ODESSA NATIONAL MEDICAL UNIVERSITY
DEPARTMENT OF DRUGS TECHNOLOGY

APPROVE
Head of Department

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

METHODICAL DEVELOPMENT OF PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course Biopharmacy

Practical lesson №9 Topic: «**Bioavailability of drugs. Absolute, relative bioavailability. Classification of factors influencing the bioavailability of drugs.»**

The practical lesson was developed by:
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The practical lesson was discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odesa – 2022

The purpose of the lesson: To acquire practical skills in calculating the main indicators of bioavailability of drugs and forecasting the bioavailability of drugs using the "Rules of the Five" Lipinski. Master the classification of factors influencing bioavailability.
Basic concepts: bioavailability, absolute and relative bioavailability.
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 2.0

Plan

I. Organizational moment.
II. Control of basic knowledge
2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):
Requirements for theoretical knowledge:

Bioavailability (F) is a pharmacokinetic parameter that characterizes the efficacy of drugs by determining the proportion of drug that enters the systemic circulation relative to the initial dose of the drug. Bioavailability is the main indicator that characterizes the amount of drug loss during transportation to the site of action in the human body (the ability of the drug to be absorbed). That is, the higher the bioavailability of the drug, the less loss will be during the assimilation and use of the body. When administered intravascularly, the bioavailability of the drug is 100%, with other routes of administration, it is much lower and almost never reaches 100%. For example, insulin is broken down by gastric enzymes, ie it has low bioavailability when taken orally, so it is used only subcutaneously or intramuscularly.

Absolute bioavailability is determined by comparing the degree and rate of entry of the substance of the study drug into the systemic circulation (subject to extrasystemic administration: orally, rectally, subcutaneously) with the standard after its intravascular administration. Bioavailability as a research method gained general recognition in the second half of the twentieth century, after the discovery of the phenomenon of therapeutic non-equivalence of drugs with the same composition, in identical dosage forms, but manufactured in different factories. Today, bioavailability is of national importance in the development, production and use of drugs and as a method underlies the parameters for determining the bioequivalence of essentially similar drugs.

The relative bioavailability is determined by comparing the degree and rate of absorption of the drug (eg tablets) with the so-called comparison standard (eg capsules) with the same or different routes of administration (eg tablets and suppositories) provided that they contain the same active substance in equal quantities. The definition of "relative bioavailability" is widely used to confirm the equivalence of the therapeutic effect of essentially similar drugs to the reference and to compare the therapeutic efficacy of the studied drugs.

The intensity and duration of pharmacological action of drugs depend on their pharmacokinetic characteristics (absorption, distribution, biotransformation,

mechanism of excretion), which, in turn, are closely related to the concept of bioavailability. The complexity of qualitative and quantitative assessment of the bioavailability of drugs is associated with a large number of factors that affect these characteristics. They are divided into exogenous (pharmaceutical or technological) and endogenous (physiological, genetic, etc.). By **exogenous factors** affecting bioavailability include: physical properties of substances (solubility, hydrophobicity, polymorphism, optical and other properties), the nature and amount of excipients that make up the drug, type of dosage form manufacturing technology and others (dose, way, speed of drug administration, use of other drugs, non-compliance with recommendations on medical nutrition, etc.), which should be taken into account at the stages of development, production and use of drugs. The bioavailability of drugs is also influenced by **endogenous** physiological (sex, age, weight), genetic and ethical parameters of the patient, the presence of comorbidities and more. Taking into account the factors influencing the bioavailability of drugs allows to optimize the mode of their production, administration and increase the effectiveness of pharmacotherapy in general. Bioavailability studies on living organisms are time consuming, expensive and may not always be applicable under normal production conditions.

There are different guidelines for **prediction of bioavailability** , the most famous of which is the " **rule of five" Lipinski** (Eng. Lipinski rule of five). This rule was formulated by Christopher A. Lipinski in 1997 based on the observation that most drugs are relatively small and lipophilic molecules. To predict the pathways of biochemical transformation of drugs, it is necessary to take into account lipophilicity, size and surface of the corresponding molecule, the presence of groups that can be attacked by enzymes and its optical properties.

The term "drug-like properties" has recently become commonplace for pharmacy and usually reflects the simple physicochemical and structural properties (molecular descriptors) characteristic of successful drugs.

The rules of five ("drug likeness" or the concept of similarity to a drug substance) are as follows: 1) LogP ≤5;

2) molecular weight ≤500;

3) the ability to be a proton acceptor ≤10;

4) the ability to be a proton donor ≤5;

5) rotation of connections ≤8.

Parameters 3 and 4 indicate the ability of the compound to form bonds in the "appropriate" region of the biomolecule, parameter 5 characterizes the "stiffness" of the structure and indicates the volume of the substance. Thus, these criteria characterize the general features of the chemical structure of the drug, taking into account sorption, distribution in the body, metabolism, elimination. However, it should be noted that these rules were developed on the basis of oral drugs, respectively, candidates for drugs for other routes of administration require different criteria for assessing the similarity. Therefore, other rules of medicinality are known. For example, Weber et al. found that most compounds with high oral bioavailability had less than 10 rotatable bonds and a polar surface area (PSA) of less than 140 Å.

Literature data indicate that compounds with a partition value of less than 3 and a PSA greater than 75 Å are 6 times less likely to cause adverse reactions in in vivo tolerance studies than compounds that did not meet these criteria. It is also proved that there is a relationship between the so-called. The "plane" of the molecule, which depends on the number of sp3 hybridized carbon atoms, and the probability of its entry into the leading compounds in the search for new drugs.

Factors influencing the bioavailability of drugs include physicochemical and pharmaceutical factors.

Didactic units:

- Bioavailability (F)
- Relative bioavailability
- Rules five

2.2. Questions (tests, tasks, clinical situations) to test basic knowledge on the topic of the lesson:

Answer the question:

1. Bioavailability of drugs.
2. The main indicators of bioavailability of drugs. Maximum (peak) concentration of the drug in the blood;
- Time to reach maximum concentration;
- The area under the curve of change in the concentration of the drug in plasma or serum over time.
3. Absolute bioavailability. Relative bioavailability.
4. Calculation of the degree of bioavailability.
5. Classification of factors influencing the bioavailability of drugs.
6. Methods for determining the degree of bioavailability. Advantages and disadvantages.
7. Optimal, high and low degree of bioavailability. Characteristics of parameters.

Solve tests:

1. Indicate which term corresponds to the following statement: "Expressed as a percentage of the amount of drug released from the dosage form, which after its introduction reaches the receptor in an amount sufficient to cause a biological effect."

A. therapeutic inequality
B. equivalence
C. pharmaceutical inequality
D. relative bioavailability
E. absolute bioavailability

2. Indicate which term corresponds to the following statement: "The amount of drug administered intravenously in a dosage form that enters the bloodstream without the effect of the effect of the first passage through the liver"

A. therapeutic inequality
B. equivalence
C. pharmaceutical inequality
D. relative bioavailability

E. absolute bioavailability

3. Indicate which term corresponds to the following statement: "Inequality of therapeutic action of the same drugs in the same doses, prepared by different manufacturers or the same plant, but different series."

A. therapeutic inequality
B. equivalence
C. pharmaceutical inequality
D. bioavailability
E. pharmaceutical equivalent

4. Indicate which term corresponds to the following statement: "Description of changes in time of concentrations of the administered drug and its metabolites in the body; covers such transport processes of the active substance and its metabolites in the body as absorption, distribution, biotransformation and elimination ".

A. bioavailability
B. equivalence
C. system availability
D. pharmacokinetics
E. absorption

5. Exogenous factors affecting bioavailability include:

A. seasons of the year;
B. temperature;
C. pharmaceutical factors;
D. clinical;
E. pathophysiological

6. Endogenous factors affecting bioavailability include:

A. body weight;
B. simple chemical modification;
C. pharmaceutical factors;
D. the physical state of the substance;
E. polymorphism

7. Until when did not pay attention to the method of manufacture of drugs as a factor influencing the effectiveness of drugs?

A. to the 60s of the twentieth century
B. until the 60s of the XVIII century
C. to the 60s of the seventeenth century
D. to the 60s of the XIX century
E. to the 60s of the sixteenth century

8. The pharmacist prepares a powder with a substance that is difficult to grind. Indicate which substance is ground in the presence of an auxiliary liquid?

A. Magnesium oxide
B. Salicylic acid
C. Zinc sulfate
D. Copper sulfate

E. Glucose

9. The pharmacist prepares a powder with a substance that is difficult to grind. Indicate which substance is ground in the presence of the auxiliary liquid

A. Magnesium oxide
B. Zinc sulfate
C. Copper sulfate
D. Thymol
E. Glucose

10. Possible causes of therapeutic non-equivalence of the same dose and dosage form of drugs, bordered by different plants:

A. technology
B. dosage of the drug
C. sex and age of the patient
D. routes of administration
E. dosage form

III. Formation of professional skills, abilities:

3.1. content of tasks:

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.

3.2. **recommendations (instructions) for performing tasks**

Task № 3

Methodical recommendations for the task

The influence of excipients (nature of the ointment base) on the process of release and absorption kinetics of drugs can also be established in model experiments on animals. To determine the excipients for the absorption of streptocide can be used different types of dosage forms: ointments, suppositories, tablets, etc. The choice as the object of study of sulfonamide drug in this case is due to the simplicity of its determination in the blood of experimental animals. According to the principle of the described method, you can also use dosage forms containing other drugs. The number of animals and study factors may also vary. To simplify the experiment (for educational purposes only), you can limit yourself to one animal for each sample of the drug.

The object of the study are 10% streptocidal ointments prepared using different bases.

Before completing the task, get acquainted with the algorithm of experimental work for task № 3 (Appendix 3).

The experiment is performed on two rabbits of the chinchilla breed of approximately the same weight and age. Animals are pre-weighed and the data recorded in a diary.

The animal on the freed from the fur area of skin measuring 5 × 5 cm in the back of the back is applied ointment at the rate of 0.5 g / kg. The ointment is rubbed with a glass shelf or plastic spatula. Blood sampling is performed after applying the ointment in 0.5; 1; 1.5 years.

Quantitative determination of sulfonamides in the blood is carried out by photocolorimetric method VN Prebsting, VI Gavrilov (1939) in the modification of IM Перцева, Д.П. Salo and VF Desenko (1975).

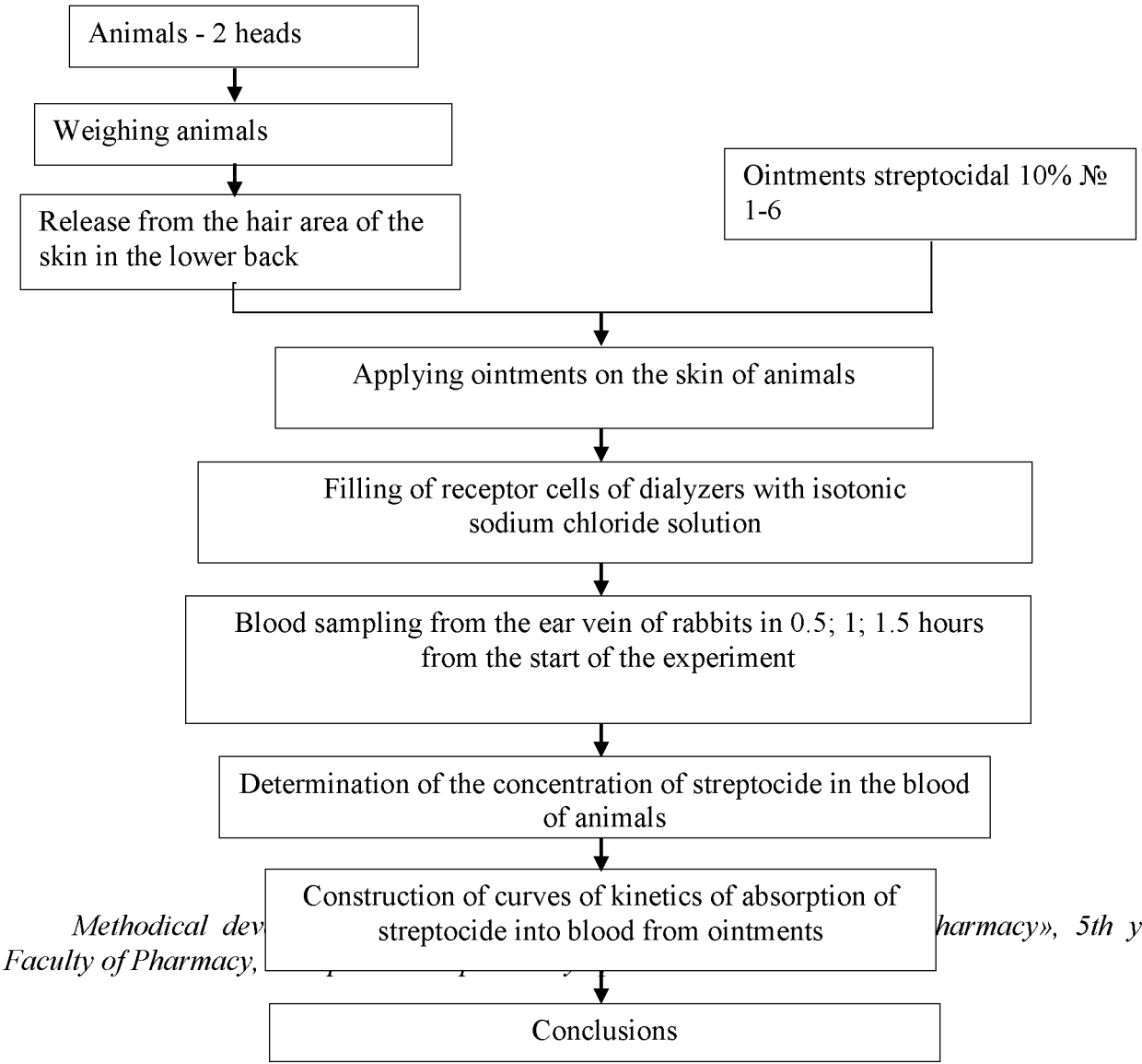
The method is based on obtaining a colored compound by combining diazotized sulfonamide with resorcinol.

