

**MINISTRY OF HEALTH OF UKRAINE**

**ODESA NATIONAL MEDICAL UNIVERSITY**

Faculty of Pharmacy

Department of clinical and general pharmacology and pharmacognosy

**CONFIRMED by**

Acting vice-rector for scientific and pedagogical work

\_\_\_\_\_ Eduard BURYACHKIVSKY

« \_\_\_\_\_ » \_\_\_\_\_ 2023

**METHODOLOGICAL DEVELOPMENT  
TO PRACTICAL LESSONS FROM THE EDUCATIONAL DISCIPLINE**

Faculty, course \_\_\_\_\_ Pharmaceutical \_\_\_\_\_ II year \_\_\_\_\_

Educational discipline: "Theoretical foundations of the technology of dosage forms."

**Approved:**

Meeting of the department of general and clinical pharmacology and pharmacognosy  
Odessa National Medical University

Protocol No. \_\_\_\_\_ dated « \_\_\_\_\_ » \_\_\_\_\_ 20 \_\_\_\_\_

Head of the department \_\_\_\_\_ (Yaroslav Rozhkovsky)

Authors:

Head of the department, doctor of medicine, prof. Rozhkovskyi J.V.

Assistant, Ph.D. in biology Eberle L.V.

## Practical lesson No. 1

### **Theme №. 1 "Historical aspects of the formation and development trends of pharmaceutical technology in the countries of the world and in Ukraine".**

**Goal.** Formation of theoretical foundations and important professional skills in students regarding the organization of provision of medicines to the population, knowledge of the basics of proper pharmacy practice; formation of students' primary professional knowledge regarding the requirements for the production activity of pharmacies, safety rules and the sanitary and anti-epidemic regime of the production department of the pharmacy.

**Basic concepts.** *Healers* - were written for the people and home treatment, not by doctors for doctors. The amount of medicine was indicated in spoons, handfuls, and glasses. In scientific treatises, where there is a reference to foreign doctors, there are Latin names, the weight is indicated in the scrolls.

*Herbalists* - they include the Russian folk names of medicinal plants and a description of the area where they grow.

*Windmills* - are translated works that contained many foreign terms, many Latin names, doses given in apothecary measure.

**Equipment:** computer, multimedia equipment.

#### **Plan:**

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

In the conditions of the formation of market relations in Ukraine, great attention is paid to the professional training of specialists in the pharmaceutical industry. The discipline is the basis for the study of ethics and deontology in pharmacy, pharmacy technology of drugs, pharmacognosy, industrial technology of drugs, which involves the integration of teaching with the above-mentioned disciplines for the formation of skills to apply knowledge in the process of further education and professional activity.

In the second half of the 9th century the Old Kievan Rus state was formed with the capital in the city of Kyiv.

It was in Kyiv that the first healers appeared who used antlers (young deer horns), onions, radishes, horseradish, garlic, and plantain. Plantain was widely used for purulent wounds externally, and garlic was used internally for intestinal diseases and in the form of garlic water for washing the whole body during epidemics (plague, dysentery).

The medical profession had a craft character and was considered an honorable occupation. Practical experience was passed down from generation to generation. City doctors had benches to sell medicines, mainly of herbal origin. In Kievan Rus', the legal status of "lychee" was in effect, that's how folk healers were called. The law established payment for the work of a layman: a person who was wounded had the

right to demand from the offender 3 hryvnias for the treatment of his wound. Later, this reward was called "healing".

In Kievan Rus, surgery was developed as an important branch of practical treatment. The need for surgery was caused by frequent wars and domestic injuries. Wine, birch water, solutions of common salt were used to treat wounds.

Medicine in Kievan Rus is characterized by the beginning of the formation of state medicine, which begins to form alongside folk and monastic medicine.

Healers, herbalists and herbalists gained the widest distribution in Russia. These collections described the healing properties of plants and gave advice on how to treat certain diseases. The healers and herbalists lacked any elements of religion and mysticism.

Pharmacy network of Ukraine since the beginning of the 19th century. is developing intensively, pharmacies are opening in all large settlements, and their number is increasing in cities. In 1873, the government was forced to issue "Rules for opening pharmacies". The permission to open a pharmacy was issued by the governor, while it was necessary to take into account the population and the number of operating pharmacies. Thus, in large cities, one pharmacy was supposed to serve 12,000 people and 30,000 prescriptions, in provincial cities – 10,000 people and 15,000 prescriptions. In other settlements, it was allowed to open pharmacies at a distance of at least 15 versts.

In 1865, 14 pharmacies operated in Kyiv. Almost all pharmacies were private. State pharmacies were preserved only in provincial and administrative centers, and even they, as a rule, were leased to private pharmacists.

In the 80s of the XIX century. advanced zemstvo intelligentsia, with the aim of improving medical care for low-income groups of the population, obtained permission to open free pharmacies, which were created at the expense of zemstvos. Medicines from independent pharmacies were dispensed free of charge or at prices lower than in private pharmacies.

During the times of the Soviet Union, pharmaceutical education was not given due attention. There were only six pharmaceutical higher education institutions. Basically, pharmacists were trained at pharmaceutical faculties of medical institutes. The financial support of pharmaceutical faculties was very poor, as the main focus was on the training of doctors. The needs of the entire industry were met by specialists of only one specialty. Specialists with the same training worked in the pharmacy, pharmaceutical company, and hospital.

