Drug technology Department

Discipline "*Biopharmacy*"

Current state and prospects of biopharmaceutics. Biopharmaceutics, key terms and story of development. Effect of the grinding degree of active pharmaceutical ingredients on the rate of their release from drugs.

LECTURE FOR ENGLISH SPEAKING STUDENTS OF SPECIALTY «PHARMACY»

Lecturer: ***ass. prof. Yuryeva A.B.***

LECTURE PLAN

1. *BIOPHARMACY AS SCIENTIFIC DISCIPLINE, ITS OBJECTIVE AND TASKS*
2. *GENERAL INFORMATION ABOUT BIOPHARMACY DEVELOPMENT*
3. *BASIC CONCEPTS AND TERMS OF BIOPHARMACY*
4. *EFFECT OF THE GRINDING DEGREE OF ACTIVE PHARMACEUTICAL INGREDIENTS ON THE RATE OF THEIR RELEASE FROM DRUGS*

Questions for individual work

1. **Works of foreign and domestic scientists that contributed to the development of biopharmaceutics.**
2. **Biopharmaceutics role in the development of drugs.**
3. **Current requirements for assessing the quality of drugs.**
4. **Disperse state, crystal structure and polymorphic forms of drugs.**

Recommended Books

- Biopharmaceutics. Practical handbook for English students of the 5th year, speciality “Pharmacy”: a handbook for the work of students / Edited by acad. A.I. Tikhonov. - Kh.: PH of NUPh, 2011. – 68 p.
- British Pharmacopoeia. – London: The Stationery Office, Vol. III, 2009. – P. 7533-7614. European Pharmacopoeia. Sixth edition. – Strasbourg: Council of Europe, Vol.1., 2008. – P. 1063-1084.
- Shargel, L. Applied Biopharmaceutics & Pharmacokinetics / L. Shargel, A. Yu, S. Wu-Pong. – 6 ed. – New-York: McGraw-Hill Medical, 2012. – 811 p. Mark P. Mathieu. PAREXEL Biopharmaceutical R&D Statistical Source-book 2014-2015 / Mark P. Mathieu. – Parexel Intl Corp., 2014. – 421 p.
- www.tl.nuph.edu.ua – site of Drugs Technology Department.
- Training portal http://pharmel.kharkiv.edu – distance learning center of NUPh.
- http://dspace.nuphedu.ua – electronic archive of NUPh.

1. BIOPHARMACY AS SCIENTIFIC DISCIPLINE, ITS OBJECTIVE AND TASKS

Biopharmacy does not substitute pharmacology. It does not study different mechanisms of action of biological-active substances. To create medicines in different dosage forms, convenient for application, storage, transportation – is the task of pharmacy.

For this purpose medicinal substances should be grinded, dissolved, mixed. Then give them different dosage forms, using various excipients, numerous mechanical devices, machinery, etc.

This way one biological effects of drugs can be strengthened, others weakened or even general activity of the drug is reduced to zero.

Studying these changes, processes, factors affecting the therapeutic efficacy of drugs is the main task of biopharmacy.

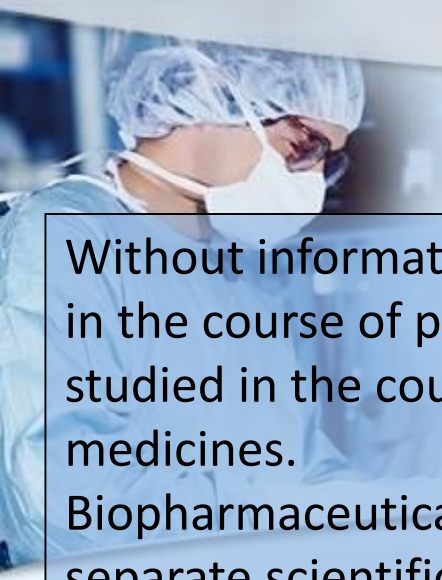
1. BIOPHARMACY AS SCIENTIFIC DISCIPLINE, ITS OBJECTIVE AND TASKS

BIOPHARMACY

DRUGS TECHNOLOGY

MEDICINAL SCIENCES

PHARMACEUTICAL CHEMISTRY



Without information about properties of medicinal substances (which are studied in the course of pharmaceutical chemistry), of plant raw material (which are studied in the course of pharmacognosy), it is impossible to correctly prepare medicines.