Construction of the calibration schedule

0.03 g (exact portion) of streptocide is quantitatively transferred to a dry volumetric flask of 200 ml, dissolved in frequent purified water and adjusted to the mark. 1 ml of solution A contains 150 μg of streptocide. From the initial solution A prepare a working solution B. To do this, 10 ml of solution A is made in a volumetric flask per 100 ml and add water

Annex 3

ALGORITHM OF EXPERIMENTAL WORK ON DETERMINATION OF THE INFLUENCE OF NATURE OF OINTMENT BASES ON THE SPEED OF SUCTION OF STREPTOCIDES FROM OINTMENTS IN ANIMAL BLOOD



cleaned to the mark with constant stirring. 1 ml of this solution B contains 15 μg of streptocide. To build a calibration graph in a series of tubes make 0.5; 1.0; 1.5; 2.0; 2.5; 3 ml of solution B and adding purified water 3.5; 3; 2.5; 2; 1.5; 1 ml, respectively, to lead solutions to a total volume of 4 ml. The contents of all tubes are mixed and add 1 ml of 15% solution of trichloroacetic acid. From each tube take 2.5 ml of solution, transfer to clean dry numbered tubes, to each sample add with vigorous shaking 0.1 ml of 0.5% sodium nitrite solution and after 10 minutes 0.1 ml of 40% urea solution. All subsequent operations are performed similarly to those described in the determination of streptocide in the blood.

After measuring the optical density of the solutions, build a calibration graph (Fig. 2). On the abscissa axis are deposited known concentrations of streptocide in solution (M kg / ml), and on the ordinate axis - the corresponding indicators of the optical density of the solution.

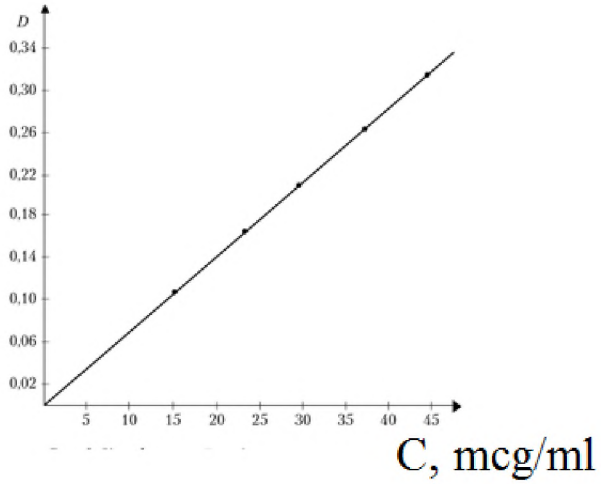


Fig. 2. Calibration graph for quantitative determination of streptocide in the blood

Determination of streptocide in the blood

4.8 ml of a 5% solution of trichloroacetic acid are added to centrifuge tubes for protein precipitation, 0.2 ml of blood taken from a rabbit's ear vein is added by micropipette, mixed by rinsing the micropipette with the contents of the tube 2-3 times, and left for a few minutes until complete hemolysis. . The tubes are centrifuged for 10 minutes at 6000 rpm. Pour 2.5 ml of centrifugate, 0.1 ml of 0.5% sodium nitrite solution into chemical tubes and mix thoroughly. At the end of 10 min add 0.1 ml of 40% urea solution and mix again.

After 10 minutes, 1.5 ml of saturated sodium acetate solution and 0.25 ml of 0.5% resorcinol solution are added to the samples and left for 15 minutes, the contents are

mixed thoroughly with a glass rod or shaken. The optical density of the solution is measured using a device FEK-56 PM (blue light filter № 4, cuvettes with a layer thickness of 10 mm). In parallel, perform photocolorimetry of a control sample that does not contain streptocide, treated similarly to test samples.

The concentration of streptocide (X, μg / ml) in the blood of experimental animals is determined by the formula:

$$X = \frac{C \cdot V \cdot K}{V_1 \cdot a},$$

where *C is the* concentration of the substance determined according to the calibration schedule (m kg / ml);

V is the total volume of the centrifuge (ml);

V_1 - *the* amount of centrifuge taken to determine streptocide (ml);

a - the amount of blood taken for analysis (ml);

K is the amount of blood that is calculated

(Usually 1 or 100 ml, in our experience 1 ml).

Example of calculation

Ointment № 2. 10% streptocidal ointment (vaseline-lanolin-based).

0,5 години $\frac{2,5 * 5 * 1}{2,5 * 2} = 25 \ \text{m}\frac{\text{kg}}{\text{ml}}$

1 година $\frac{4,7 * 5 * 1}{2,5 * 2} = 47 \ \text{m}\frac{\text{kg}}{\text{ml}}$

1,5 години $\frac{3,6 * 5 * 1}{2,5 * 2} = 36 \ \text{m}\frac{\text{kg}}{\text{ml}}$

Enter the results in table. № 4.

Table 4

INFLUENCE OF EXCIPIENTS ON THE SUCTION OF STREPTOCIDE IN THE BLOOD FROM OINTMENTS

№ p / p	The name of the ointment	Diameter of the painted zone, mm		
		0.5 years	1:00	2 hours
1	10% streptocidal ointment on Vaseline			
2	10% streptocidal ointment on vaseline-lanolin basis			
3	10% streptocidal ointment on vaseline-lanolin basis with dimethyl sulfoxide			
4	10% streptocidal ointment			

	based on Kutumov			
5	10% streptocidal ointment on a methylcellulose gel			
6	10% streptocidal ointment on a polyethylene oxide basis			

Using the data in Table № 4, construct the kinetics of streptocide absorption into the blood depending on the nature of the base used in the coordinates: the concentration of the substance (m kg / ml) along the abscissa and the ordinate - time (*t* , h).

After completing the task, draw conclusions about the influence of the nature of the ointment base on the rate of absorption of streptocide into the blood of animals. Compare the experimental data obtained by the methods "in vivo" and "in vitro".

Draw a conclusion about the correlation of these methods.

3.3. requirements for work results, including before registration;

In accordance with the recommendations (instructions) for the tasks.

3.1. control materials for the final stage of the lesson: tasks, tasks, tests, etc .:

1. The pharmacist begins to work. Specify what solution to treat your hands:
   A. Ethyl alcohol
   B. 1% chloramine solution
   C. A solution of chloramine 0.5%
   D. Chlorhexidine solution
   E. Alcohol - ether mixture
2. The pharmacist begins to work. Specify what solution to treat your hands:
   A. Ethyl alcohol
   B. 1% chloramine solution
   C. A solution of chloramine 0.5%
   D. Chlorhexidine solution
   E. Alcohol - ether mixture
3. What does the term “in vivo” mean?
   A. experiments performed on living tissues and whole organisms or inside them
   B. is a technique of performing an experiment in vitro, or, more generally, in a controlled environment outside a living organism
   C. done with a computer or with a computer simulation
   D. study of the process at the same place where it takes place (without moving the object of observation to any special conditions, in a special environment)
   E. means that events occur outside the living organism
4. Which of the following disciplines is not the basis for the development of biopharmacy?
   A. pharmaceutical chemistry
   B. drug technology

C. anatomy
D. pharmacokinetics
E. pharmacodynamics

5. What is the main task in biopharmacy as a science?
A. theoretical and experimental substantiation of the creation of new drugs
B. improvement of existing drugs
C. quality control of medicines
D. synthesis of new substances
E. theoretical and experimental substantiation of creation of new medicines, improvement of already existing medicines

6. Which of the following factors is pharmaceutical?
A. concomitant pathologies
B. become ill
C. dosage form and ways of its introduction into an organism
D. time of taking the drug
E. age of the patient

7. Which of the following factors does not apply to pharmaceuticals?
A. excipients
B. simple chemical modification
C. dosage form and ways of its introduction into an organism
D. age of the patient
E. technological process

8. Which of the following factors does not apply to pharmaceuticals?
A. excipients
B. concomitant pathologies
C. dosage form and ways of its introduction into an organism
D. physical condition of the drug
E. technological process

9. Which method does not apply to in vitro methods?
A. chromatographic
B. direct diffusion across the membrane
C. "solubility" test
D. agar plates
E. on laboratory animals

10. Which method does not apply to in vitro methods?
A. direct diffusion across the membrane
B. on healthy volunteers
C. agar plates
D. chromatographic
E. "solubility" test

21. Which scientists were the founders of biopharmacy in Ukraine?
A. Pertsev IM, Chernykh VP
B. Hajai YI, Salo DP

C. Pertsev IM, Salo DP
D. Tikhonov AI, Pertsev IM
E. Bashura OG, Yarnykh TO

IV. Summing up

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 PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course: Biopharmacy

Practical lesson №10 Topic: «**Molecular weight, solubility, acidity, alkalinity, physical state and polymorphism as physicochemical factors influencing the bioavailability of drugs.»**

The practical lesson was developed by:
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signature
The practical lesson was discussed at the methodical meeting of the department
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Protocol № 1

Odesa – 2022

The purpose of the lesson: To acquire practical skills of forecasting the influence of physicochemical factors on pharmacokinetic characteristics, dynamics of bioavailability, therapeutic effect of drugs and stability of drugs during storage. Master the methods of determining the main physicochemical properties that affect the bioavailability of drugs. Be able to analyze the possible effects of the substance on the body, taking into account certain quantitative characteristics.
Basic concepts: Molecular weight, solubility of drugs.
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 2.0

Plan

I. Organizational moment.
II. Control of basic knowledge
2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):
Requirements for theoretical knowledge:

Molecular weight and solubility of drugs are important physicochemical factors that affect the absorption, distribution and excretion of the drug. The degree of absorption and selection of the appropriate route of administration of the drug depends on the solubility.

There are four groups of drugs by solubility and absorption:

1. Medicinal substances that dissolve well and are well absorbed.

For such substances it is not necessary to determine the test of "dissolution", because the active substance in a few minutes goes into solution.

2. Medicinal substances that dissolve well but are poorly absorbed.

3. Medicinal substances that are poorly soluble but well absorbed. To prevent the insolubility of substances in liquid dosage forms, a simple chemical modification can be used: An example of the effect of a simple chemical modification is the use of active substances in the form of acids, alkalis, salts, ethers, etc., the structure of which does not change.

To improve solubility use:

a) replacement of the insoluble drug substance by its pharmacological analogue (codeine - codeine phosphate, theophylline - euphylline, barbital - birbital sodium, erythromycin with its ether - erythromycin propionate, sodium salt of benzylpenicillin - alisylpenicillin - aryl).

b) addition of excipients capable of improving solubility due to complexation (for example, potassium iodide for dissolving crystalline iodine in aqueous and alcoholic solutions);

c) addition of substances that create the optimal pH value (sodium bicarbonate, boric acid, buffer solutions). Therefore, the study of a simple chemical modification of the active substance can increase the effectiveness of pharmacotherapy by improving bioavailability.

4. Medicinal substances that are poorly soluble and poorly absorbed. For this group of drugs, it is preferable to use parenteral routes of administration.

Among the physicochemical characteristics of drugs that affect absorption and excretion, the relative molecular weight is of great importance. For example, according to Hirom and co-authors, only substances with a molecular weight of less than 300 are excreted in the urine. In cases where the molecular weight of the substance is greater than 300, a proportion of the drug is excreted in the bile.