The first steps of independent Ukraine in this direction in the early 1990s were the birth of a national system of institutions designed to regulate the creation, analysis, research, introduction into medical practice and production of pharmaceuticals.

National Pharmacological and Pharmacopoeial Committees were created as guarantors of the quality of domestic and imported medicinal products entering the pharmaceutical market of Ukraine, the Committee for Drug Control, the Committee for Immunobiological Medicines, the State Inspectorate for Quality Control of Medicines, the Medicines Registration Bureau, etc.

With the declaration of independence of Ukraine in 1991, the form of ownership of pharmaceutical enterprises and pharmacy establishments underwent significant changes.

The modern stage of development of health care in Ukraine, which is characterized by the growth of the production of medicines, enterprises of various forms of ownership, with the use of mostly imported substances, as well as the arrival of large volumes of imported medicines on the domestic pharmaceutical market, puts forward strict requirements for their quality and requires improvement of the service their control.

**2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).**

- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);

- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.

### Tests

**1. In Kievan Rus, surgery was developed as an important branch of practical treatment, and the main antiseptic for treating wounds was:**

A wine

B snake venom,

C water,

D mushrooms,

E saliva.

**2. Define the term herbalists...**

A were written for the people and home treatment, not by doctors for doctors,

B they include the Russian folk names of medicinal plants and a description of the area where they grow,

C -,

D translated works containing many foreign terms, many Latin names, doses given in apothecary measure,

**3. In the handwritten "Uvariv herbalist" (1614), all known in Russia are described**

....

A medicinal plants,

B mushrooms,

C bacteria,

D diseases,

E -.

**4. In 1865, pharmacies functioned in Kyiv. Specify their number at the moment:**

A 14,

B 20,

C 30,

D 25,

E 15.

**5. The special development of the pharmaceutical industry in the 20th century was observed in:**

- A Galicia,
- B Odeshchyna,
- C Donetsk,
- D Lviv region
- E -.

**6. The first information about pharmacies in Western Ukraine is dated to the end of:**

- A of the seventeenth century,
- B of the 16th century
- C of the 14th century,
- D of the 18th century,
- E of the 15th century.

**7. At the end of the XX century. on the pharmaceutical market of Ukraine there are about ..... pharmaceutical companies**

- A 200;
- B 150,
- C 300,
- D 50,
- E 100.

**8. The first steps of independent Ukraine in the early 1990s were the birth of a national system of institutions designed to regulate the creation, analysis, research, and pharmaceutical products, therefore the following were created:**

- A Pharmacological and Pharmacopoeial Committees,
- B Pharmacies,
- C Pharmaceutical enterprises,
- D State Inspection,
- E -.

**9. Home pharmacies were more often created in small towns or provinces to help doctors. The main condition for opening such pharmacies was....**

- A lack of a pharmacy within a 1-mile radius of the doctor's residence,
- B the presence of a population that could purchase medicine,
- C if the pharmacist was a doctor part-time,
- D the presence of a railway,
- E -

**10. An outstanding event in Ukraine in the 1970s was the opening of a pharmaceutical enterprise. Specify the name of the company?**

- A Lvivfarm,
- B Odesafarm,
- C Kharkivfarm,
- D Kyivfarm,
- E -

**3. *Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):***

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

### 3.1. Tasks for fixing the material

№.№ C.E.	Main tasks	Instructions	Answers
1	2	3	4
1.	Development of medicine and pharmacy in Ukraine?	your answer	
2.	Pharmacy in Kyevan Rus in the XVI-XVII centuries?	your answer	
3.	Name the main achievements in pharmacy in Kyevan Rus?	your answer	
4.	Prominent figures in the field of medicine in Kyevan Rus?	your answer	
5.	Creation of the first pharmacies in Ukraine?	your answer	
6.	The development of pharmacy in Europe during the XVI-XVII centuries?	your answer	
7.	Name the outstanding figures in the pharmacy of Europe?	your answer	
8.	What diseases were noted in the period of the XVI-XVII centuries? The main ways of treatment?	your answer	
9.	What was the basis of the apothecary order.	your answer	
10.	Name the owners of the first pharmacies opened in Ukraine?	your answer	

### 3.2. Questions for self-control:

1. The development of medicine and pharmacy in Ukraine from Ancient Rus to the beginning of the 20th century.
2. Pharmacy in Kyevan Rus during the XVI–XVII centuries.

3. Medical professions of the 16th century. Pharmacy order.
4. Pharmacy at the beginning of the 18th century.
5. Development of Ukrainian medicine and pharmacy in the XIII–XIX centuries.
6. Development of the pharmacy business in Ukraine in the 18th century.
7. Historical aspects of pharmaceutical education in Ukraine and abroad.
8. Outstanding scientists and their contribution to the development of medicine and pharmacy.
9. Development of pharmaceutical production in European countries.