Biopharmaceutical branch is new in the technology of medicines. It formed in separate scientific discipline at the beginning of 60-th years of last century.

Nowadays biopharmacy is a theoretical base of different medicinal forms technology.

1. BIOPHARMACY AS SCIENTIFIC DISCIPLINE, ITS OBJECTIVE AND TASKS

The objective and task of biopharmacy as scientific discipline

- Studying students of the pharmacists work, as technologist - researcher;
- study of the theoretical bases, the acquisition of professional skills in the selection of scheme of research while developing of compositions and technologies of new drugs and improving existing;
- use bases of biopharmacy in justification of optimal drugs technology;
- prediction of pharmacokinetic processes of biologically active substances in the manufactured and extemporaneous drugs in various dosage forms.

2. GENERAL INFORMATION ABOUT BIOPHARMACY DEVELOPMENT

THE MAIN CAUSES OF BIOPHARMACY OCCURRENCE AS A SCIENCE

establishment of therapeutic factors of nonequivalence of drugs

different therapeutic efficacy of drugs that contain an equal number of the same components in identical dosage forms produced by different pharmaceutical companies

2. GENERAL INFORMATION ABOUT BIOPHARMACY DEVELOPMENT

THE MAIN OBJECTIVE OF BIOPHARMACY

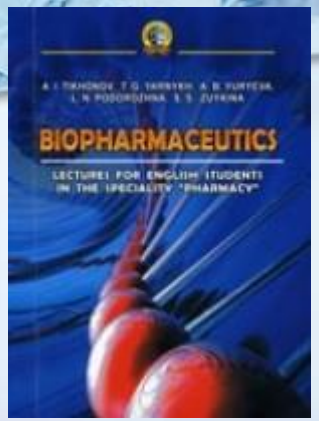
theoretical and experimental justification of development of new drugs and improving existing considering increasing their therapeutic effects and reducing the side effects on the body

2. GENERAL INFORMATION ABOUT BIOPHARMACY DEVELOPMENT

Biopharmacy

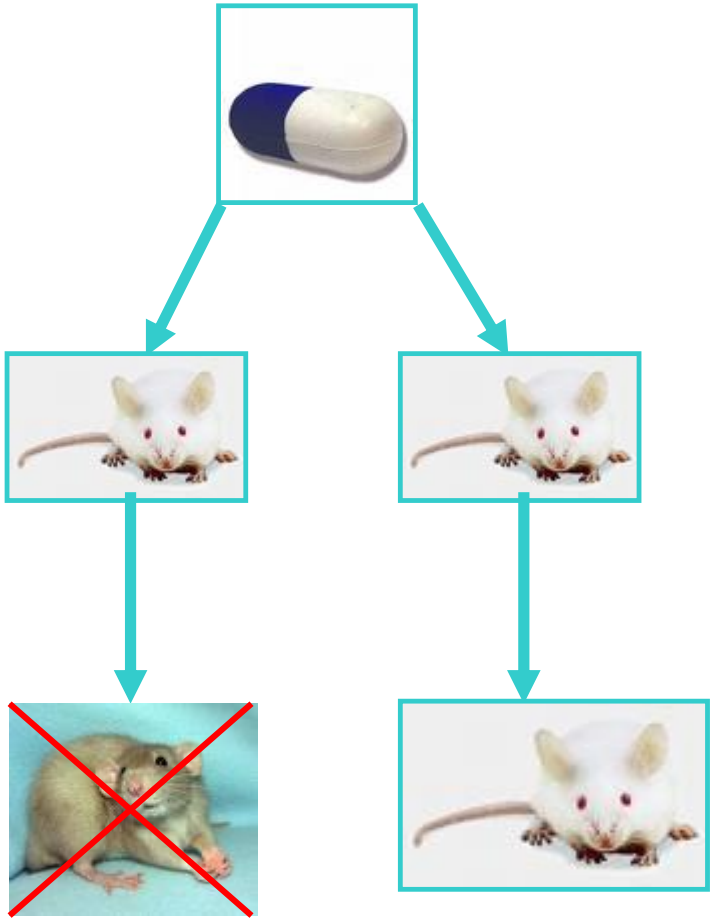
science that studies the dependence of therapeutic action of drugs on the body from a variety of factors

studying the impact of physical and chemical properties of active substances and excipients in medicines in various dosage forms in the same doses of the therapeutic effect



2. GENERAL DATA ABOUT THE DEVELOPMENT OF BIOPHARMACY

- An example became already a reading-book: in the 60x years of XX of century at setting in one of clinics of the USA of pills of one medicinal preparation, that operates specifically on the processes of the hemopexis, purchased from two different pharmaceutical firms that contain identical doses, it was suddenly discovered that the pills of one firm appeared in 2 times more active pills of other firm.