One of the indicators of the ability of a substance to penetrate the blood-encephalic barrier in addition to the molecular weight is the polarity of the surface of the molecules.

Simple chemical modification can have a significant effect on the pathways of drug biotransformation. A new functional group introduced into the molecule of a substance, as a result of chemical reactions occurring in the body, can change its solubility and, in turn, the nature and strength of therapeutic action both to increase its pharmacological activity (prodrugs) and to decrease it. This changes the effect of the first passage through the liver, which is the main organ of metabolism of most drugs. As a result of metabolism, the substance can become electrophilic in chemical nature and interact with biological macromolecules, causing toxic effects, mutagenesis, carcinogenesis, etc. An example of a simple chemical modification is the conversion to salt. For example, the alkaloid quinine-base can be converted into salts: sulfate, chloride, bromide. Their solubility is different and is 1: 800, 1:34, 1:16, respectively, which, in turn, determines the unequal bioavailability and severity of antimalarial action.

The pharmaceutical industry produces the following dosage forms of quinine hydrochloride: tablets of 250 and 500 mg and 50% solution in ampoules of 1 ml. Quinine hydrobromide, the solubility of which is twice as high as that of quinine hydrochloride, due to the possibility of side effects - the phenomenon of "bromism" is practically not used.

The pH of drugs has a significant effect on excretion. Drugs with acidic properties are rapidly excreted in the alkaline reaction of urine. Conversely, weak bases - in an acidic urine. For example, the elimination of morphine hydrochloride, codeine phosphate, quinine sulfate, novocaine increases with the acid reaction of urine, and in an alkaline environment are excreted faster derivatives of barbituric acid, salicylates and sulfonamides.

Didactic units:

- Molecular weight of drugs
- solubility of drugs

2.2. Questions (tests, tasks, clinical situations) to test basic knowledge on the topic of the lesson:

Answer the question:

1. Description of the appearance of the drug substance and assessment of its solubility as general indicative characteristics of the bioavailability of the test substance.
2. The influence of the solubility of the drug on the choice of the appropriate route of administration.
3. Key approaches for determining the solubility of a molecule in water or in fats.
4. Definition of "solubility" according to SPU.
5. The effect of acid-base properties of the drug on absorption
in the gastrointestinal tract. Explain with specific examples.
6. The effect of pH on the pharmacological action of drugs. Chemical incompatibility and acid-base properties. Give specific examples.
7. Ways of "chemical modification of the molecule" (introduction of functional groups) in order to increase the solubility and thus bioavailability.
8. The essence of the phenomenon of polymorphism. Its use in the creation of new drugs to increase their bioavailability.
9. The influence of physicochemical factors on the stability of drugs during storage.

Solve tests:

1 Indicate which term corresponds to the following statement: "Two-phase coarsely dispersed systems with a particle size of 100 to 1000 nm and more".

A. heterogeneous systems
B. homogeneous systems
C. binary systems
D. bicomponent systems
E. does not have the correct answer

2. Indicate which term corresponds to the following statement: "Constant rate constant, during which the active substance is removed from the body by excretion or biotransformative processes."

A. biotransformation
B. elimination constant
C. suction constant
D. equivalence
E. does not have the correct answer

3. Indicate which term corresponds to the following statement: “Single-phase ionic or molecularly dispersed systems. True solutions.

A. heterogeneous systems
B. homogeneous systems
C. binary systems
D. bicomponent systems
E. does not have the correct answer

4. Indicate which term corresponds to the following statement: "The process of transition of the drug from the place of reception to the bloodstream."

A. bioavailability
B. equivalence

C. system availability
D. biotransformation
E. resorption

5. Indicate which term corresponds to the following statement: "It is the property of a chemical to form in different crystallization conditions crystals that differ from each other by a class of symmetry or shape, physical and sometimes chemical properties."
A. optical activity
B. polymorphism
C. degree of purity
D. crystallinity
E. amorphous

6. Indicate which term corresponds to the following statement: "This is the process of involuntary transition to a stable solution using surfactants insoluble or sparingly soluble in this solvent."
A. hydrotopy
B. solubilization
C. recrystallization
D. hydration
E. hydrolysis

7. To which group of substances belongs arsenic anhydride?
A. Substances that are difficult to grind
B. Fragrant
C. Indifferent
D. Colored
E. Substances that are easily sprayed

8. A batch of injectable solution of apomorphine green was obtained at the plant. What processes caused the color change.
A. as a result of redox processes that occurred when the pH changed
B. due to caramelization of apomorphine
C. as a result of redox processes and caramelization of apomorphine
D. due to polymorphism
E. as a result of simple chemical modification

9. How long do you leave the agar gel to swell?
A. 10 min.
B. 20 min
C. 30 min
D. 40 min
E. 60 min

10. In the manufacture of streptocide ointment 10% pharmacist mixed without pre-grinding the drug substance with an ointment base, which led to a decrease in the rate of release of streptocide. To improve the quality of the ointment it is necessary to disperse the streptocide, pre-grinding:

A. with ethanol or diethyl ether;
B. half the weight of the drug substance of Vaseline oil;
C. with half or part of Vaseline melting;
D. with all Vaseline;
E. with dichloroethane.
E. Potassium iodide

III. Formation of professional skills, abilities:

3.1. content of tasks:

Complete an individual task set by the teacher:

Task 1: 1. Give examples of consideration and rational use of the phenomena of polymorphism of medicinal substances in pharmaceutical and medical practice.

Task 2. Explain the example of 5-aminosalicylic acid and sodium salt absorption in the gastrointestinal tract of acids and their salts.

3.2. recommendations (instructions) for performing tasks

According to the course of practical training to carry out registration of the individual task in a workbook.

3.3. requirements for work results, including before registration

In accordance with the recommendations (instructions) for the tasks.

3.4. control materials for the final stage of the lesson: tasks, tasks, tests, etc .:

1. In the manufacture of eye drops with collargol pharmacist-technologist used sodium chloride to create an isotonic concentration of the solution. Evaluate the actions of the technologist.

A. Sodium sulfate should be used for isotoning
B. Boric acid must be used for isotoning
C. Glucose solution should be used for isotoning
D. Sodium nitrate should be used for isotoning
E. Eye drops with collargol do not isotonic

2. In the manufacture of suppositories by pouring the mass stratification is possible. What you need to do to prevent this:

A. Avoid high temperatures
B. reduce the content of LR
C. cool before pouring
D. increase the fusion temperature of the base and LR
E. add plasticizers

3. The pharmacist prepared an ointment against edema. Indicate which of the following ointment bases has osmotic activity?

A. Polyethylene oxide
B. Vaseline
C. Esylon-aerosil
D. Hydrogenated fats

E. Gelatin-glycerol

4. The pharmacist prepared an ointment-solution on a lipophilic basis. Specify the substance, creating an ointment of this type?

A. Menthol
B. Novocaine
C. Dermatol
D. Starch
E. Sulfur

5. The pharmacist prepared the ointment. Specify a foundation that absorbs skin secretions and cleanses wounds?

A. Polyethylene oxide
B. Gelatin-glycerol
C. Vaseline
D. Spermacet
E. Hydrogenated fats

6. The pharmacist prepared powders with a dye. What is the best option for powder technology he chose?

A. Added last
B. Placed between layers of uncolored substance
C. Added first
D. Grind with alcohol and mix with other ingredients
E. Mixed with alcohol-water-glycerol mixture

7. The pharmacist prepared powders with this substance in a separate mortar, in a separate workplace, using the method of "three-layer". Specify the substance for which the following technology is characteristic:

A. Sulfur
B. Riboflavin
C. Protargol
D. Glucose
E. Copper sulfate

8. The pharmacist prepared a suspension ointment on a lipophilic basis. Specify the substances that form an ointment of this type?

A. Xeroform
B. Protargol
C. Menthol
D. Tannin
E. Plant extracts

9. The pharmacist prepared a suspension ointment. Specify the substances that create an ointment of this type?

A. Bismuth nitrate basic
B. Protargol
C. Wax

D. Ichthyol

IV. Summing up

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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«29» august 2022 y.

METHODICAL DEVELOPMENT OF PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course Biopharmacy

Practical lesson №11 Topic: «**Influence on bioavailability and therapeutic activity of spatial isomerism and optical properties of drugs.»**

The practical lesson was developed by:
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signature
The practical lesson was discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odesa – 2022

The purpose of the lesson: To master the influence of the spatial location of the molecule on the physicochemical, pharmacological properties and bioavailability of drugs; to study the pharmacokinetic and pharmacodynamic features of individual isomers of known drugs.
Basic concepts: Conformational isomerism, optical isomerism, enantiomers.
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 2.0

Plan

I. Organizational moment.
II. Control of basic knowledge
2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):
Requirements for theoretical knowledge:

Changing the spatial arrangement of the same groups in the molecule of biologically active substances can have as significant consequences as changes in the chemical nature of these groups. Spatial isomerism is geometric (cis-trans-isomerism) and optical. The CIS configuration of tripolidine is inactive, in contrast to the trans configuration, which has antihistamine, anticholinergic action, is a drug for colds and colds.

Spatial geometric isomers are divided into two types: conformational and configurational. *Conformational isomerism is* caused by the rotation of atoms or atomic groups around one or more simple σ□-bonds. As a result of rotation around CC-bonds, molecules can have different spatial forms, which are called conformations.

Configuration isomers are stereoisomers whose molecules have different arrangements of atoms in space without conformation.

Optical isomerism (mirror isomerism, enantiomerism) is observed in substances that exhibit optical activity, ie able to rotate a plane-polarized light beam. These substances have one asymmetric carbon atom and are called enantiomers. There are D, L- (relative) and R, S-classification of optical isomers.

Enantiomers (optical isomers, mirror isomers, antipodes) are stereoisomers whose molecules are related to each other as an object and incompatible mirror image. All chemical and physical properties of enantiomers are the same, except for two: the rotation of the plane of polarized light and biological activity.

Conditions of enantiomerism: 1) the carbon atom is in a state of sp 3 - hybridization; 2) the absence of any symmetry; 3) the presence of an asymmetric (chiral) carbon atom, ie an atom having four different substituents.

For example, there are 2 enantiomers of ibuprofen - R (-) and S (+). The inactive enantiomer R (-) is converted in vivo to the active isomer S (+). The improved gastrointestinal tolerability of ibuprofen is due to the competition of the inactive isomer R (-) with the isomer S (+) for the binding site to COX-1, resulting in a decrease in the inhibitory effect of the latter on prostaglandin synthesis. Therefore, the presence of variant biologically active substances based on their various enantiometric

characteristics in the substance can lead to: · undesirable side effects, toxicity caused by one of the isomers, manifestation of a significant difference in absorption, manifestation of significant variations in sulfate-protein bonds degree of metabolism, transformation into a toxic substance (deterioration of metabolism), the effect on the metabolism of other drugs taken simultaneously.

The optical properties of drugs significantly affect the pharmacokinetics and pharmacodynamics. For example, (S) - (+) sodium naproxen exhibits antipyretic, analgesic and anti-inflammatory activity. In contrast, R - (-) sodium naproxen is inactive.

Levophanol has an analgesic effect, while dextophan its dextrorotatory isomer has an antitussive effect.

The right-handed isomer of quinine sulfate, in contrast to the left-handed counterpart, has antiarrhythmic activity. It is released in the form of tablets of prolonged action - quinidine sulfate, which in the body evenly releases the drug in 8-10 hours. The reversible isomer - pachycarpine hydrochloride stimulates labor. Its left-handed isomer, sparteine, reduces heart rate in sinus tachycardia (antiarrhythmic).

Among the enantiomers may be symmetrical molecules that do not have optical activity, they are called mesoisomers.

The above data show that changes in the spatial arrangement of the same groups in the molecule of biologically active substances can have as significant consequences as changes in the chemical nature of these groups. One of the reasons for the different physiological activity of stereoisomers of drugs is the difference in their penetration into the body. These differences can be related both to the structural features and properties of biological membranes, which are themselves built of optically active, asymmetric material, and to the presence in the membranes of special systems that carry out the transfer of metabolites across the membranes. There are stereospecific transport membrane systems, under the action of which the concentration of L-amino acids inside the cells increases by about 500 times compared to the environment. D-amino acids are not transported by these systems.

If there are more than 2 asymmetric carbon atoms in the molecule, there are stereoisomers, which are mirror (optical) antipodes. They are called diastereomers.

