific activity according to several criteria;
   2. General pharmacology.

Pharmacokinetics

1. Dynamics of suction and excretion;
2. Bioavailability.

4. Drugs with modified technology for obtaining known pharmacological substances without changing the type and composition of the dosage form:

Harmlessness

1. Acute toxicity on one species of animals when the drug is administered in dosage form;
2. Subacute toxicity;
3. Local irritant and (or) ulcerogenic action;
4. Possible allergenic properties.

Pharmacological activity

1. Specific activity.

Pharmacokinetics

2.2.5. Medicines based on resynthesized pharmacological substances (by known technology):

Harmlessness

1. Acute toxicity on one type of animals when administered drug in dosage form compared to the dosage form based on origami - tional substance;
2. Subacute toxicity;
3. Local irritant and (or) ulcerogenic action;
4. Possible allergenic properties.

Pharmacological activity

1. Specific activity.

Pharmacokinetics

2.2.6. Combined drugs that contain two or more known pharmacological substances:

Harmlessness

1. Acute toxicity to three species of animals;
2. Subacute toxicity;
3. Chronic toxicity;
4. Local irritant and (or) ulcerogenic action;
5. Possible cumulative effect;
6. Possible allergenic properties;
7. Toxic effect on the immune system;
8. Teratogenicity; embryolethality; fetotoxicity; gonadotoxicity;
9. Possible mutagenic properties;
10. Drug dependence: if necessary.

Pharmacological activity

1. Specific activity according to several criteria;
2. General pharmacology.

Pharmacokinetics

1. Dynamics of suction and excretion;

2. Bioavailability.

7. Drugs are combined, which, along with the known ones, contain new pharmacological substances:

Harmlessness

1. Acute toxicity to three species of animals;
2. Subacute toxicity;
3. Chronic toxicity;
4. Local irritant and (or) ulcerogenic action;
5. Possible cumulative effect;
6. Possible allergenic properties;
7. Toxic effect on the immune system;
8. Teratogenicity; embryolethality; fetotoxicity; gonadotoxicity;
9. Possible mutagenic properties;
10. Possible carcinogenic effect;
11. Drug dependence: if necessary; required - for prin - Tipova new drugs;
12. Treatment of poisoning in case of overdose in the experiment.

Pharmacological activity

1. Specific activity according to several criteria;
2. General pharmacology.

8. Drugs with a change in the composition of subsidiary Pharmaceuti - these substances on the basis of known pharmacological substances in a certain dosage forms:

Harmlessness

1. Acute toxicity to three species of animals;
2. Subacute toxicity;
3. Local irritant and (or) ulcerogenic action;
4. Possible allergenic properties.

Pharmacological activity

1. Specific activity by one criterion.

Pharmacokinetics

1. Dynamics of suction and excretion;
2. Bioavailability.

9. Medicines recommended for new indications without changing the type, composition of the dosage form and mode of administration.

Harmless Studies are not performed.

Pharmacological activity

1. Specific activity by one criterion;
2. Specific activity according to several criteria. *Pharmacokinetics*

10. Medicines registered in the former USSR before 01.12.91, NTD (regulatory and technical documentation) for which developed in Ukraine;

- to the Pharmacological Committee of Ministry of Health Ukraine provided mat - ly that were considered in the Pharmacological Committee of the USSR. Additional clinical trials are not performed.

2.2.11. Drugs produced by domestic technology, using imported pharmaceutical substances and (or) import of pharmaceutical substances suitable dosage forms which zareyest - Rowan in Ukraine if the former Soviet Union:

Harmlessness

1. Acute toxicity in one species.

Pharmacological activity

1. Specific activity by one criterion.

Pharmacokinetics

2.2.12. Drugs manufactured by the licensed technology using pharmacological and pharmaceutical substances, dosage forms which correspond registered in Ukraine or in co - ex USSR:

Harmlessness

1. Acute toxicity in one species.

Pharmacological activity

1. Specific activity by one criterion.

Pharmacokinetics

2.2.13. Homeopathic medicines:

Harmlessness

1. Chronic toxicity;
2. Possible allergenic properties.

Pharmacological activity

Pharmacokinetics

2.2.14. Drugs manufactured by new technology inc - a handling import tabletmasy, granules, appropriate dosage forms which are registered in Ukraine if the former Soviet Union:

Harmlessness

1. Acute toxicity in one species.

Pharmacological activity

1. Specific activity by one criterion.

2.2.15. Drugs manufactured by new technology inc - a handling imported pharmaceutical substances and (or) import pharma - tsevtychnyh substances suitable dosage forms which are registered in Ukraine if the former Soviet Union:

Harmlessness

1. Acute toxicity in one species.

Pharmacological activity

1. Specific activity by one criterion.

2.2.16. Medicines made from “in bulk” (packaging of the finished dosage form), registered in the form “in bulk”:

Preclinical studies are not performed.