#### 4. Summing up.

#### 5. List of recommended literature (main, additional, electronic information resources):

##### Basic literature:

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

##### Additional

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.
3. State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 1. -1128 p.
4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
5. History of medicine and pharmacy: teaching. manual for pharmacy students. education closing and pharmacy Faculty of Higher Education of the Ministry of Health of Ukraine / A. A. Kotvitska, V. V. Gorbanev, O. O. Surikov and others. – Kharkiv: National Institute of Economics and Technology: Golden Pages, 2016. – 168 p.



6. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N MOZU42 – 4.5: 2015 //Edited by Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. -109 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).

### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>
3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine <https://library.gov.ua/>
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbuv.gov.ua/>
7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/](http://StateExpertCenteroftheMinistryofHealthofUkrainehttps://www.dec.gov.ua/index.php/ua/)
8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen.

## Practical lesson No. 2

**Theme № 2 "Pharmaceutical technology. Modern tasks and prospects of pharmaceutical technology. Basic terms and concepts of pharmaceutical technology".**

**Goal.** Formation of students' knowledge of regulatory and technical documentation in the industrial production of medicinal products. To study the general principles of the organization of pharmaceutical production. To master the principles of classification of medicinal forms.

**Basic concepts.** *Pharmaceutical technology* – (pharmaceutical technology; medicinal technology) is a branch of science that studies the theoretical foundations of the technological processes of obtaining and processing medicinal products into prophylactic, therapeutic, rehabilitative, diagnostic and other medicinal products in the form of various medicinal forms.

*Pharmacy drug technology* - is carried out by preparing drugs according to individual prescriptions, preparing intra-pharmacy blanks, packaging, and is carried out in a pharmacy. It is distinguished by a large range of small-batch products. Manufactured medicinal products are unstable during storage, have a complex composition and individual dosages;

*Technology of pharmaceutical production* (factory (industrial) drug technology) - is characterized by large-scale production and is produced by mechanized pharmaceutical enterprises, plants and factories.

*Technological parameter* - a physical or chemical parameter that has a quantitative or qualitative scale of measurements, which determines the limits of the technological norm and / or safety, the departure of which exceeds the limit values, leads to a decrease in the quantity or quality of the product obtained and / or the occurrence of extraordinary situations.

**Equipment:** computer, multimedia equipment.

**Plan:**

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

Pharmaceutical drugs are products of interdisciplinary importance and wide application, on which the life, health and well-being of a person primarily depend. Saturation of the Ukrainian market with domestically produced pharmaceuticals is associated with the formation of new approaches to the organization of production, assessment of the quality of raw materials used and finished products, and the use of new technologies. Solving these problems is within the power of specialists who have appropriate training in solving issues arising in the pharmaceutical industry.

*The main tasks of pharmaceutical technology as a science:*

- development of technological foundations and methods of production of new medicinal substances and preparations;
- improvement of existing medicines;
- search, study and use of new auxiliary substances in the production of medicinal products;
- studying the stability and establishing the expiration date of medicinal substances, preparations, semi-finished products and other products;
- study of the effectiveness of the technological process, the main indicators of which are: specific consumption of raw materials, energy and labor costs per unit of production; output and quality of finished products; intensity of technological process; production cost.

*Pharmaceutical technology:*

If auxiliary work (dissolution and drying of raw materials, preparation of solutions of a given concentration, etc.) is carried out in separate equipment for one stage of the main technological process, then such auxiliary work is included in this stage of the main technological process.

*Auxiliary work* carried out in separate equipment for several stages of the same production or several productions are allocated to independent stages of auxiliary work (for example, preparation of demineralized water, solutions of acids or alkalis with a given concentration for the entire workshop, etc.).

*If waste processing* or their disposal is carried out as independent work, they may not be included in the technological scheme of production. At the same time, the technological scheme with an arrow indicates where the waste goes for processing (disposal)

*Technical means* - a set of production tools necessary for the implementation of the technological process.

*Intermediate products* are partially processed products obtained at any stage of the technological process, excluding the final stage, and intended for further processing before they become finished products.

*An intermediate product* is a product received by a manufacturing company from a supplier that has undergone one or more stages of processing (at the supplier) necessary for the production of finished products (from the consumer). An intermediate product for a supplier is a finished product.

Waste is a modified or low-quality residue of raw materials, materials or semi-finished products, which cannot be used for the preparation of a finished product without appropriate processing.

If production waste has consumer value and can be further processed, they are called by-products. Production waste, which is not subject to further processing and does not represent consumer value, is called emissions.

A series of finished medicinal products is a set of units of a medicinal product, which is manufactured from one series of raw materials, materials and intermediate products in one technological process, including the same sterilization stage.

The State Register of Medicinal Products of Ukraine (Law of Ukraine "On Medicinal Products and Medicinal Products") is a regulatory document containing information on medicinal products that are permitted for production and use in medical practice.

The quality of a medicinal product is a set of properties that give the medicinal product the ability to satisfy consumers in accordance with its purpose and meet the requirements established by law.

The quality of the medicinal product is standardized by the Pharmacopoeia article - a regulatory document that defines the composition, packaging, expiration date and requirements for the quality of the medicinal product (medicinal substance or excipient) and has the status of a state standard.

*The certificate* is a written certificate (guarantee) that the quality of the medicinal product (efficacy, safety) meets the established requirements of the specification, and the production process meets the rules of good manufacturing practice (GMP).

Stability is the ability of a medicinal product (preparation) to retain its physicochemical and microbiological properties for a certain period of time from the moment of its release.