In the last decade, a new direction of pharmacokinetics began to develop - stereopharmacokinetics. According to the literature, the use in medical practice of chiral drugs having in the structure of one or more optically active centers (mixture of enantiomers), significantly affects the pharmacological activity and bioavailability. Stereoisomerism is inherent in the molecules of living organisms. Moreover, biopolymers are usually chirally pure substances, ie contain enantiomers of the same species. Thus, the composition of natural proteins consists mainly of left-rotating amino acids (L-form), and complex carbohydrates and nucleotides (DNA and RNA monomers) include right-rotating sugars (D-isomers). Chirality is the basis of cell synthesis, highly specific enzymatic and immune reactions, ie all the most important processes in a living organism. An example is the interaction reaction between a cellular receptor and a ligand, a substance that is able to bind to the corresponding

receptor. Each receptor has a characteristic spatial structure, including a region that interacts with the ligand. These structures must fully correspond to each other - on a "key-lock" basis. If we consider such a mechanism of interaction in relation to drugs, the pharmacological activity of the drug will directly depend on the degree of conformity of its spatial structure to the receptor. That is, the pharmacological characteristics of the drug are largely determined by the stereospecificity of its action. Hence another important conclusion: since nature is stereospecific, to ensure optimal pharmacological action, the "ideal" drugs must be chirally pure. By type of symmetry, all stereoisomers are divided into enantiomers and diastereomers.

Optical isomers that are not mirror isomers, differing in the configuration of several but not all asymmetric carbon atoms and that have different physical and chemical properties, are called σ□-diastereoisomers.

π□-Diastereomers (geometric isomers) are stereomers having in molecules π□-bond.

All diastereoisomers are stereoisomeric compounds that are not enantiomers. In other words, the terminology "diastereoisomer" includes compounds containing both conjugated systems and double bonds simultaneously. For contrast in comparison with "enantiomers", diastereoisomers certainly show different physical and chemical characteristics, ie have different solubility, melting point, boiling point.

Based on the physicochemical properties, the distribution of diastereoisomers can be efficiently performed using approved technologies of standard chemical distribution of crystallization and column chromatography. It should be noted that the "enantiomers" cannot be separated by any of the above methods until they are converted to diastereoisomers.

L-Carnitine is one of the essential essential acids because it plays a major role in the transport of fatty acids in the mitochondria. In clinical practice, L-carnitine is successfully used in the treatment of a wide range of diseases such as anorexia, chronic fatigue syndrome, cardiovascular disease, hypoglycemia, male infertility, kidney disease and carnitine deficiency in hemodialysis. D-Carnitine is biologically inactive and causes a number of side effects manifested by the interaction of the D-form with the natural L-form of carnitine.

The results of experimental and clinical studies to evaluate the effectiveness of L-, D- and DL-carnitine indicate the advantage of the L-form of carnitine in comparison with its optical isomer or racemate.

Traditionally, modern drug production technologies provide racemic mixtures. A racemic is a mixture of equal amounts of two enantiomers, right- and left-rotating. However, currently accumulated enough information about the different effects on the body of R- and S-enantiomers of drugs. As a rule, the main pharmacological activity of racemic drugs is associated with the action of one of the enantiomers. The second - less active, or exhibits other pharmacological properties. A striking example of the influence of the spatial configuration of the drug on physiological activity is morphine. The substance contained in natural plant raw materials is left-handed. Administration

of this drug to animals and humans causes severe and prolonged analgesia. The dextrorotatory isomer of morphine has no analgesic effect. A similar situation is associated with the action of insulin - physiological activity is shown only by the left-rotating form. There are known examples of the use in therapeutic practice of racemic drugs (thalidomide), when one of the stereoisomers had a strong toxic effect, which led to tragic cases. Knowledge of the mechanism of influence of steric features on the physiological activity of the molecule allows using stereospecific methods of synthesis to create drugs that have the highest efficiency or lowest toxicity. Therefore, at the stage of drug development, a comparative analysis of therapeutic activity, toxicity, metabolism, pharmacodynamics and pharmacokinetics of individual stereoisomers is required.

Didactic units:

- Conformational isomerism,
-optical isomerism,
- enantiomers.

2.2. Questions (tests, tasks, clinical situations) to test basic knowledge on the topic of the lesson:

Answer the question:

1. Types of isomerism.
2. Determination of optical isomerism. Optical isomers.
3. Influence of optical isomers on bioavailability and pharmacological activity.
4. Structural isomerism. Give examples.
5. Spatial isomerism. Conformational and configurational isomers.
6. Stereochemistry. Its role in the development of new biologically active substances.

Solve the test:

1. Indicate which term corresponds to the following statement: "Total constant that determines the rate of penetration of the drug from the injection site through the biological membrane into the body."

A. biotransformation
B. elimination constant
C. suction constant
D. equivalence
E. resorption

2. The pharmacist must prepare an ointment which contains silver nitrate (up to 5%) on an emulsion basis. How to introduce this substance into a dermatological ointment:

A. Dissolution in a small amount of water
B. In the form of a fine powder of the suspension type
C. Dissolution in a submerged base
D. Dissolution in a liquid suitable for the base
E. Fusion with the base

3. The pharmacist must prepare an ointment that contains substances that are insoluble in the base or in water in an amount of more than 5%. How to introduce them to the base?

A. grind with part of the melted base
B. grind with all the unmelted base
C. grind with part of the unmelted base
D. grind with a liquid related to the base
E. grind with an alcohol-water-glycerin mixture

4. Which of the following areas is not used in the scientific study of biopharmacy?
A. search for major bioavailability modulators
B. study of bioequivalence of drugs
C. conducting preclinical studies
D. study of the influence of pharmaceutical and other variables
E. definition of biological synergism

5. Indicate which term corresponds to the following statement: "This is a factor when the same substance can be used as a drug in various chemical compounds (salt, base, acid, ether, etc.), in which part of the molecule is completely preserved. a drug responsible for the pharmacological effect. "
A. polymorphism
B. simple chemical modification
C. the degree of ionization of the substance
D. solubilization
E. hydrotopy

6. To which group of substances belongs camphor?
A. Narcotic
B. Potent
C. Colored
D. Substances that are easily sprayed
E. Substances that are difficult to grind

7. Patient Yu. Usually took atropine, but due to its absence, hyoscyamine, which contains only the active L-isomer, was administered. The effect developed faster. What influenced the acceleration of the effect?
A. The difference in elimination
B. The difference in biotransformation
C. The difference in the action of stereoisomers.
D. The difference in bioavailability
E. Suction difference

8. Which of the following terms does not apply to crystalline systems (syngony)?
A. monoclinic
B. diclin
C. trigonal
D. tetragonal
E. pentagonal

9. Which of the following terms does not apply to crystalline systems (syngony)?
A. monoclinic
B. nanoclinic

C. trigonal
D. tetragonal
E. hexagonal

10. Which of the following factors does not apply to pharmaceuticals?
A. excipients
B. technological process
C. dosage form and ways of its introduction into an organism
D. physical condition of the drug
E. time of drug administration

III. Formation of professional skills, abilities:

3.1. content of tasks:

1. Vigabatrin (4-amino-hexen-5-acid) is prescribed as an anticonvulsant in epilepsy. Give the structural formulas of possible isomers and explain the difference in their activity.
2. Give the structural formulas of all possible isomers of Meprobamate (2-methyl-2-propyl-propanediol-1,3) which is used in medical practice in the initial stage of hypertension as a sedative. Explain the difference in isomer activity.
3. Give the structural formulas of isomers of Diethylstilbestrol. Explain why the isomer of trans-diethylstilbestrol shows higher estrogenic activity than the cis-isomer?

3.2. requirements for work results, including before registration;

According to the course of practical training to carry out registration of the individual task in a workbook.

3.3. requirements for work results, including before registration

In accordance with the recommendations (instructions) for the tasks.

3.4. control materials for the final stage of the lesson: tasks, tasks, tests, etc.:

1. Which of the following factors does not apply to pharmaceuticals?
A. excipients
B. pregnancy
C. dosage form and ways of its introduction into an organism
D. physical condition of the drug
E. technological process

2. Patient P., 45 years old, has had angina pectoris for a long time. Nitrate intake is not always regular due to the nature of work. The doctor advised long-acting nitrate, which does not require control during the day. What form of drug allows you to do this?
A. Granule.
B. Tablet.
C. Plaster.
D. Capsule
E. Solution

3. Who first discovered the phenomenon of polymorphism?
A. Boucher
B. Halabala

C. Dewey
D. Fat
E. Hajj

4. The dissolution time for suppositories on a hydrophilic basis should not exceed:
A. 20 min
B. 30 min.
C. 45 min
D. 1 hour
E. 2 years

5. Is it permissible to arbitrarily replace any ion in the drug molecule, based on purely technological or economic considerations:
* A. inadmissible
B. admissible
C. is permissible only for technological reasons
D. is permissible only for economic reasons
E. is permissible only with the permission of the head of the enterprise

6. What is meant by the term aggregate state of drugs?
A. electrical conductivity
B. solubility
C. amorphous
D. polymorphism
E. pH

7. What is meant when using the term physical state of drugs?
A. electrical conductivity
B. solubility
C. crystallinity
D. polymorphism
E. pH

8. What is meant by the use of the term physicochemical properties of drugs?
A. pH
B. polymorphism
C. physicochemical properties
D. degree of purity
E. all the answers are correct

9. Which of the following compounds does not belong to the polymorphic modifications of carbon?
A. coal
B. diamond
C. graphite
D. granite
E. gravel

10. Which of the following indicators affects the size of the colored area during the study of streptocide ointment by agar plates?

A. the physical state of streptocide
B. the degree of grinding of streptocide
C. the phenomenon of polymorphism in the ointment
D. quantitative content of streptocide
E. purity of the substance

IV. Summing up

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.

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METHODICAL DEVELOPMENT OF PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course: Biopharmacy

Practical lesson №12 Topic: «**Lipophilicity and its impact on pharmacokinetic characteristics and dynamics of bioavailability of drugs.»**

The practical lesson was developed by:
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«29» august 2022 y.
Protocol № 1

Odesa - 2022

The purpose of the lesson: To study the effect of lipophilicity on pharmacokinetic characteristics and dynamics of bioavailability of drugs; to acquire practical skills in calculating the lipophilicity coefficient with the help of computer programs and its use for predicting the bioavailability of drugs.
Basic concepts: Lipophilicity
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 2.0

Plan

I. Organizational moment.

II. Control of basic knowledge

2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):

Requirements for theoretical knowledge:

To assess the bioavailability of drugs and their dosage forms, along with such characteristics as molecular structure, molecule size, stereochemical features, physical state, the ability of the substance to dissolve in the aqueous or lipid layer of biological membranes is important. The concept of "lipophilicity" is used to estimate this parameter.

Lipophilicity is a physicochemical constant of a substance that characterizes the ability of a chemical compound to dissolve in fats, oils, lipids, and nonpolar solvents (toluenes, hexanes, etc.). This parameter determines the pharmacokinetics of the drug and its behavior in the body, passing through the bilipid layer of the cell membrane. Lipophilic (fat-soluble) substances are quickly and almost completely (90%) absorbed in the gastrointestinal tract. The intake of fat-soluble drugs decreases with a decrease in the absorption surface (after resection of the stomach, part of the intestine), diarrhea, increased peristalsis, edema of the gastrointestinal mucosa, circulatory disorders of the gastrointestinal tract. Hydrophilic compounds are not completely and unevenly absorbed in the intestine.

Lipophilicity is usually described by the processes of distribution between two phases - non-polar (organic phase) and polar (mostly aqueous). Quantitative characteristic of lipophilicity - partition coefficient P - is defined as the ratio of the concentrations of the neutral compound in organic (corg) and aqueous (aqueous) solutions under equilibrium conditions (1):

$$P = \frac{c_{org}}{c_{water}} \quad (1)$$

Experimentally, the lipophilicity coefficient is determined using a standard binary system n-octanol - water. This system is a convenient model for assessing lipophilicity: n-octanol is chosen as the standard solvent due to its formal similarity to lipids (long alkyl chain and functional group having both proton-donor and acceptor properties). The concentration of the substance is determined by spectrophotometric method or high performance liquid chromatography. LogPo / w values began to be used as a

parameter of lipophilicity after Hench discovered a correlation between the biological activity of a substance and its distribution constant in this system.

There are several theoretical approaches to estimating logP. Among them, the additive method is especially popular, which assumes that the total lipophilicity of the molecule can be decomposed into structural components. One of the first schemes to assess the lipophilicity of substituents was proposed by Hench.

The increase in lipophilicity of the molecule is observed with the introduction of functional groups or radicals in the following sequence:

1. For hydrophilic groups:

Carboxyl> hydroxyl> aldehyde> keto group> amino group> imino group> amido group> imido group

2. For hydrophobic radicals:

Methyl> methylene> ethyl> propyl> higher alkyl> phenyl> chlorophenyl> bromophenyl> iodophenyl.

The value of logP between -1 and +5 is optimal for substances intended for oral use: if the value is less than -1, the substance is poorly absorbed from the intestine; when logP> 5 - the compound has significant lipophilicity and is able to linger in the lipid layers, which also complicates its absorption.