3.3.Recommended literature:

Main literature:

1. OI Tikhonov, TG Yarnykh, OI Zupanets, OS Dankevich, OS Bogutska, NV Bezditko, YMAzarenko, YV Levachkova Biopharmacy.-NFAu.- 2010.- 240p. Approved by the Ministry of Education and Science of Ukraine

2. Biopharmacy: Textbook. for students. pharmacy. universities and faculties. / AITikhonov, TG Yarnykh, IA Zupanets, OS Dankevich, EE Bogutskaya; Ed. AI Тихонова. - H .: Published by NUPh; Golden Pages, 2003.-240p .: 18 fig.

3. Workshop on biopharmacy: Textbook. manual for university students / AITikhonov, EE Bogutskaya, TG Yarnykh, etc .; ed. AITikhonova.- Kharkiv: NUPh Publishing House: Golden Villages, 2003.- 96p.

Additional literature:

1. Харкевич Д.А. Pharmacology: - Textbook. - 8th ed., Revised, Additional. and ispr. - M .: GEOTAR-Media, 2005.- 736 p.

2. Tikhonov, OI Pharmacy technology of drugs. Biopharmaceutical aspects of geriatric drugs: a lecture for graduate students special. "Technology of drugs and the organization of pharmaceutical business" / OI Tikhonov, TG Yarnykh, OE Bogutska. - H .: NUPh Publishing House, 2009. - 20 p.

3. Tikhonov, AI Influence of biological factors and environmental factors on the bioavailability of drugs: a lecture for extracurricular activities. work stud. special "Pharmacy" / AI Tikhonov, TG Yarnykh, EE Bogutskaya. - H .: NUPh Publishing House, 2009. - 36 p.

Questions for self-control

1. The concept of simple chemical modification of drugs and its impact on the bioavailability and stability of drugs.
2. Classification of excipients and their role in the preparation of dosage forms. The influence of the nature of excipients on the rate of absorption of drugs and their therapeutic efficacy.
3. The influence of the dosage form on the rate of absorption of the drug, its concentration in biological fluids and the stability of drugs.
4. Ways of introduction of drugs into an organism and their influence on therapeutic activity.
5. Influence of technological factor on pharmacotherapy.
6. The concept of drug stability. The role of stabilizers in drug technology.
7. nfluence of drug storage conditions on their stability.
8. The concept of pharmacodynamics and pharmacokinetics of drugs.
9. The main biological factors influencing the absorption of drugs.
10. The influence of the physiological state of the patient on the pharmacodynamics and pharmacokinetics of drugs.
11. Variable biochemical factors. Metabolism and elimination of drugs.

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic

2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	The main tasks	Instructions	Answers
1.	The procedure for clinical study of drugs.	Define the term	Tikhonov, OI Pharmacy technology of drugs. Biopharmaceutical aspects of geriatric drugs: a lecture for graduate students special. "Technology of drugs and the organization of pharmaceutical business" / OI Tikhonov, TG Yarnykh, OE Bogutska. - H .: NUPh Publishing House, 2009. - 74 p.
2.	Where certification of preclinical study of drugs and control over their activities is carried out.	Give an explanation	Certification of databases of preclinical study of drugs and control over their activities in order to facilitate compliance with the requirements for planning and conducting research, the order of registration of results obtained by the Pharmacological Committee of the Ministry of Health of Ukraine through the Center for Preclinical Study of Medicines and relevant expert groups.

II. Practical work (tasks) that will be performed in class:

III. Test tasks for self-control

http://info.odmu.edu.ua/chair/drugs technology / Tests Step-2 on the following topics:

-Industrial production of pharmaceutical solutions of syrups, extraction preparations. Quality assessment

-Industrial production of biogenic stimulants. Aerosols. Quality assessment

IV. Individual tasks for students on the topic of the lesson

Prepare a presentation (abstract): The main directions of improvement of drugs and development of biopharmaceutical research.

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.

3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.
4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p

ODESSA NATIONAL MEDICAL UNIVERSITY
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«29» August 2022 y.