Expiry date - approved by the legislative body on the basis of the results of special studies, the storage time of the medicinal product (preparation), during which it retains its physico-chemical, microbiological and therapeutic properties in an unchanged form or within the limits established for them, subject to compliance with the storage conditions.

Medicinal (pharmaceutical) raw materials - medicinal products, medicinal plant raw materials, auxiliary substances allowed for medical use for the purpose of the production of medicinal products or other pharmaceutical products or semi-finished products. In fact, the composition of raw materials includes all raw materials that enter production for processing in order to obtain a finished product or semi-finished product, with the exception of packaging materials.

Active substances (Law of Ukraine "On Medicinal Products") are biologically active substances that can change the state and functions of the body or have a prophylactic, diagnostic or therapeutic effect and are used for the production of finished medicinal products.

Medicinal product (medicinal substance) - a substance (mixture of substances) of synthetic or natural origin, which has a certain biological activity and is allowed for medical use, production and import for the purpose of diagnosis, prevention or treatment of humans or animals.

Auxiliary substance - a chemically and biologically indifferent substance, allowed for medical use for the purpose of obtaining a dosage form, providing or preserving certain properties of the medicinal product.

Medicinal form - the form given to a medicinal product or medicinal plant material, convenient for use and providing the necessary therapeutic effect.

Medicinal product (medicinal product, medicinal product) is a medicinal form in a packaged, packaged and labeled form in accordance with the requirements of regulatory and technical documentation, which has a certain expiration date and is convenient for medical use, transportation and storage.

## **2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).**

- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);

- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.

## **Tests**

### **1. Define the term validation:**

*A is a documentary confirmation of compliance of the equipment, production conditions, technological process, quality of the intermediate product and the finished product with the current regulations and / or requirements of regulatory documentation.*

*B is a documentary confirmation of the conformity of production equipment.*

*C is the conformity of production conditions, technological process.*

*D is a documentary confirmation of the quality of the intermediate product and the finished product in accordance with current regulations and / or requirements of regulatory documentation.*

*E -.*

### **2. The State Register of Medicinal Products of Ukraine is...**

*A regulatory document containing information on medicinal products approved for production and use in medical practice.*

*B a set of properties that give the medicine the ability to satisfy consumers in accordance with its purpose and to meet the requirements established by law.*

*C the ability of a medicinal product (preparation) to retain its physico-chemical and microbiological properties for a certain period of time from the moment of its release.*

*D form given to the medicinal product or medicinal plant material is convenient for use and provides the necessary therapeutic effect.*

### **3. Biologically active substances that can change the state and functions of the body, diagnostic or therapeutic effect and are used for the production of ready-made medicinal products are called...**

*A Active substances,*

*B Pharmaceutical form,*

*C Medicine,*  
*D Certificate,*  
*E -.*

**4. A written certificate that the quality of the medicinal product meets the established requirements of the specification, and the production process - the rules of good manufacturing practice (GMP) is called...**

*A Certificate,*  
*B Patent for an invention,*  
*C Mark of quality,*  
*D Utility model patent,*  
*E Article.*

**5. Solid, soft, liquid and gaseous dosage forms are classified according to...**

*A aggregate state,*  
*B composition of auxiliary components,*  
*C by the presence of active substances,*  
*D stages of production.*  
*E-.*

**6. A mixture of several types of chopped, ground into coarse powder or whole medicinal plant raw materials, sometimes with the addition of other medicines is called...**

*A fee,*  
*B powders*  
*C granules,*  
*D dragee*  
*E capsules.*

**7. Systems in which a solid substance is suspended in a liquid and the particle size ranges from 0.1 to 10  $\mu\text{m}$  are called:**

*A suspension;*  
*B emulsions,*  
*C liniments,*  
*D mucus,*  
*E solutions.*

**8. The classification of dosage forms, depending on the routes of administration, is divided into:**

*A enteral and parenteral;*  
*B injectable and inhaled,*  
*C rectal and vaginal,*  
*D sublingual and percutaneous,*  
*E -.*

**9. The State Pharmacopoeia is...**

*A set of mandatory national standards and norms that regulate the quality of medicinal products,*  
*B some norms that regulate the quality of medicinal products,*

- C a set of selective criteria that indicate a certain quality of medicinal products,*  
*D articles on individual medicinal substances and medicinal products,*  
*E -*

**10. The Commission of the European Pharmacopoeia currently has... members:**

- A 38 countries,*  
*B 40 countries,*  
*C 20 countries,*  
*D 5 countries,*  
*E 15 countries.*

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

**3.1. Tasks for fixing the material**

<b>№№ п.п.</b>	<b>Mein tasks</b>	<b>Instructions</b>	<b>Ansvers</b>
<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>
1.	Name the main tasks of technology?	your answer	
2.	Name the main criteria for the organization of pharmaceutical production?	your answer	
3.	Main departments in a pharmaceutical company?	your answer	
4.	Define the term pharmaceutical technology?	your answer	
5.	State the common and distinctive features between pharmacy drug technology and pharmaceutical manufacturing technology?	your answer	
6.	Define the term validation?	your answer	
7.	Name the main principles of classification of dosage forms?	your answer	

8.	How is the quality of the medicinal product determined?	your answer	
9.	Indicate the classification of medicinal forms depending on the method of introduction into the body?	your answer	
10.	Name the main regulatory and technical documents for the industrial production of medicinal products?	your answer	

### 3.2. Questions for self-control:

1. The main tasks of pharmaceutical technology as a science.
2. General principles of pharmaceutical production organization.
3. Basic terms and concepts in the field of drug production.
4. Principles of classification of dosage forms.
5. Classification of dosage forms depending on the method of administration of drugs into the body.
6. Classification of dosage forms depending on the field of action.
7. Classification of dosage forms according to Yu. I. Khadzhai.
8. Regulatory and technical documentation for the industrial production of medicinal products.
9. State Pharmacopoeia of Ukraine.