The value of logP can theoretically be calculated based on the structural formula of the substance using special computer programs such as ACD / labs 10, ACD / LogP, Dragon, Instant JChem, Gaussian, Molinspiration, Chemoffice 6.0 and others.

The increase in lipophilicity correlates with the accumulation of the substance in adipose tissue, decreased water solubility, increased rate of penetration through the skin, increased binding to plasma proteins, accelerated metabolism and excretion, accelerated peak activity and, in some cases, reduced duration of action.

Features of metabolism and excretion of lipophilic drugs are important in the treatment of patients with impaired renal and hepatic function.

The amount of lipophilicity of cardiac glycosides significantly affects their pharmacokinetics, namely absorption in the digestive tract, which determines the rate of onset, duration of their cardiotonic effect and the route of their introduction into the body. The more and more strongly the cardiac glycosides bind to proteins, the longer their action lasts.

Thus, the drug digitoxin, which belongs to the non-polar lipophilic cardiac glycosides, is well soluble in lipids and easily penetrates cell membranes. It is used orally (in the form of tablets). It is completely absorbed in the digestive tract (100%), strongly binds to plasma proteins (60%), biotransformed in the liver, has a high ability to accumulate in tissues. The effect occurs after 1.5-2 hours, is completely eliminated after 14-21 days.

Cardiac glycosides with moderate polarity and lipophilicity - digoxin, celanide - are used orally and intravenously, because they are absorbed in the digestive tract only by 60-80% and 15-40%, with plasma proteins are bound by 20-30% and 20-25%, in accordance. The onset of action is observed after 30-120 minutes. when administered orally, after 5-30 minutes - with intravenous. Complete elimination occurs in 5-7 days.

The drugs are partially converted in the liver, are mainly excreted in the urine and have a lower potential for accumulation than digitoxin.

Polar hydrophilic cardiac glycosides - strophanthin, corglycone - when taken orally, they are practically not absorbed (3-7%), do not bind to proteins, slightly biotransformed in the liver, almost do not accumulate, excreted unchanged mainly in the urine, so they are used head intravenously (rarely intramuscularly). Drugs of this group show unstable (within 1-3 days), but fast effect (the beginning of action is observed in 3-5 minutes and reaches a maximum within 30-60 minutes), complete elimination occurs in 1-3 days. Strophanthin is a drug for primary health care.

Differences in the duration of action of β-blockers with a low selectivity index depend on the characteristics of the chemical structure, lipophilicity and elimination pathways. Lipophilicity of β-blockers promotes their penetration through the blood-encephalic, hystero-placental barrier into the eye chamber. Lipophilic β-blockers are rapidly and completely (over 90%) absorbed in the gastrointestinal tract, their metabolism in the liver is 80-100%, the bioavailability of most of them (propranolol, metoprolol, alprenolol, etc.) due to the effect of "first pass" »Through the liver is slightly more than 10-40%. These drugs with prolonged use can themselves reduce hepatic blood flow, slow down their own metabolism and the metabolism of other lipophilic drugs. This explains the increase in the half-life and the possibility of reducing the single (daily) dose and the frequency of their reception, increasing the effect, the threat of overdose. In addition, the high lipophilicity of β-blockers determines their higher effectiveness in the prevention of adverse cardiovascular diseases, in particular in patients with hypertension or coronary heart disease.

Didactic units:

- Lipophilicity

Answer the question:

1. Define the concept of "Lipophilicity".
2. Coefficient of distribution and methods of its determination.
3. Computer programs for calculating the lipophilicity of biologically active compounds.
4. Hench method and its use in medical chemistry.
5. The value of lipophilicity for drug absorption.

Solve the test:

1. Indicate which term corresponds to the following statement: "A complex process in which lipoid-dissolved molecular drug substances in the process of biochemical reactions are replaced by catalytic enzymes (oxidation, reduction, hydrolysis, synthesis) into metabolites."

A. bioavailability
B. equivalence
C. system availability
D. biotransformation
E. absorption

2. Indicate which term corresponds to the following statement: "Constant rate of transition of the drug from the circulatory system to any or any part of the body."
   A. biotransformation
   B. elimination constant
   C. suction rate constant
   D. equivalence
   E. distribution rate constant
3. Lipophilic bases are used for preparation of ointments. Specify the lipophilic component of the bases, which is a representative of hydrocarbons.
   A. Esilon-4.
   B. Spermacet.
   C. Paraffin.
   D. Combi.
   E. Phytosterol.
4. The pharmacist prepared the ointment. Specify the substance that is injected into the lipophilic base, heated to 40C?
   A. Camphor
   B. Anesthesia
   C. Benzoic acid
   D. Streptocide
   E. Vinyl
5. Ointment bases are subject to the following requirements:
   A. compatibility with medicinal substances;
   B. low melting point;
   C. transparency;
   D. strength;
   E. purity.
6. The doctor prescribed a superficial ointment on a hydrophobic basis. What is the basis that a pharmacist should use?
   A. Vaseline
   B. Wax
   C. Cocoa butter
   D. Spermacet
   E. Bentonite
7. The doctor prescribed rectal suppositories and did not specify their weight. Indicate the mass of the suppository to be prepared at the pharmacy:
   A. 4.0
   B. 1.0
   C. 3.0
   D. 5.0
   E. 2.0
8. The doctor prescribed the patient a simple sulfur ointment for the treatment of scabies. Choose the basis that provides the desired therapeutic effect:

A. vaseline;
B. emulsion consistency base EM Kutumova "water-vaseline";
C. lanolin;
D. lard;
E. bentonite base.

9. Medicinal substances in multiphase ointments are administered depending on their properties. How should a pharmacist introduce novocaine into a vaseline-lanolin base?
A. Grind with alcohol or ether.
B. Grind with glycerin.
C. Rub with part of the melted base.
D. Dissolve in water.
E. Dissolve in the molten base.

10. Medicinal substances in multiphase ointments are administered depending on their properties. How should a pharmacist introduce diphenhydramine into a vaseline-lanolin base?
A. Grind with alcohol or ether.
B. Grind with glycerin.
C. Rub with part of the melted base.
D. Dissolve in water.
E. Dissolve in the molten base.

III. Formation of professional skills, abilities:

3.1. content of tasks:

Complete an individual task set by the teacher:

Task: to calculate the value of the distribution coefficient P to assess the lipophilicity of salicylic acid

3.2. **recommendations (instructions) for performing tasks**

According to the course of practical training to carry out registration of the individual task in a workbook.

The partition coefficient P is calculated by the formula:

P = lg (Akints.) / (Avih.-Akints.),

deAkinc. –Value of the optical density of the octanol solution after shaking with water;

Avih. - the value of the optical density of the initial solution before shaking with water

3.3. requirements for work results, including before registration

In accordance with the recommendations (instructions) for the tasks.

3.4. control materials for the final stage of the lesson: tasks, tasks, tests, etc.:

1. Medicinal substances in multiphase ointments are administered depending on their properties. How should a pharmacist inject analgin into a vaseline-lanolin base?
A. Grind with alcohol or ether.
B. Grind with glycerin.
C. Dissolve in a minimum amount of water.

D. Rub with part of the melted base.
E. Dissolve in the molten base.

2. Soft dosage forms and bases can be divided into hydrophilic and hydrophobic on the following grounds:
A. on rheological properties
B. by affinity for water,
C. on concentration and a dispersed condition of auxiliary and medicinal substances.
D. on the ability to adsorb water
E. by type of dispersion of systems

3. Ointments must have certain rheological characteristics. These include:
A. plasticity;
B. homogeneity
C. hydrophilicity
D. elasticity
E. a certain pH value

4. Ointments must have certain rheological characteristics. These include:
A. hydrophilicity;
B. homogeneity
C. period of relaxation;
D. elasticity
E. a certain pH value

5. Ointments must have certain structural and mechanical characteristics. These include:
A. homogeneity;
B. elasticity;
C. hydrophilicity;
D. elasticity;
E. a certain pH value

6. Ointments must have certain structural and mechanical characteristics. These include:
A. a certain pH value
B. elasticity
C. hydrophilicity
D. homogeneity;
E. viscosity

7. Ointment of suspension type on a lipophilic basis forms?
A. Bismuth subnitrate
B. Novocaine
C. Dicaine
D. Diphenhydramine
E. Camphor

8. Ointment of suspension type on a lipophilic basis forms:

A. Novocaine
B. Dicaine
C. Diphenhydramine
D. Zinc oxide
E. Camphor

9. The patient is prepared nasal ointment containing protargol. How should a pharmacist inject protargol into an ointment base?
A. Grind with alcohol.
B. Grind with water.
C. Rub with glycerin and then with water.
D. Rub with a base and then with glycerin
E. Pour a thin layer on the surface of the ointment base.

10. Which of the following factors is pharmaceutical?
A. physical condition of the drug
B. become ill
C. concomitant pathologies
D. time of taking the drug
E. pregnancy

IV. Summing up

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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«29» august 2022 y.

METHODICAL DEVELOPMENT OF PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course: Biopharmacy

Practical lesson №13 Topic: «**Classification of pharmaceutical factors: physical state; excipients (their nature, physical condition and quantity).** »

The practical lesson was developed by:
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The practical lesson was discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odesa – 2022

The purpose of the lesson: To master the theoretical foundations of the classification of pharmaceutical factors and be able to use them to predict the distribution of substances, effects on the body and bioavailability.
Basic concepts: Excipients, crystalline modifications.
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 2.0

Plan

I. Organizational moment.

II. Control of basic knowledge

2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):

Requirements for theoretical knowledge:

Pharmaceutical factors influencing the therapeutic efficacy of drugs:

1) Physical state of active substances and polymorphism;

2) Excipients (physical condition, origin and quantity);

The physical state of the active substance can also affect the rate of its dissolution, absorption, the degree of activity and toxicity. Therefore, in each case, the starting substance is ground to such an extent that provides optimal therapeutic and minimal unwanted side effects of drugs. For example, calciferol is able to be absorbed and have a therapeutic effect only when its particle size is less than 10 microns. At the same time, the reduction of erythromycin particles leads to a decrease in its antimicrobial activity, and the micronized form of sulfonamide powder significantly increases the undesirable nephrotoxic effect.

The drug substance can be represented by several crystalline modifications, each of which has specific properties (physical and pharmacotherapeutic). The same drug substance in the crystalline state may have a different spectrum of action than in the amorphous form. In addition, different types of crystal structure of the same drug act differently. For example, the duration of action of a suspension of microcrystalline form of insulin is almost twice as long as a suspension of insulin of amorphous form.

The stability and effectiveness of the drug depend on the crystal modification. Crystal modifications, which are characterized by greater solubility in physiological fluids and better absorption, are usually less stable. The ability of the same substance to form several crystalline modifications, which differ in terms of crystal structure and, as a consequence, are characterized by different physical properties is called polymorphism. Obtaining a polymorphic modification of the substance determines a set of external conditions, of which the best studied - the temperature factor, the nature of the solvent, its presence or absence, the introduction of various excipients in dosage forms, drying, pressure. In two or more crystalline modifications there are 30% of all organic substances. Two different polymorphic forms of riboflavin were discovered by Shimizu in 1956. These forms differ in physical and chemical properties. Metastable form dissolves at a concentration of 1200 mg / l, stable - 60 mg / l. 49 polymorphic modifications are known for sulfonamides, and about 120 for antibiotics. Sertraline

hydrochloride has 5 polymorphic modifications, each of which has different antidepressant activity.

Excipients also affect the efficacy and bioavailability of drugs. Excipients are a large conditional group of components that are part of pharmaceuticals (except active substance), which, in turn, are determined by the purpose of their use in the manufacture of drugs: the creation of a certain pharmaceutical form or therapeutic system, giving them certain properties (shelf life, action, consistency, etc.) or to optimize technological processes (creating a shell, coating etc.). Scientific substantiation of rational use of excipients is important during the development of the composition of any drug, for example, for the purpose of their production, prolongation of action, stability, etc. As a peculiar component of drugs, they are in constant contact with the active substances and, depending on certain conditions, can often determine the cause of therapeutic inequality, pharmacokinetics and other properties (technological, consumer, economic) characteristics of pharmaceuticals.

Didactic units:

-Physical state of active substances and
- polymorphism;
- excipients;

Answer the question:

1. Pharmaceutical factors that impact on therapeutic efficacy drugs: constant and variable; their classification.
2. Variable pharmaceutical factors.
3. The physical state of drugs and its effect on the rate of their release and absorption from drugs.
4. The influence of the degree of dispersion of drugs and excipients that used in the production of powders for bioavailability and stability medicines.
5. The role of excipients in the technology of dosage forms and their classification.
6. The influence of the nature of excipients on the rate of absorption of drugs drugs, the effectiveness of various dosage forms and their stability.
7. Dependence of therapeutic efficacy of drugs on pharmaceutical technology.
8. Impact of simple chemical modification of medicinal substances on their biological accessibility.