METHODICAL DEVELOPMENT OF INDEPENDENT WORK OF STUDENTS (IWS)

Course 5 Faculty of Pharmaceutical

Course Biopharmacy

Topic №8 **«Conducting clinical trials of drugs.»**

Methodical recommendations on IWS developed by:
Ph.D. of Pharmaceutical Sciences
_____ (Fisor N.S.)
signature

Methodical recommendations of IWS were discussed at the methodical meeting of the department
«29» August 2022 y.
Protocol № 1

Odessa - 2022

Topic: "Conducting clinical trials of drugs" - 4 hours.
Objective: To deepen knowledge in the consideration of clinical trials of drugs.

Basic concepts: Clinical trials

Plan

I. Theoretical questions for the lesson:

Order of the Ministry of Protection
health of Ukraine
from 25.09.2002 № 355

REGISTERED at the Ministry of
Justice of Ukraine on October 14, 2002
for № 825/7113

CHANGES AND ADDITIONS
to the instructions for conducting clinical trials
of drugs
and examination of clinical trial materials

1. In section 2:

1. Sub-clause 2.1.1 of clause 2.1 after the words “patients (volunteers)” shall be supplemented with the words “and (or) healthy volunteers”.
2. Paragraph 2.1 shall be supplemented with sub-clauses 2.1.7, 2.1.8 as follows:

«2.1.7. *Bioavailability* - the speed and degree with which it is active
the substance or its active part is absorbed from the dosage form and becomes available at the place of its intended action.

«2.1.8. *Bioequivalence* - two drugs are considered bioequivalent if they are pharmaceutically equivalent or pharmaceutically alternative and their bioavailability after administration in the same molar doses is similar to the extent that they can be expected to be equally effective and safe.

1.3. Paragraph 2.3 shall be supplemented with sub-clause 2.3.1 as follows:

«2.3.1. *A generic drug* is a finished drug that can replace a new drug after the expiration of the patent.

1.4. Paragraph 2.16, after the words "Examination materials" add the words "and preclinical study" and after "assessment of materials" add the words "and pre-clinical study."

2. Section 3 shall be worded as follows:

«3.1. To conduct a clinical trial of a medicinal product, the customer submits to the Center an application of any form, to which are attached:

materials that contain general information about the drug;

the results of its pre-clinical studies and clinical trials (if any);

like drug with a certificate of origin, Approval - Jen customer [1, 2];

information on where the medicinal product submitted for clinical trials was manufactured; [1 2]

information on the technology of manufacturing (production) of the medicinal product and documentation on which the control of the manufacturing and quality of the medicinal product was carried out [2].

3.2. Available materials are subject to examination at the Center, which Provo - is in a manner prescribed by Section 4 hereof. In case of positive conclusions provided by the customer, the Center determines the clinical base (bases), type and scope of clinical trials. The Center informs the customer about the decision.

If a non-mass drug is submitted for clinical trials, the Center may check the conditions of its manufacture.

3.3. After determining the clinical bases, the customer submits to the Center materials:

Protocol clinical trial that will develop - lyayetsya according to the type and phase of drug testing, guidelines and regulations of the Center and the European Economic Community. The structure of the protocol is given in Annex 1;

the researcher's brochure (summary of the results of preclinical and clinical (if any) studies of the drug that are important for its study in humans) or instructions for medical use of the drug. The structure of the researcher's brochure is given in Annex 2;

information for the subject and (or) a form of informed written consent;

individual registration form (if necessary);

the results of previous examinations and (or) decisions of the Center concerning preclinical study and clinical trial of the medicinal product (if any) ".

3. In section 4:

1. The title of section 4 shall be worded as follows: "Examination of materials of preclinical study or clinical trial of medicinal products".
2. In paragraph 4.1, replace the words "in paragraph" with the words "in section".
3. Paragraph 4.2 shall be worded as follows: “Examination of materials of pre-clinical study of a medicinal product or clinical trial shall be carried out under the terms of an agreement between the customer and the Center. The examination of the materials of the pre-clinical study and clinical trial in accordance with the protocol (excluding the number of clinical databases) and amendments to the protocol is subject to payment.
4. Paragraph 4.3 after the words "additional data on" add the words "preclinical study or". The second sentence of paragraph 4.3 to read as follows: "The time required to prepare them, not part of the thermo - well, expert works."

4.3 second paragraph after "the materials" with the words - "we preclinical or".

3.5. The first paragraph of paragraph 4.4 after the words "to the materials" add the words "preclinical study or". In the second paragraph of paragraph 4.4 after the words "the materials" delete the words "clinical trial".