### 4. Summing up.

#### 5. List of recommended literature (main, additional, electronic information resources):

##### Basic literature:

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

##### Additional

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V.



- Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.
  3. State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 1. -1128 p.
  4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
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### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>
3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine <https://https://library.gov.ua/>
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbu.gov.ua/>
7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/](http://State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/)
8. Compendium online – <https://compendium.com.ua/uk/>
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## Practical lesson No. 3

### Theme № 3. "Pharmaco-technological properties of powdered materials."

**Goal.** Formation of theoretical foundations in students about the physico-chemical properties of loose materials and their influence on the technology of tablet production and definition of concepts: bulk density of powders, density after shrinkage, fluidity (flowability), extrusion pressure and their influence on the technology of tablet production.

#### **Basic concepts.**

*Powder* - is a solid medicinal form for internal and external use, consisting of one or more solid particles of varying degrees of fineness and having the property of flowability.

**Equipment:** computer, multimedia equipment.

#### **Plan:**

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

The rational method of tableting largely depends on the pharmaco-technological and physico-chemical properties of the active substances and the selection of the assortment and number of auxiliary substances. As active materials, loose substances in the form of powdery or granular particles, which have certain physico-chemical and technological properties, are used.

Powdered substances consist of polydisperse systems with different shapes and sizes of crystalline particles (an amorphous structure is less common in the production of tablets). The shape and size of powder particles depend: in the case of crystalline substances (chemical-pharmaceutical preparations) - on the structure of the crystal lattice and the conditions of growth of particles in the process of crystallization, in the case of crushed plant materials - on the anatomical and morphological features of the crushed plant organs and the type of grinding machine.

Tablets obtained by pressing have different geometric shapes, weights and sizes. The domestic industry mainly produces round tablets with a flat or biconvex surface

The size of the tablets varies from 4 to 25 mm in diameter. Tablets with a diameter of more than 25 mm are called briquettes. The most common are tablets with a diameter of 4 to 12 mm. Tablets with a diameter of more than 13 mm should be chewed, resorbed or dissolved before use; with a diameter of 9 mm and more should have a line (one or two), which allows you to divide them into two or four parts and thus facilitate the dosing of the medicinal substance.

The production of tablets begins with the study of the properties of the original medicinal substances, which in many ways determine the rational method of tableting, the choice of the range and amount of auxiliary substances. As a starting material, loose substances are used in the form of powdery forms (particle size up to 0.2 mm) or granular (particle size from 0.1 to 3 mm), which have the following properties:

- physical - density, shape, size and character of the surface of the particles, adhesion (sticking on the surface) and cohesion (sticking of particles inside the body), surface activity, melting point, etc.;
- chemical - solubility, reactivity;
- technological - bulk density, degree of compaction, flowability, moisture, fractional composition, dispersion, compressibility, etc.;
- structural and mechanical - plasticity, strength, elasticity, viscosity of the crystal lattice, etc.

**2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).**

- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);
- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.

## Tests

**1. According to the method of production, tablets are divided into two classes:**

- A pressed and molded tablets,
- B molded and effervescent,
- C tablets with a shell and a film,
- D enteric and effervescent,
- E for oral and vaginal.

**2. The sizes of tablets in diameter range from ...**

- A 4 to 25 mm,
- B 2 to 14 mm,
- C 5 to 40 mm,
- D 10 to 50 mm.

**3. The true density of the powder is determined by the ratio .....**

- A of the mass of the drug to its volume, with zero porosity of the powder,
- B of the volume of the drug to its density,
- C mass of the drug to its moisture content,
- D concentration of the drug to its volume, with zero porosity of the powder.
- E -.

**4. The following chemical properties are important for tableting, namely:**

- A presence of water of crystallization, solubility, wettability and hygroscopicity,
- B the presence of impurities, solubility, irrigability and flowability,
- C presence of hygroscopicity and homogeneity of particles,
- D presence of good solubility and wettability.