Solve the test:

1. For the patient it is necessary to prepare an ointment containing ephedrine hydrochloride, novocaine, zinc oxide on a water-emulsion basis. Specify the correct sequence of introduction of components at manufacturing of such basis:

A. Zinc oxide, base, ephedrine hydrochloride, glycerin, novocaine, water
B. Zinc oxide, base, ephedrine hydrochloride, novocaine, water
C. Zinc oxide, water, base, ephedrine hydrochloride, novocaine

D. Zinc oxide, ephedrine hydrochloride, novocaine, base, water
E. Zinc oxide, water, glycerin, base, ephedrine hydrochloride, novocaine

2. The pharmacist prepares an ointment containing 1% novocaine. How should novocaine be added to a hydrophobic base?

A. Dissolve in purified water, emulsify with anhydrous lanolin
B. Dissolve in ethyl alcohol, add Vaseline
C. Grind with Vaseline oil, add Vaseline.
D. Grind with alcohol or ether, emulsify with anhydrous lanolin
E. Grind with glycerin, add Vaseline

3. The pharmacist prepares powders with a substance that is easily sprayed. Specify the following substance:

A. Calcium chloride
B. Calcium gluconate
C. Bromocamphor
D. Bismuth nitrate basic
E. Barbamyl

4. In the pharmaceutical industry, hard gelatin capsules are obtained, the walls of which are thin and brittle. At what stage of the technological process are violations of technological regimes?

A. at the stage of manufacturing (forming) gelatin shells of capsules
B. at the stage of manufacturing gelatinous mass
C. at the stage of pressing
D. at the stage of encapsulation
E. at the stage of coating

5. At high concentrations of emulsifier type o / v in drugs, it tends to:

A. accelerate absorption due to the formation of micellar complexes
B. slow down the absorption due to the formation of micellar complexes
C. increase the solubility of insoluble substances
D. affect the polymorphism of LR
E. affect a simple chemical modification

6. When preparing powders in pharmacies take into account the physico-chemical properties of individual ingredients. Indicate which drug substance is mixed with the powder mass without additional grinding:

A. Camphor

B. Starch
C. Menthol
D. Salicylic acid
E. Streptocide

7. At low concentrations of emulsifier type o / v in drugs, it tends to:

A. accelerate absorption due to the formation of micellar complexes
B. slow down the absorption due to the formation of micellar complexes
C. increase the solubility of insoluble substances
D. affect the polymorphism of LR
E. affect a simple chemical modification

8. When preparing a carbopol base, what should be the pH?

A. 2
B. 4
C. 6
D. 7
E. 10

9. In preparing the powders, the pharmacist used a substance that changes under the action of carbon dioxide. Which capsules should be used for packaging:

A. Cardboard
B. Waxed
C. Paper
D. Cellophane
E. Semi-parchment

10. When preparing a powder of 1.0 difficult-to-grind substance, the pharmacist used 5 drops of ethyl alcohol. Specify this substance:

A. Salicylic acid
B. Xeroform
C. Iodine
D. Porcelain
E. Phenylsalicylate

III. Formation of professional skills, abilities:

3.1. content of tasks:

Complete an individual task set by the teacher:

1. Give examples of the use of prodrugs in medical practice .

Illustrate the equations of the reaction of release of the drug from them and determine

conditions necessary for this.
2. To make the forecast of distribution of substance and influence on an organism on the basis
received data.

3.2. **recommendations (instructions) for performing tasks**

According to the course of practical training to carry out registration of the individual task in a workbook.

3.3. requirements for work results, including before registration

In accordance with the recommendations (instructions) for the tasks.

3.4. control materials for the final stage of the lesson: tasks, tasks, tests, etc .:

1. When preparing powders with this substance, the pharmacist used separate scales, a separate mortar and a separate workplace. Specify the substance for which this technology is characteristic

A. Sulfur
B. Copper sulfate
C. Talc
D. Etacredine lactate
E. White clay

2. When preparing powders with this substance, the pharmacist used separate scales, a separate mortar and a separate workplace. Specify the substance for which the following technology is characteristic:

A. Magnesium oxide
B. Copper sulfate
C. Routine
D. Bismuth subnitrate
E. Potassium permanganate

3. The pharmacist-technologist prepares an emulsion ointment for the nose, which includes diphenhydramine and protargol. He mixed the prescribed drugs in a mortar, dissolved in water and emulsified the solution with anhydrous lanolin. Evaluate the actions of the pharmacist.

A. The pharmacist did the right thing
B. It is necessary to separately dissolve and emulsify substances and add them to the ointment base.
C. Diphenhydramine and collargol are incompatible
D. This solution must be heated in a water bath and then emulsified
E. Vaseline should be emulsified

4. The third-year student asked the undergraduate student, "In what package are easily degradable substances released from the pharmacy?" Enter the correct answer:

A. Paper bags
B. Glass jars with corks
C. Plastic boxes
D. Waxed capsules
E. Cardboard boxes

5. The third-year student asked the undergraduate student, "What drugs are added last without grinding?" Enter the correct answer

A. Glucose
B. Milk sugar
C. Magnesium oxide
D. Menthol
E. Camphor

6. In ointments-suspensions drugs are rubbed with a liquid related to the ointment base, if the concentration of the ointment:

A. Less than 5%
B. More than 5%
C. More than 10%
D. More than 15%
E. More than 25%

7. The pharmacist gave for analysis the prepared suspension ointment (up to 5%). How to determine the homogeneity of suspension ointments

A. When considering 4 samples on a glass slide
B. When rubbing in a mortar
C. When examining samples through a microscope
D. When smeared on the back of the palm
E. When dissolved in vitro

8. The pharmacist prepares a dermatological ointment. Specify the substance that must be introduced into the ointment base in the form of an aqueous solution:

A. Bismuth subnitrate
B. Starch
C. Xeroform
D. Ephedrine hydrochloride

E. Wax

9. The pharmacist prepares a dermatological ointment. Specify the substance that must be introduced into the ointment base in the form of an aqueous-glycerol solution:

A. Protargol
B. Camphor
C. Starch
D. Zinc oxide
E. Menthol

10. The pharmacist prepares an emulsion ointment. What determines the type of emulsion system - in / about, about / in

A. The number of bases
B. The nature of the emulsifier
C. The amount of water
D. The ratio of ingredients
E The order of mixing the ingredients

IV. Summing up

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.

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3. Janicki S., Sznitowska M., Zielinski W. Dostepnosc farmaceutyczna I dostepnosc biologiczna lekow. – Warshawa, 2001.–242 s.

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«29» august 2022 y.

METHODICAL DEVELOPMENT OF PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course: Biopharmacy

Practical lesson №14 Topic: «**The choice of dosage form and route of administration of the drug into the body.** »

The practical lesson was developed by:
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The practical lesson was discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odesa – 2022

The purpose of the lesson: To be able to predict the possible impact of the dosage form and routes of administration of the drug on the kinetics of release and absorption of the active substance and its bioavailability **.**
Basic concepts: Dosage form.
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 2.0

Plan

I. Organizational moment.

II. Control of basic knowledge

2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):

Requirements for theoretical knowledge:

Numerous studies on the effect of the dosage form on the therapeutic efficacy of drugs have shown that the optimal activity of the drug is achieved only when prescribed in a rational dosage form. In addition, in this case, you can avoid many side effects of drugs on the body.

Dosage form is a rational from a pharmacological point of view, convenient for reception and storage form of the drug, which provides its optimal therapeutic effect with minimal side effects. According to modern ideas, the dosage form is a material norm of manifestation of the dialectical unity of active and auxiliary substances, as well as technological operations that provide the optimal therapeutic effect of the drug.

The most important task in the development and preparation of the dosage form is to ensure optimal conditions for the release and subsequent absorption of the substance. All other requirements to which the dosage form must meet are subject to these conditions.

The degree of influence of the dosage form on the processes of absorption is determined by the ability to release the active substance from the oral dosage form and the possibility of contact with the mucous membranes of the stomach, intestines and interaction with their secretions. From here, as release and, consequently, better bioavailability, all oral drugs can be arranged in the following order: solution → emulsion → suspension → powders → granules → tablets.

The choice of dosage form simultaneously determines the method (path) of administration of the drug into the body. Each route of administration has its advantages, but not every one is effective. For one reason or another, sometimes even intravenous administration of the drug does not provide bioavailability. In the case of cardiac decompensation, injections and rectal dosage forms should be considered rational dosage forms of cardiac glycosides, because oral administration causes intestinal irritation (ulcer, bleeding, pain), which is associated with impaired absorption of mucous membranes in such patients. Thus, the dosage form should be advantageous and rational not only economically, aesthetically, convenient for use of the parties, but first of all from the point of view of pharmacodynamics of drug and maintenance of modern requirements of pharmacotherapy.

The rationality of the dosage form and the ways of its administration is assessed by the rate of release of the drug from the dosage form, its absorption and excretion from the body.

Long-term therapy with indomethacin in suppositories proceeds without complications, with a good therapeutic effect, while the use of the drug in tablets is accompanied by dyspeptic symptoms, disorders of the central nervous system and other complications.

Insulin is used parenterally, because when taken orally it is completely inactivated in the gastrointestinal tract, and there are dosage forms that provide high (rapid) or less high rate of effect and different duration of hypoglycemic action (prolonged forms).

Didactic units:

-Dosage form

Answer the question:

1. Describe the routes of administration of drugs into the body.
2. Definition and characteristics of types of dosage forms.
3. Classification of dosage forms. Requirements for dosage forms.
4. Study of pharmaceutical and bioavailability of drugs in different dosage forms.
5. Relationship between the dosage form and by drug administration substances.

Solve tests:

1. Some types of capsules have their own names. Choose the definition that corresponds to tubatin:

   A. soft gelatin capsules with an elongated neck
   B. hard gelatin capsule with microcapsules with a film shell
   C. hard gelatin capsules with microdraggering with a fatty shell
   D. individual particles of LR with a thin shell, the size of which is 1 - 5000 microns .;
   E. soft elastic capsule

2. Patient R., 23 years old, developed a headache due to emotional overload. The doctor advised taking analgin. In what way it is expedient to enter this preparation to the patient?

   A. In a tablet per os.
   B. In a solution in / m.
   C. In a solution in / in.
   D. In solution per rectum.
   E. In solution per os.

3. The patient was administered cerucal intravenously, considering that this way will increase the bioavailability of drugs. How is this concept defined?

A. The proportion of the dose of the drug that changed during passage through the gastrointestinal tract
B. The proportion of the dose of the drug, which in unchanged form has reached the systemic circulation.
C. The proportion of the dose of the drug, which is excreted unchanged from the body.
D. The proportion of the drug dose that bound to albumin
E. The proportion of the dose of drugs that have undergone glucuronidation in the liver.

4. Patient B., 33 years old, started taking NSAIDs for joint pain. The doctor prescribed him a lower dose than a woman of the same age with this disease. How can you explain the doctor's action?

A. Men have higher COX activity.
B. Women have less COX activity.
C. Women are hypersensitive to NSAIDs
D. Women are more likely to metabolize NSAIDs in the liver.
E. Men are more likely to metabolize NSAIDs in the liver.

5. Patient K., 54 years old, suffers from coronary heart disease. The patient had an attack of angina, which lasted about 30 minutes and was accompanied by changes in the ECG. Which route of administration of nitroglycerin should be used to treat the attack in this case?

A. Sublingual reception.
B. Parenteral administration.
C. Applying ointment to the skin.
D. Buccal patch
E. Admission per os ..

6. Patient T. is taking amlodipine. Explain what is the "target" of this drug?

A. Ion channels.
B. Enzymes.
C. Transport proteins.
D. Receptors
E. Genes

7. Patient A., 45 years old, was prescribed the second-generation cephalosporin antibiotic for pneumonia in a dose that the doctor called "shock." What is included in this concept?

A. Equal to one-time.
B. Exceeds the highest daily.
C. Exceeds the average therapeutic.
D. Equal to supportive.
E. Equal to the minimum therapeutic.

8. The patient needs to prepare vaginal suppositories. Indicate what should be the weight of the vaginal suppository, if it is not specified in the recipe?

A. 3.0 g
B. 4.0 g
C. 2.5 g
D. 2.0 g

9. The doctor prescribed the drug to the patient. The patient's condition requires the achievement of maximum bioavailability. What parameter of the drug itself can achieve this goal?