2. GENERAL DATA ABOUT THE DEVELOPMENT OF BIOPHARMACY

- It is found out a chemical analysis no rejections in maintenance of medicinal substance in the pills of both firms. This was the first case (that was got by wide publicity) of the exactly set therapeutic inadequacy, nonequivalence of preparations that contain the identical doses of the same active substance, but made by different manufacturers. The later like phenomenon found out at many antibiotics (tetracyclines, levomycetine, erythromycine), steroid hormones, sulfanilamidums, cardiac glycosides and other.

2. GENERAL DATA ABOUT THE DEVELOPMENT OF BIOPHARMACY

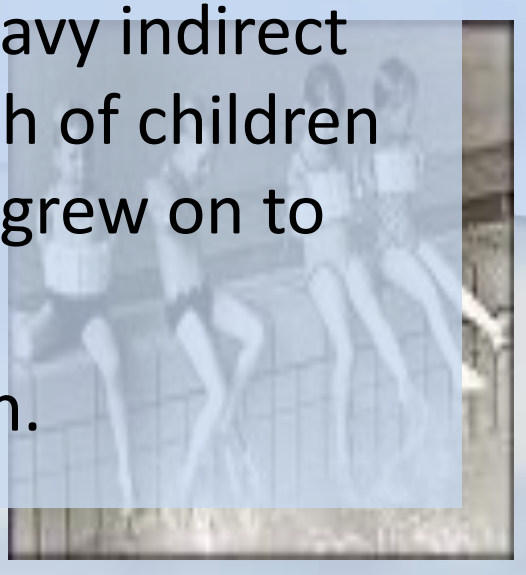
- For specialists that are engaged in a production and analysis of medicinal preparations, this phenomenon was unexpected. All preparations answered the requirements of pharmacopoeia, and that is why, in accordance with the conception generally accepted by then, must be equivalent.
- Explaining to this phenomenon of therapeutic inadequacy was given by new branch of pharmacy, medicine, biology - biopharmacy that signifies birth of the biological stage of pharmacy.

2. GENERAL DATA ABOUT THE DEVELOPMENT OF BIOPHARMACY

Tragic history is known for the whole world with the pills of preparation of talidomide (contergan), that was produced in Western Germany.

- Talidomide is a calming and easy sleeping-pill, however this preparation destroys tissues of fetus in the womb of mother, that's why it can not be applied to the pregnant mothers. But about such heavy indirect action of preparation knew only after birth of children without hands and feet, with hands that grew on to the trunk and other

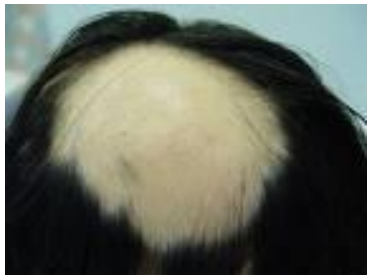
A case with talidomide is not an exception.



2. GENERAL DATA ABOUT THE DEVELOPMENT OF BIOPHARMACY

In the middle of 1970th in the USA a scandal grew round medicine called “**Mer-29**". "**Mer-29**" was considered the newest preparation that reduced the level of cholesterol in blood and prevented development of atherosclerosis and cardiovascular diseases. Such illnesses are an epidemic of the modern world, and that is why fully naturally, that this remedy (expensive enough) was applied by most Americans.

And only it turned out then, that "**Mer-29**" had not only justified hopes as medicine but also caused not irreparable harm to the health of most people. It was marked plenty of cases, when the long reception of preparation resulted in the heavy diseases of skin, baldness, blindness.