**5. Bulk density is:**

- A is the mass of a unit volume of freely poured powder, which depends on the density of the substance, the shape and size of the particles, their stacking,
- B is the mass of a unit volume of freely poured powder, which depends on the moisture content of the substance, the shape and their stacking,
- C is the volume of the free space between the powder particles,

**D** is the ratio of bulk density to true density.

**E** -.

**6. The volume of free space (pores, voids) between powder particles:**

**A** Porosity,

**B** Bulk density,

**C** Relative density,

**D** Raw material moisture,

**E** Fractional composition.

**7. Knowing which value allows you to predict the standard sizes of tablets, to correctly choose the amount of pressing pressure for obtaining tablets.**

**A** Flowability of the substance;

**B** Bulk density,

**C** Fractional composition,

**D** Porosity,

**E** -.

**8. The shape, size and nature of the surface of the powder particles are determined using...**

**A** Microscope,

**B** Dandruff,

**C** Telescope,

**D** Without devices,

**E** -.

**9. The true density of the powder is determined using ....**

**A** Volume meter,

**B** Microscope,

**C** pH meter,

**D** spectrophotometer,

**E** -

**10. Relative density (ton, %) is calculated as:**

**A** Percentage ratio of bulk (bulk) density to true density,

**B** percentage ratio of humidity to true density,

**C** is the percentage ratio of bulk (bulk) density to grinding.

**D** is the percentage ratio of bulk density to concentration.

**E** -

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);

- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);

- requirements for work results, incl. to registration;

- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

### 3.1. Tasks for fixing the material

№№ c.e.	Mein tasks	Instructions	Answers
1	2	3	4
1.	Classification of tablets by structural feature.	your answer	
2.	Determination of moisture content.	your answer	
3.	Determination of fractional composition.	your answer	
4.	Determination of bulk density.	your answer	
5.	Determination of true density.	your answer	
6.	Determination of relative density.	your answer	
7.	Definition of flowability.	your answer	
8.	Determination of compressibility.	your answer	
9.	Determination of the force of pushing out tablets from matrices.	your answer	
10.	Determination of the shape, size and nature of the powder surface.	your answer	

### 3.2. Questions for self-control:

1. Physico-chemical properties of powdered materials.
2. Technological volume density, degree of compaction, flowability of powdered materials.
3. Moisture, fractional composition of powdered materials.
4. Dispersity, compressibility of powdered materials.
5. Structural and mechanical properties: plasticity, strength, elasticity, viscosity of the crystal lattice, etc.
6. Determination of the shape, size and nature of the powder surface, determination of moisture content.
7. Setting fractional composition, bulk density, true density, relative density.
8. Determination of porosity, flowability, compressibility, etc.

### 4. Summing up.

## **5. List of recommended literature (main, additional, electronic information resources):**

### **Basic literature:**

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

### **Additional**

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.
3. State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 1. -1128 p.
4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
5. History of medicine and pharmacy: teaching. manual for pharmacy students. education closing and pharmacy Faculty of Higher Education of the Ministry of Health of Ukraine / A. A. Kotvitska, V. V. Gorbanev, O. O. Surikov and others. – Kharkiv: National Institute of Economics and Technology: Golden Pages, 2016. – 168 p.
6. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N MOZU42 – 4.5: 2015 //Edited by Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. -109 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).

### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>

3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine <https://https://library.gov.ua/>
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbuv.gov.ua/>
7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/](http://StateExpertCenteroftheMinistryofHealthofUkrainehttps://www.dec.gov.ua/index.php/ua/)
8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen.

## Practical lesson No. 4

### Theme № 4 «Theoretical foundations of grinding of solid bodies. Theories of crushing of solid bodies».

**Goal.** Students' formation of theoretical foundations about grinding, classes of grinding, degree of grinding and methods of grinding. To learn the theoretical basics of grinding solid bodies.

**Basic concepts.** *Splitting* - the body breaks into particles in the places of concentration of the greatest loads, which arise as a result of the action of wedge-shaped working elements. The method of splitting in comparison with crushing allows you to adjust the size of the obtained particles.

*Breaking* - the body is destroyed under the action of bending forces. The size and shape of the particles obtained by breaking are approximately the same as by splitting.

*Cutting* - the body is divided into particles of predetermined sizes and shapes.

*Abrasion* - the body is crushed under the action of compressive, stretching and shearing forces. At the same time, a fine dust-like product is obtained.

*Impact* - the body is destroyed into particles under the action of a dynamic load. There is a difference between compressed and free stroke.

**Equipment:** computer, multimedia equipment.

#### Plan:

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

The intensity of physical and chemical processes involving the solid phase increases with an increase in the surface of a solid material, which is achieved by reducing its size. In this regard, various solid materials are subjected to mechanical grinding in many chemical industries, which is of great importance in the manufacture of dosage forms.

Grinding is the process of reducing the size of material particles by destroying them under the action of external forces that overcome the internal forces of adhesion that bind the particles of a solid substance together.

The characteristics of the crushed material are the following parameters: dispersion (fractional, granulometric composition), passage  $D$  (residue  $R$ ), fraction  $\Delta D$  or  $\Delta R$ .

To determine the complete picture of the fractional composition of the crushed material, distribution functions are used, which represent the dependence of the passage  $D$  or the residue  $R$  on the diameter (size) of the particles.

One of the characteristics of the material is the specific surface, that is, the surface of the particles, which refers to a unit of mass or volume of the material.



Average particle diameter, median diameter, and others are used as conventional indicators.

The material can also be characterized by the permissible percentage content of a certain fraction: large, medium and small.

Grinding methods mean the kind of impact on a solid material that leads to its destruction.

Solid material can be destroyed by the following grinding methods: crushing, splitting, breaking, cutting, sawing, abrasion, impact and various combinations of these methods.