A. Parenteral route of administration.
B. Dose.
C. Brand.
D. Therapeutic breadth of action.
E. The half-life

10. Hard gelatin capsules are designed for dosing of loose powder, granular and microencapsulated substances. They have the shape of a cylinder and consist of two parts. Name them:

A. stem and capillary
B. body and capillary
C. body and lid
D. body and body
E. pulp and lid

III. Formation of professional skills, abilities:

3.1. content of tasks:

Complete an individual task set by the teacher:

1. Predict the use of indomethacin in suppositories and tablets.

How do the selected dosage forms affect the development of the therapeutic effect?

2. Explain the parenteral use of insulin. What drugs

forms of insulin provide a high or less high rate of development hypoglycemic effect. How does the prolonged dosage form affect duration of therapeutic effect?

3.2. **recommendations (instructions) for performing tasks**

According to the course of practical training to carry out registration of the individual task in a workbook.

3.3. requirements for work results, including before registration

In accordance with the recommendations (instructions) for the tasks.

3.4. control materials for the final stage of the lesson: tasks, tasks, tests, etc .:

1. The maximum allowable ratio when mixing powders

   A. 1: 1
   B. 1: 5
   C. 1:20
   D. 1: 2
   E. 1: 7

2. Some types of capsules have their own names. Select the definition that corresponds to the medulla:

   A. soft gelatin capsules with an elongated neck
   B. hard gelatin capsule with microcapsules with a film shell
   C. hard gelatin capsules with microdraggering with a fatty shell
   D. individual particles of LR with a thin shell, the size of which is 1 - 5000 microns .;
   E. soft elastic capsule

3. Some types of capsules have their own names. Select the definition that corresponds to the nanocapsules:

   A. soft gelatin capsules with an elongated neck
   B. individual particles of LR with a thin shell, the size of which is less than 1 μm
   C. hard gelatin capsules with microdraggering with a fatty shell
   D. hard gelatin capsule with film-coated microcapsules
   E. soft and elastic capsule of various shapes

4. Some types of capsules have their own names. Select the definition that corresponds to the microcapsules:

   A. soft gelatin capsules with an elongated neck
   B. individual particles of LR with a thin shell, the size of which is 1 - 5000 microns
   C. individual particles of LR with a thin shell, the size of which is less than 1 μm

D. hard gelatin capsule with film-coated microcapsules
E. soft and elastic capsule of various shapes

5. In order to prolong the action of nitroglycerin it is used in the form

A. patch
B. capsules
C. suppository
D. injections
E. infusion

6. A patient who needs to prepare camphor ointment went to the pharmacy. What concentration of ointment should be prepared by a pharmacist, guided by the requirements of regulatory documents?

A. 10%
B. 1%
C. 15%
D. 20%
E. 5%

7. The patient must undergo treatment with methindol (indomethacin). Which dosage form will be rational:

A. tablets
B. capsules
C. suppositories
D. ointment
E. gel

8. When the influence of the type of dosage form on the process of analgin release by the method of "in vitro", as the medium used:

A. water
B. acid
C. meadow
D. formalin
E. acetone

9. How will the quality of gelatin capsules change if the temperature of the mass specified in the regulations is reduced during their formation by the immersion method?

A. the walls of gelatin capsules will be thick

B. the walls of gelatin capsules will be thin and brittle
C. the walls of the gelatin capsules will be with the inclusion of air
D. the walls of gelatin capsules do not dissolve
E. The walls of the gelatin capsules will be very hard

10. What are the acid-resistant coatings used in the manufacture of tablets and capsules:

A. plasticizers
B. enteric
C. disintegrating
D. thixotropic
E. insoluble

IV. Summing up

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.

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«29» august 2022 y.

METHODICAL DEVELOPMENT OF PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course: Biopharmacy

Practical lesson №15-1 Topic: «**Interaction of drugs with food.** »

The practical lesson was developed by:
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The practical lesson was discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odesa – 2022

The purpose of the lesson: To be able to predict the possible interaction of drugs with food and the possible impact of drugs on the biochemical processes of the human body.
Basic concepts: Dosage form.
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 1.0

Plan

I. Organizational moment.

II. Control of basic knowledge

2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):

Requirements for theoretical knowledge:

Ways of possible influence of food on pharmacokinetic parameters of the drug: on the absorption of drugs from the digestive tract; on the bioavailability of drugs; competitive antagonism or synergy of drugs and food components at the level of the mechanism of action; effect on the rate of excretion of the substance (metabolites). The most significant effect on food affects the process of absorption of drugs in the gastrointestinal tract. The following variants of interaction are possible: chemical and physical interaction of medicinal substances and food components (adsorption, mucus coating of drugs, etc.); change in pH in the stomach and, as a consequence, change in the degree of ionization of drugs; competitive antagonism of drugs and food components with an active transport mechanism; change in the residence time of the drug in the stomach (intestine); metabolism of drugs under the influence of intestinal microflora.

Factors such as the degree of gastric filling, physicochemical properties of drugs (molecule size, solubility, stability, degree of ionization, etc.), their ability to complex, chelate and ion formation, the effect of volume can also affect the absorption stage. , composition and viscosity of secretions, permeability of the mucous membrane of the digestive tract for the drug substance and food, the impact on the microflora involved in the metabolism of the drug. The dosage form of the drug also has a significant effect on the severity of the interaction of drugs with food.

Drugs in liquid dosage forms are less susceptible to food because they can move relatively freely from the stomach to the intestines. Solid dosage forms when taken with food can be delayed for a long time in the stomach cavity, which disrupts the absorption of active substances. For solid dosage forms, the degree of interaction with food depends on the size of the particles, fillers, coating material. Drugs obtained on the basis of microgranules and particles with a film coating are the least exposed to food. Intestinal-soluble coated tablets are particularly sensitive to food, their concomitant intake with food delays the drug in the stomach and significantly prevents the absorption of the drug. When the drug is combined with alkaline food (liquid), the shell may dissolve and the active substance may be destroyed when the drug is in the stomach. Hence the general recommendations for the combination of drugs: resorptive drugs are most rational to take 30-40 minutes before a meal, drinking 50-100 ml of boiled or distilled water; the bioavailability of drugs that are poorly soluble in water

increases if you drink plenty of fluids; the bioavailability of drugs that are well soluble in water does not depend on the amount of fluid consumed.

In addition, it is necessary to take into account some general provisions: when taking drugs before meals reduces the possibility of their interaction with food components, eliminates the influence of food components on drug absorption and limits the negative impact of digestive juices on drugs; food stimulates the secretion of bile, which promotes the absorption of lipophilic substances, so lipophilic drugs should be prescribed after a meal; meat and plant foods, milk change the pH of urine in the alkaline direction and cause the excretion of drugs - weak acids (salicylates, barbiturates, etc.); foods rich in acidic equivalents (citrus, cranberries, olives, etc.) cause the excretion of drugs - weak bases and enhance the action of drugs - weak acids.

Didactic units:

-pharmacokinetics,
-chelation,
-resorptive action,
-lipophilicity.

Answer the question:

1. Ways of food exposure to drugs.
2. The reasons for changes in the bioavailability of drugs when eating.
3. Physical interaction medicinal preparations from food stuffs (adsorption of the drug on the food lump, etc.)
4. Antagonism or synergism at the level of the mechanism of action of drugs and food components.
5. The effect of food on the rate of drug excretion.

Solve the test:

1. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. Some drugs that irritate the gastrointestinal tract are washed down with milk. The pharmacist recommended that the patient drink pancreatin tablets with milk. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Pancreatin tablets should be chewed
   C. Pancreatin tablets should be washed down with alkaline water
   D. Milk will not affect pancreatin
   E. Pancreatin tablets should be taken with strong tea
2. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. Some drugs that irritate the gastrointestinal tract are washed down with milk. The pharmacist recommended that the patient drink Bisacodyl tablets with milk. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Bisacodyl tablets should be chewed
   C. Bisacodyl tablets should be washed down with a glass of water
   D. Milk will not affect bisacodyl
   E. Bisacodyl tablets should be taken with strong tea

3. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. Some drugs that irritate the gastrointestinal tract are washed down with milk. The pharmacist recommended that the patient drink Oxytetracycline tablets with milk. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Oxytetracycline tablets should be chewed
   C. Insoluble complexes are formed, poorly absorbed
   D. Milk will not affect Oxytetracycline in any way
   E. Oxytetracycline tablets should be taken with strong tea
4. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. When dispensing Indomethacin tablets, the pharmacist recommended that the patient drink them with milk. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Indomethacin tablets should be chewed
   C. Insoluble complexes are formed, poorly absorbed
   D. Milk will not affect Indomethacin in any way
   E. Indomethacin tablets should be taken with strong tea
5. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. When releasing tablets 5. Biseptol pharmacist recommended that the patient drink them with alkaline mineral water. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Biseptol tablets should be chewed
   C. Insoluble complexes are formed, poorly absorbed
   D. Milk will not affect Biseptol in any way
   E. Biseptol tablets should be taken with strong tea
6. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. When dispensing Citramon tablets, the pharmacist recommended that the patient drink them with alkaline mineral water. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Citramon tablets should be chewed
   C. Insoluble complexes are formed, poorly absorbed
   D. Milk will not affect Citramon in any way
   E. Citramon tablets should be taken with strong tea
7. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. When dispensing Streptocide tablets, the pharmacist recommended that the patient drink them with alkaline mineral water. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Streptocide tablets should be chewed
   C. Insoluble complexes are formed, poorly absorbed
   D. Milk will not affect Streptocide in any way

E. Streptocide tablets should be taken with strong tea

8. The bioavailability of drugs is influenced by many factors, including the nature and amount of food consumed with the drug. When dispensing Tetracycline tablets, the pharmacist recommended that a patient following a dairy-vegetable diet drink them with milk or kefir. Evaluate the actions of the pharmacist.
   A. The pharmacist did the right thing
   B. Tetracycline tablets should be chewed
   C. Insoluble complexes are formed, poorly absorbed
   D. Milk will not affect Tetracycline in any way
   E. Tetracycline tablets should be taken with strong coffee
9. Indicate which term corresponds to the following statement: "Biologically active part of the drug that is responsible for the therapeutic effect."
   A. effective substance
   B. efficiency
   C. distribution
   D. biotransformation
   E. system availability
10. Indicate which term corresponds to the following statement: "Biologically active part of the drug that is responsible for the therapeutic effect."
   A. effective substance
   B. efficiency
   C. distribution
   D. biotransformation
   E. system availability

III. Formation of professional skills, abilities:

3.1. content of tasks:

Complete an individual task set by the teacher:

Using the literature, fill in the table of drug -food interactions products:

Drug	Food product	Result of interaction
Sulfanilamides	Products containing foil acid: beans, tomatoes, liver, kidneys	
Iron supplements, orally	Food containing phytin acid (millet, semolina, beans, peas, etc.)	
Iron supplements orally	Meat dishes, fresh fruit, vegetables	
Macrolides, lincosamides, tetracyclines	Tonic drinks, "Fanta", Pepsi-Cola, etc.	
Calcium antagonists (except amlodipine, diltiazem),	Grapefruit juice	

terfenadine, cyclosporine		
Antibiotics group Tetracycline	Milk	
Antibiotics group penicillins and cephalosporins		
Sulfanilamides		
Salicylates, barbiturates, acetazolamide, nitrofurans, buformin	Sour fruit and vegetable juices	
Erythromycin, ampicillin, cyclosporine		

3.2. **recommendations (instructions) for performing tasks**

According to the course of practical training to carry out registration of the individual task in a workbook.

3.3. requirements for work results, including before registration

In accordance with the recommendations (instructions) for the tasks.