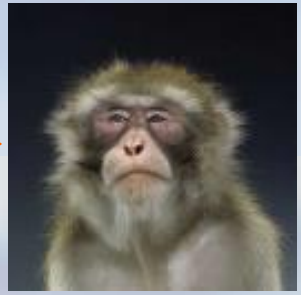


2. GENERAL DATA ABOUT THE DEVELOPMENT OF BIOPHARMACY

Government of the USA attracted a company-producer to criminal responsibility.

Every new preparation, before it is got by a pharmacy or a hospital for treatment of that or other disease, the long and difficult way of researches and control passes. At first preparation is investigated on animals - guinea-pigs, dogs and, finally, on primacies (monkeys). Comprehensively and for a long the degree of it's safety is investigated, operating on different organs, tissues and systems of organism.





2. GENERAL DATA ABOUT THE DEVELOPMENT OF BIOPHARMACY

Till recent time auxiliary substances concerned as indifferent forming products, the value of which was taken to giving of corresponding form and volume to the medicinal substance, with the aim of comfort of it's reception, transporting, storage.

However discoveries of the last decades resulted in confession of biological role of auxiliary substances. These substances enter into a contact with organs and tissues of organism, that's why to these substances pull out certain requirements. They must be biologically harmless and consonant with tissues of organism, and also not to own an allergic and toxic actions.

3. BASIC CONCEPTS AND TERMS OF BIOPHARMACY

Equivalence –

- suitability of the quantity of medicinal substances in the drug under analytical documentation
- suitability of pharmacological effect of the investigational drug to comparison product

Pharmaceutical equivalent (chemical)

Medicinal product containing the same substance and dose in specific dosage form and meets the requirements defined by technological standards

Clinical equivalent

Medicinal product that contains the same substance and dose, and after application gives the same therapeutic effect

3. BASIC CONCEPTS AND TERMS OF BIOPHARMACY

Bioequivalence

Medicines made by different manufacturers or the same plant, but different series after putting them in the same dosage form for the same patients in the same dose, showing the same biological (therapeutic) effect

Therapeutic non-equivalence

Inequality of therapeutic effects of the same drugs in the same doses and dosage forms produced by different manufacturers or the same plant, but different series

Pharmaceutically equivalent drugs will not always be therapeutically equivalent

SCIENTIFIC DIRECTIONS AND PROSPECTS OF DEVELOPMENT OF BIOPHARMACY

Biopharmacy

determines the new system of going near co-operation "medicinal preparation is an organism of patient"

studies influence of variable factors on therapeutic efficiency of medicinal preparations

gives a scientific ground to therapeutic nonequivalence of medicinal preparations

biopharmaceutical researches allow to work out rational composition and technology of medicinal preparations

SCIENTIFIC DIRECTIONS AND PROSPECTS OF DEVELOPMENT OF BIOPHARMACY

the results of researches allow to perfect existent medicines

the results of researches forecast and correct bioavailability of medicines

the results of researches allow purposefully to manage pharmacological and toxicological properties of medicines in different medicinal forms.

SCIENTIFIC DIRECTIONS AND PROSPECTS OF DEVELOPMENT OF BIOPHARMACY

Basic criteria of biopharmacy is providing of optimal therapeutic effect of medicine under minimal dosage of medicinal substance and minimal side effect.

Biopharmacy had successfully solved a range of tasks of applied pharmacy and medicine, and made an essential influence on further development of theory of modern studying of drugs.

EFFECT OF THE GRINDING DEGREE OF ACTIVE PHARMACEUTICAL INGREDIENTS ON THE RATE OF THEIR RELEASE FROM DRUGS

Physical state of drugs in the first place influences their pharmacokinetics (the rate of release, absorption) and the stability of the dosage form

Physical state of the medicinal substances include such parameters:

- **Degree of grinding (dispersity)** MS introduced in the solid state
- **Polymorphism (crystal structure)** MS introduced in the solid state
- **Aggregate state** of MS in medicinal form (method of administration)
- **Optical isomerism** (using different spatial isomers of MS)
- Using of anhydrous forms or crystalline hydrates of MS
- **Purity of MS** (type and quantity of impurities, the presence of micro-organisms)

EFFECT OF THE GRINDING DEGREE OF ACTIVE PHARMACEUTICAL INGREDIENTS ON THE RATE OF THEIR RELEASE FROM DRUGS

With the introduction of drugs in the solid aggregate state a significant effect on the bioavailability has degree of grinding (dispersity) of medicinal substances

Grinding of medicinal substances – the most simple and common technological operation, which is performed in the preparation of most drugs.