Crushing is a type of failure in which the deforming load acting on the body leads to an increase in internal stress above the compressive strength limit.

As a result of such destruction, particles of different sizes and shapes are obtained.

*Splitting* - the body breaks into particles in the places of concentration of the greatest loads, which arise as a result of the action of wedge-shaped working elements. The method of splitting in comparison with crushing allows you to adjust the size of the obtained particles.

*Breaking* - the body is destroyed under the action of bending forces. The size and shape of the particles obtained by breaking are approximately the same as by splitting.

*Cutting* - the body is divided into particles of predetermined sizes and shapes.

*Abrasion* - the body is crushed under the action of compressive, stretching and shearing forces. At the same time, a fine dust-like product is obtained.

*Impact* - the body is destroyed into particles under the action of a dynamic load. There is a difference between compressed and free stroke.

With a compressed impact, the body is destroyed between two working bodies of the shredder. The effect of such destruction depends on the kinetic energy of the impacting body.

With a free impact, the destruction of the body occurs as a result of its collision with the working body of the shredder or other bodies in flight. The effect of such destruction is determined by the speed of their collision, regardless of whether the body that is destroyed or the working body of the shredder moves. In most cases, these types of influence on the material are used in combination, while most often only one of them is decisive.

Depending on the physical and mechanical properties, particle sizes of the starting material and the final product, one or another method of grinding is chosen, while it is also necessary to take into account the moisture content of the material and other properties.

## **2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).**

- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);

- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.

## Tests

**1. The process of reducing the size of material particles by destroying them under the action of external forces that overcome the internal forces of adhesion that connect the particles of a solid substance is called:**

- A grinding,
- B dissolution,
- C dispersion,
- D extraction,
- E solution.

**2. The ratio of the particle sizes of the original and crushed material is called...**

- A degree of grinding,
- B solubility,
- C concentration,
- D dispersion.

**3. According to the Mohs hardness scale, quartz .....**

- A scratches the glass,
- B scratches with his fingernail,
- C cuts glass,
- D has the hardness of window glass.
- E -.

**4. The strength limit ( $10^{-5}$  N/m<sup>2</sup>) of quartz is:**

- A 1200-1500,
- B 1450,
- C 300-1500,
- D 1000-2500.

**5. How to grind a viscous, medium-hard material:**

- A abrasion with impact,
- B crushing, impact,
- C splitting, abrasion,
- D crushing.
- E-.

**6. According to the surface theory (Rittinger theory)...**

- A the useful work of grinding is spent on the formation of new surfaces,
- B the useful work of abrasion is spent on reducing the formation of new surfaces.
- C useful work of grinding is spent on volumetric deformation of particles that are destroyed,
- D useful grinding work is spent on the partial deformation of the particles.
- E -

**7. What is the name of the theory that shows that the useful work of grinding is spent on the volumetric deformation of the particles that are destroyed.**

- A Volumetric theory (Kirpychov-Kick theory),
- B Surface theory (Rittinger theory),
- C Rebinder's theory,
- D Benedict's theory.
- E -.

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

**3.1. Tasks for fixing the material**

№№ c.e.	Mein Tasks	Instruction's	Answers
1	2	3	4
1.	Grinding classes.	your answers	
2.	Shredding by crushing and splitting.	your answers	
3.	Shredding by breaking and cutting.	your answers	
4.	The method of grinding according to the Mohs scale.	your answers	
5.	Strength limit and modulus of elasticity of materials.	your answers	
6.	Groups of materials depending on strength.	your answers	
7.	Grinding methods depending on the type of material.	your answers	
8.	Gates of Energy	your answers	
9.	Surface theory (Rittinger's theory).	your answers	
10.	Bulk theory (Kirpychov-Kick theory).	your answers	

**3.2. Questions for self-control:**

1. Grinding. Grinding classes, degree of grinding.
2. Methods of grinding (crushing, splitting, breaking, cutting).
3. Mohs hardness scale.
4. Strength limit and modulus of elasticity of some materials.
5. Groups of materials depending on strength.
6. Grinding methods depending on the type of material.
7. Physico-mechanical basics of grinding.
8. Energy consumption.
9. Stages and main grinding schemes.
10. Classification of shredders.
11. Comparison and selection of shredders.

#### **4. Summing up.**

#### **5. List of recommended literature (main, additional, electronic information resources):**

##### **Basic literature:**

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

##### **Additional**

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.
3. State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 1. -1128 p.
4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
5. History of medicine and pharmacy: teaching. manual for pharmacy students. education closing and pharmacy Faculty of Higher Education of the Ministry of

Health of Ukraine / A. A. Kotvitska, V. V. Gorbanev, O. O. Surikov and others.  
– Kharkiv: National Institute of Economics and Technology: Golden Pages, 2016.  
– 168 p.

6. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N MOZU42 – 4.5: 2015 //Edited by Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. -109 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).

### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>
3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine <https://https://library.gov.ua/>
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbuv.gov.ua/>
7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/](http://StateExpertCenteroftheMinistryofHealthofUkrainehttps://www.dec.gov.ua/index.php/ua/)
8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen.

## Practical lesson No. 5

### Theme № 5 «Methods of determining the size of particles of solid bodies. Sifting and mixing of powdered materials. Theoretical foundations of pressing.»