3.4. control materials for the final stage of the lesson: tasks, tasks, tests, etc .:

1. Indicate which term corresponds to the following statement: "The ability of a drug substance or drug to achieve the desired effect."
   A. effective substance
   B. bioavailability
   C. efficiency
   D. biotransformation
   E. clinical equivalent
2. Indicate which term corresponds to the following statement: "A condition that allows a drug substance introduced into the body to reach the site of exposure."
   A. therapeutic inequality
   B. equivalence
   C. pharmaceutical inequality
   D. bioavailability
   E. pharmaceutical equivalent
3. Indicate which processes relate to the direct study of biopharmacy?
   A. derivation, effect
   B. release of the substance from the dosage form, absorption
   C. metabolism, excretion
   D. absorption, distribution, metabolism, excretion

E. destruction

4. Indicate which processes relate to the direct study of biopharmacy?
   A. derivation, effect
   B. release of the substance from the dosage form, absorption
   C. metabolism, excretion
   D. absorption, distribution, metabolism, excretion
   E. LADMER
5. Hard gelatin capsules are designed for dosing of loose powder, granular and microencapsulated substances. They have the shape of a cylinder and consist of two parts. Name them:
   A. stem and capillary
   B. body and capillary
   C. body and lid
   D. body and body
   E. pulp and lid
6. Pharmaceutical factors influencing the therapeutic activity of drugs:
   A. excipients
   B. material losses of production
   C. dosage of the drug
   D. compliance with GMP rules
   E. compliance with DSTU
7. Digoxin was prescribed to patient D., 87 years old, who suffers from hypertension, coronary heart disease with atrial fibrillation and heart failure. The patient recently had a transient cerebrovascular accident. The doctor prescribed digoxin in half the therapeutic dose. What is this doctor's decision connected with?
   A. Economic reasons
   B. The presence of hypertension.
   C. The presence of heart failure.
   D. Age of the patient
   E. The presence of arrhythmia.
8. What does the term “in vitro” mean?
   A. experiments performed on living tissues and whole organisms or inside them
   B. is a technique of performing an experiment in vitro, or, more generally, in a controlled environment outside a living organism
   C. done with a computer or with a computer simulation
   D. study of the process at the same place where it takes place (without moving the object of observation to any special conditions, in a special environment)
   E. means that events occur outside the living organism
9. What does the term “in vivo” mean?
   A. experiments performed on living tissues and whole organisms or inside them
   B. is a technique of performing an experiment in vitro, or, more generally, in a controlled environment outside a living organism
   C. done with a computer or with a computer simulation

D. study of the process at the same place where it takes place (without moving the object of observation to any special conditions, in a special environment)

E. means that events occur outside the living organism

10. Which of the following disciplines is not the basis for the development of biopharmacy?
    A. pharmaceutical chemistry
    B. drug technology
    C. anatomy
    D. pharmacokinetics
    E. pharmacodynamics
11. What is the main task in biopharmacy as a science?
    A. theoretical and experimental substantiation of the creation of new drugs
    B. improvement of existing drugs
    C. quality control of medicines
    D. synthesis of new substances
    E. theoretical and experimental substantiation of creation of new medicines, improvement of already existing medicines

IV. Summing up

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

APPROVE
Head of Department

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

METHODICAL DEVELOPMENT OF PRACTICAL LESSON

Course: 5 Faculty: Pharmaceutical

Course: Biopharmacy

Practical lesson №15-2 Topic: «**Interaction with other drugs.»**

The practical lesson was developed by:
Ph.D., Assoc.

_____(Fizor. N.S.)
signature
The practical lesson was discussed at the methodical meeting of the department
«29» august 2022 y.
Protocol № 1

Odesa – 2022

The purpose of the lesson: To be able to predict undesirable interactions of drugs of different pharmacological groups and to predict the occurrence of chemical and pharmacological incompatibilities.
Basic concepts: Pharmaceutical interaction, Physico-chemical interaction, Pharmacokinetic interaction.
Equipment: according to the requirements of Good Pharmacy Practice (GPP).
Study time: 1.0

Plan

I. Organizational moment.

II. Control of basic knowledge

2.1. Requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):

Requirements for theoretical knowledge: In practical medicine, several drugs are often used simultaneously. Under the interaction of drugs means a change in the effect of one or more drugs with simultaneous or previous use of another drug. In this case, the interaction of drugs may be therapeutically appropriate or therapeutically unreasonable, which is understood as the incompatibility of drugs. With therapeutically appropriate interaction, it is possible to enhance the therapeutic effect or reduce side effects and complications.

In case of drug incompatibility, there is a loss or violation of the effect of drugs, or an increase in their side or toxic effects.

Interaction of drugs can be divided into physicochemical, pharmaceutical and pharmacological.

Physico-chemical interaction - a direct interaction between drugs that have a chemical or physical nature (physical - adsorption; chemical - drug molecules react with each other, forming new substances). Chemical interaction reactions - oxidation, neutralization, substitution.

Pharmaceutical interactions may occur before the drug is administered to the body. Thus, in the process of manufacturing drugs or their storage, as well as when mixing in a single syringe or infusion system due to the interaction of the components of the mixture there is a change as a result of which the initial activity of drugs is reduced or lost, or toxic properties are formed. In addition, with incorrect prescriptions in recipes due to chemical interaction, precipitates can form, change color, odor, consistency, etc.

Pharmaceutical incompatibility is also possible in the manufacture and storage of combined drugs.

Pharmacological interactions occur after the introduction of drugs into the body and may be associated with changes in pharmacokinetics and pharmacodynamics of drugs. Pharmacological interactions also include cases of changes in the effects of drugs associated with physicochemical and chemical interactions in the patient's environment.

Interaction of drugs is a change in the effectiveness and safety of one drug with simultaneous or sequential use with another drug, as well as xenobiotics, food, alcohol,

smoking. Clinically significant interactions of drugs that change the effectiveness and safety of pharmacotherapy.

Types of drug interactions

The mechanism of interaction of drugs is pharmacokinetic and pharmacodynamic.

Pharmacokinetic interaction is the effect of one drug on the pharmacokinetic processes (absorption, distribution, metabolism, excretion) of another. The result of the pharmacokinetic interaction is a change in the concentration of drugs in the blood plasma, and hence on specific target molecules of drugs (receptors, etc.). All types of pharmacokinetic drug interactions have a common feature - a change in the bioavailability of the drug, ie the amount of drug entering the specific receptor, or the time of its stay in the receptor.

Pharmacodynamic interaction is the effect of one drug on the formation and realization of the pharmacological effect of another, while the concentration of the drug in blood plasma may not change.

Didactic units:

-physico-chemical interaction;
- pharmaceutical interaction;
- pharmacokinetic interaction;
- pharmacodynamic interaction.

Answer the question:

1. Pharmacodynamic interactions of drugs.
2. Interaction of drugs with herbal components.
3. Interaction of drugs with ethyl alcohol
4. Types of drug interactions.
5. The concept of chemical incompatibilities.
6. The concept of pharmacological incompatibilities.
7. Physico-chemical reactions of drugs in pharmaceutical interaction.

Solve tests:

1. How long have you not paid attention to the method of manufacturing drugs as a factor that affects the effectiveness of drugs?
   A. to the 60s of the twentieth century
   B. until the 60s of the XVIII century
   C. to the 60s of the seventeenth century
   D. to the 60s of the XIX century
   E. to the 60s of the sixteenth century
2. In the Pharmacopoeia to determine the kinetics of release of drugs from prolonged dosage forms using media:
   A. acidic;
   B. alkaline;
   C. buffer;
   D. purified water;
   E. chloroform.

3. The pharmacist must order components for the preparation of Lassar paste. What components are included in this drug
   A. Zinc oxide, vaseline, lanolin, starch, zinc sulfate
   B. Zinc sulfate, talc, vaseline, kaolin, novocaine
   C. Zinc oxide, starch, salicylic acid, Vaseline
   D. Zinc salicylates, boric acid, bismuth subnitrate, Vaseline
   E. Zinc sulfate, magnesium chloride, citric acid, Vaseline
4. Factors affecting microbiological contamination of drugs:
   A. excipients
   B. type of dosage form n route of administration
   C. technological scheme of production
   D. material losses of products
   E. compliance with GMP rules
5. The pharmacist prepares a nasal ointment containing ephedrine hydrochloride. How should a pharmacist introduce ephedrine hydrochloride into a water-emulsion ointment base?
   A. Dissolve in a minimum amount of purified water.
   B. Dissolve in ethyl alcohol.
   C. Grind with alcohol or ether.
   D. Grind with glycerin.
   E. Pour a thin layer on the surface of the water.
6. The pharmacist prepares a powder, which includes bismuth nitrate basic and magnesium oxide, which are prescribed in equal amounts. Specify rational technology:
   A. Rub the pores of the mortar with an indifferent substance, add a mixture of bismuth nitrate basic and magnesium oxide
   B. Rub the pores of the mortar with the whole amount of magnesium oxide, add bismuth nitrate basic, mix
   C. Rub the pores of the mortar with an equal amount of bismuth nitrate basic and magnesium oxide, which together are added to the mortar
   D. Rub the pores of the mortar of bismuth nitrate with the main, add all the magnesium oxide
   E. Rub the pores of the mortar with a small part of magnesium oxide, add bismuth nitrate basic and the remainder of magnesium oxide
7. The pharmacist prepares the workplace for work. Specify what solution to treat the table
   A. 1% chloramine solution
   B. Ethyl alcohol
   C. A solution of chloramine 0.5%
   D. Chlorhexidine solution
   E. Alcohol - ether mixture
8. The pharmacist calculated water from aqueous lanolin for the introduction of water-soluble substances into the ointment. How much water does 5 g of lanolin contain?
   A. 1ml
   B. 1.5ml

C. 2ml
D. 2.5ml
E. 3ml

9. The pharmacist prepared powders with hygroscopic substances. Which capsules should be used for packaging:
   A. Waxed
   B. Cardboard
   C. Paper
   D. Cellophane
   E. Semi-parchment
10. The pharmacist prepared powders with substances that are easily weathered. Which capsules should be used for packaging:
   A. Waxed
   B. Cardboard
   C. Paper
   D. Cellophane
   E. Semi-parchment

III. Formation of professional skills, abilities:

3.1. content of tasks:

Complete an individual task set by the teacher:
Using the literature, fill in the table:

Stage Phk	Mechanism	Example	Result
Absorption	Formation chelated compounds and complexes	Tetracycline and antacids (calcium, magnesium, aluminum)	Reduction antibacterial actions
Distribution			
Biotransformation			
Excretion			

3.2. **recommendations (instructions) for performing tasks**

According to the course of practical training to carry out registration of the individual task in a workbook.

3.3. requirements for work results, including before registration

In accordance with the recommendations (instructions) for the tasks.

3.4. control materials for the final stage of the lesson: tasks, tasks, tests, etc .:

1. The pharmacist prepared powders containing menthol and thymol. Which capsules should be used for packaging:
   A. Simple
   B. Parchment
   C. Paraffin

D. Cellophane
E. Waxed

2. The pharmacist prepared a complex powder with substances prescribed in different quantities. Specify the correct cooking sequence that ensures uniformity of mixing:
A. Wipe the pores of the mortar with a strong substance, then add drugs from "smaller to larger"
B. Wipe the pores of the mortar with a substance prescribed in a smaller amount, then add drugs from "smaller to larger"
C. Wipe the pores of the mortar with a substance prescribed in larger quantities, the part is selected, then add drugs from "smaller to larger"
D. Wipe the pores of the mortar with a substance prescribed in smaller quantities, then mix the ingredients in the order of their prescription in the recipe
E. The pores of the mortar are rubbed with a poisonous substance, then mixed with substances of the general list

3. Patient D., 55 years old suffering from coronary heart disease, cannot take isosorbide dinitrate due to a significant headache. For adequate treatment, the doctor prescribed retard nitrate with a modern galenic structure. What is this drug?
A. Olicard.
B. Cardiket
C. Nitrosorbide
D. Molsidomine
E. Trimetazidine.

4. Patient L., 56 years old, suffers from hypertension. Constantly taking nifedipine. Complains about the need to take the drug 3-4 times a day for effective blood pressure control. What form of this drug can be advised to the patient for easier administration of the drug with the same effectiveness?
A. Coated tablets.
B. Drops.
C. Retard form.
D. Capsules.
E. Injectable solution.

5. An ointment containing menthol and ephedrine hydrochloride on a vaseline lanolin basis is prepared. Specify the correct sequence of administration of drugs in the base.
A. First dissolve the base of menthol, then emulsify an aqueous solution of ephedrine hydrochloride
B. Grind both components with alcohol and then with part of the molten base.
C. First dissolve the ephedrine hydrochloride in the base, and then menthol.
D. Grind both components with purified water and then emulsify the base.
E. Both components are dissolved by melting Vaseline and lanolin

6. The pharmacist prepares a nasal ointment containing ephedrine hydrochloride. How should a pharmacist introduce ephedrine hydrochloride into a water-emulsion ointment base?
A. Dissolve in ethyl alcohol.
B. Dissolve in purified water.

C. Grind with alcohol or ether.
D. Grind with glycerin.
E. Pour a thin layer on the surface of the water.

7. The pharmacist prepares an ointment on Vaseline. What substance does he use to reduce the melting point of the base?
A. Vaseline oil
B. Lard
C. Butanol
D. Chloroform
E. Ethanol

8. The pharmacist in the preparation of powders used alcohol to grind one of the substances. Specify this substance:
A. Analgin
B. Protargol
C. Phenylsalicylate
D. Glucose
E. Sulfur

9. Which method refers to in vivo methods?
A. direct diffusion across the membrane
B. on isolated organs
C. chromatographic
D. solubility test
E. agar plates

10. Which method does not apply to in vitro methods?
A. agar plates
B. on rats
C. "solubility" test
D. direct diffusion across the membrane
E. chromatographic

IV. Summing up

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.

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