EFFECT OF THE GRINDING DEGREE OF ACTIVE PHARMACEUTICAL INGREDIENTS ON THE RATE OF THEIR RELEASE FROM DRUGS

Grinding of medicinal substances provides:

Obtaining the dosage form with the required physical and chemical properties (homogeneity, accuracy of medicinal substances dosing and other technological indicators)

At the same time, dispersity of the particles significantly affects on pharmacological effects of medicinal substances

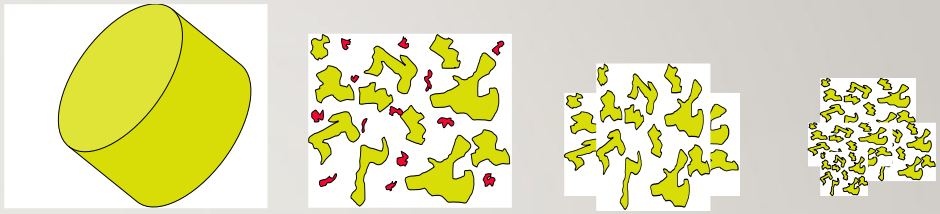
SPU regulates degree of grinding
(SPU art. 2.9.35. Grinding of powders)

The term	The average size of the particles, μm (мкм)
Rough	>355
Average	180-355
Small	125-180
Very small	<125

EFFECT OF THE GRINDING DEGREE OF ACTIVE PHARMACEUTICAL INGREDIENTS ON THE RATE OF THEIR RELEASE FROM DRUGS

PHYSICAL STATE OF THE DRUGS DISPERSITY

GRINDING OF DRUGS



Release rate (dissolution) of solids is directly proportional to its surface area

While grinding the surface area of solids is increased

Therefore, grinding ensures faster dissolution, absorption and pharmacological effects of medicinal substances

PHYSICAL STATE OF THE DRUGS
DISPERSITY

High decreasing of the particle size of the drug can cause adverse effects

- **inactivation of the active substances**
- **fast elimination from the organism**
- **toxic action**
- **reducing of the drug stability**

Micronized powder of sodium nitrate is easily decomposed with the release of toxic nitrogen oxides

Micronization of penicillin and erythromycin for oral use, leads to a sharp decrease of their antimicrobial activity

Medicinal substance in the drug must have the optimal degree of grinding, which provides the necessary therapeutic effect with the least possible side effects

Conclusions:

The main goal of the biopharmacy in the modern technology of medicines is maximum rise of therapeutical efficiency of medicinal substances and reduction to minimum of their side effects on organism. When working at these problems investigations in valuing of biological accessibility of drugs play an important role. That means that to pharmaceutical complex of knowledge, where firstly and only criteria were their physicochemical constants, are introduced new regulations, which have purely biological, medical grounds.

The term "biopharmaceuticals" first appeared in the scientific pharmacy of the United States in the 1960's and was soon widely recognized internationally.

The emergence of biopharmaceuticals was prepared by the gradual development of pharmacy, medicine, chemistry and other sciences. It is precisely at the crossroads of several branches of knowledge and biopharmacy takes its place

The term LADMER describes individual areas of drug interaction with the body: includes biopharmaceuticals, pharmacokinetics and pharmacodynamics (Liberation, Absorption, Distribution, Metabolism, Elimination, Response).

Under the physical condition of medicinal substances it is understood:

- Degree of shredding or dispersion (particle size) of medicinal substances;

- polymorphism of medicinal substances;

- aggregate state (amorphous, crystalline, shape and character of crystals);

- physical and chemical properties (pH, solubility, optical activity, electrical conductivity, melting temperature);

- surface properties of the medicinal substance (surface tension, film, etc.);

- Degree of purity (type and amount of contaminants, including the presence of microorganisms, allergens, astringents, etc.).

The physical state of the drugs affects the stability of the drug during storage, therapeutic efficacy, the rate of absorption, distribution and excretion of the drug from the body.

THANK YOU FOR YOUR ATTENTION!