3.6. Paragraph six of paragraph 4.7 after the word "(volunteers)" add the words "and healthy volunteers".

4. In section 5:

1. Item 5.1 the following sentence: "The drug is transmitted by an act of transfer, stating the number and batch number of the medicinal product, which were submitted to the Laboratory of Drug Quality Control Center for Quality Control (international multicenter clinical trials according to August - tyfikata quality medicinal product provided by the manufacturer) ".
2. Paragraph 5.8 shall be supplemented with the following sentence: "If necessary, the Center has the right to withdraw the investigational medicinal product in the amount required for re-analysis of quality in the Laboratory of Quality Control of Medicinal Products of the Center, as well as for other examinations."

5. In section 6:

1. Item "6.2. Examination of the results of a clinical trial is free of charge "- to exclude.
2. Paragraph 6.9 shall be worded as follows: "In case of positive conclusions of the examination, the Center approves the results of the clinical trial presented in the report and recommends or does not recommend the continuation of the clinical trial of the medicinal product. The Center informs the customer about the decision made. "

6. To supplement the Instruction on conducting clinical trials and examination of clinical trial materials with section 6 of the following content:

«6. *Features of clinical trials of drugs to establish bioequivalence*

6.1. Clinical trials and examination mat - Live on clinical trials to establish bioequivalence studies conducted in accordance with sections 3-7 hereof.

6.2. The object of study in a clinical trial to establish bioequivalence are generic drugs that are intended for extravascular administration, provided that their action is mediated by the appearance of the substance in the systemic circulation.

6.3. Appropriate drugs with proven bioavailability are used as a comparison drug, the list of which is determined by the Center.

6.4. Patients (volunteers) or healthy volunteers may be involved in a clinical trial to establish bioequivalence.

6.5. Persons between the ages of 18 and 55 may be involved in a clinical trial to establish bioequivalence as healthy volunteers. Healthy volunteers can be people who do not have chronic diseases of the cardiovascular and neuroendocrine systems, liver, kidneys, as well as people who do not have a burdensome history of allergies.

Until research can not involve minors, pregnant women and women who are breastfeeding, people who are in pre iso - modulator, in prisons and military terms - ing service.

6.6. Appropriate studies of antitumor, psychotropic and medicinal products used in HIV infections may be performed with the involvement of patients who are shown the purpose of the study drug.

7. In this regard, section 6 of this Instruction shall be considered section 7.

Questions for self-control

1. The impact factor **and** the environment on pharmacotherapy.
2. Interaction of drugs with food.
3. The concept of therapeutic non-equivalence of drugs and the causes of its occurrence.
4. Brands and generics. Replacement of drugs by their analogues.
5. Types of bioavailability of drugs. Determination of absolute and relative bioavailability of drugs.
6. "In vivo" methods, which are performed on living organisms of laboratory animals, healthy human volunteers and on isolated organs with single and multiple injections.
7. Distinctive features in the reactivity of different species of animals to the introduction of biologically active substances.
8. "In vitro" methods used in biopharmacy (direct diffusion through the membrane, "agar plates", chromatographic, solubility test, etc.).
9. Modern methods for determining the concentration of drugs in biological fluids (blood, urine, and other body secretions).
10. Graphical method of calculating the area of the pharmacokinetic curve and the relative degree of absorption depending on pharmaceutical factors. Determination of absorption and elimination constants

Approximate tasks for the study of theoretical material

1. Make a dictionary of basic concepts on the topic
2. Fill in the orientation card for self-preparation of the student using the literature on the topic :

№ z.p.	**The main tasks**	**Instructions**	**Answers**
1.	Conducting clinical trials of drugs	Define the term	Tikhonov, AI Influence of biological factors and environmental factors on the bioavailability of drugs: a lecture for extracurricular. work stud. special "Pharmacy" / AI Tikhonov, TG Yarnykh, EE Bogutskaya. - H .: NUPh Publishing House, 2009. - 83 p.
2.	Generic drug	Define the term	A generic drug is a finished drug that is able to replace a new drug after the expiration of the patent.

II. Practical work (tasks) that will be performed in class:

http://info.odmu.edu.ua/chair/drugs_technology / Tests Step-2 on the following topics: Industrial production of parenteral drugs Quality assessment

III. Test tasks for self-control

IV. Individual tasks for students on the topic of the lesson

Prepare a presentation (abstract):

- In vitro research methods
- In vivo research methods

List of recommended reading

Main:

1. .Biopharmaceutics. Збірник текстів лекцій./ Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S., НФаУ Оригінал, 2011. – 140 с.
2. Biopharmaceutics. Практикум / Tikhonov A.I., Bogutskaya Ye.Ye., Yarnykh T.G., Kotenko A.M., Garkavtseva O.A., НФаУ Оригінал, 2011. – 80 с.
3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.
4. Biopharmaceuticals: Biochemistry and Biotechnology, 2nd Edition. – 2013. – 544 p