**Goal.** Formation of theoretical foundations for students about the main stages and features of sieving and mixing of solids with subsequent production of medicinal forms.

**Basic concepts.** *Sifting* – is the process of obtaining a product with the same particle size. Sifting is regulated according to the State Federal Office of Internal Affairs and Communications I.

*Mixing* – is a mandatory operation in the manufacture of powders. It can be carried out simultaneously with powdering or independently, if a complex powder is prepared from an already crushed substance. In pharmacies, powders are mixed mainly in a mortar. This operation should be carried out with frequent collection of powder from the walls of the mortar and pestle to the center of the mortar with the help of a celluloid capsule.

**Equipment:** computer, multimedia equipment.

#### **Plan:**

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

An important point in the production of powders is familiarization with the main operations and equipment necessary for the production of powders; to study the peculiarities of the technology of solid dosage forms. Peculiarities of sieving and mixing of powdered materials.

Depending on the medical purpose and the method of application, powders have different requirements for dispersion. Crystalline powders intended for dissolution before use by patients (magnesium sulfate, boric acid, etc.) are usually produced in the form of powders with a particle size of 0.2 to 0.3 mm. Powder powders intended for the treatment of various injuries of the skin or mucous membranes must be ground very finely (0.090-0.093 mm) in order to increase the total surface of the particles of these substances and reduce their traumatic effect.

When obtaining complex powders in industrial conditions, each substance included in the composition of the mixture is crushed separately and sifted through a suitable sieve. When sieving mixtures through the holes of the sieves, first of all, particles that are smaller and have a higher specific mass pass through. Then lighter and larger particles are sifted out. As a result of this, the screening is arranged in layers of different quality. Therefore, after sifting, the materials must be thoroughly mixed again.

In industrial conditions, mechanical designs of sieves are used: rotating, oscillating, vibrating. According to the construction of vibrating devices, there are 3 types of vibrating sieves: electromagnetic, gyrational, inertial.

Sifting of crushed material is carried out with the help of sieve mechanisms of various designs: rotating, swinging and vibrating. Wet material can be sifted on vibrating sieves.

Mixing of powdered products is carried out in special mixers, which are classified as:

- by the nature of the mixing process (convection or diffusion),
- a design feature (drum mixers with a rotating body and rotating blades),
- by the method of action on the mixture (gravitational, centrifugal),
- the nature of the mixing process (periodic or continuous) and other features.

A qualitative characteristic of the mixing process is the homogeneity of the composition of any of the samples taken from different zones of the mixer.

The mixing process is influenced by the following factors: surface forces (electrostatic, molecular, van der Waals), shape and size of particles and their density. The time of mixing simple and complex prescriptions in the dry state is from 3 to 12 min., and in the moistened state - from 5 to 20 min. To obtain a homogeneous mixture of bulk materials, fluidized bed mixers are used. The basic principle of mixing is that a smaller quantity is added to a larger quantity in order to avoid the loss of small quantities of substances. The simplest and easiest method of mixing is one in which the ingredients are part of the powder in approximately equal quantities, with particles of the same size and close in density. All components are poured into a mixer and mixed until a homogeneous mixture is obtained. If, under the specified equal conditions, the specific mass of the mixed powders is different, then the duration of mixing increases. If a small amount of a poisonous or potent substance or essential oil needs to be added to a large amount of substances, then they must first be thoroughly mixed with one of the ingredients or with an indifferent powdery substance. In some cases, substances that are part of the mixture in small quantities, it is better to dissolve in a small amount of solvent.

## ***2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).***

- *requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);*
- *questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.*

## **Tests**

### **1. Grinding machines are classified according to the method of grinding the material into:**

- A.** disc, ball, rotary machines;
- B.** disk, cutting, fine grinding machines;

- C. crushers for medium, fine, colloidal, fine grinding;
- D. cutting, grinding, crushing, impact, impact-centrifugal machines;
- E. grass cutters, root cutters.

**2. When determining the technological properties of powders, flowability is determined. What devices are used to determine this indicator?**

- A. vibrating watering can;
- B. disintegrator;
- C. dismembrator;
- D. set of sieves;
- E. friabilator.

**3. At pharmaceutical enterprises, in the production of powders, the operation of grinding medicinal substances is used. What machines are used for fine grinding of substances:**

- A. dismembrators;
- B. drum mills, vibrating mills;
- C. grass and root cutters;
- D. roll shredders;
- E. disintegrators.

**4. The pharmaceutical enterprise produces powders for various purposes. Specify the degree of grinding of the powders given in the DFU:**

- A. large, medium, thin;
- B. large, medium-large, medium-small, small, smaller, smallest;
- C. large, medium-large, medium-fine, smaller, colloidal;
- D. large, medium, small, colloidal;
- E. large, medium, small, smallest.

**5. Grinding equipment is classified by the method of grinding. What machines does a roller crusher include:**

- A. percussion;
- B. erasing;
- C. crushing;
- D. cutting;
- E. shock-centrifugal

**6. Mixers are used to obtain a homogeneous mixture of loose materials. Which faucets do not have rotating parts:**

- A. double-cone mixers;
- B. drum mixers;
- C. blade mixers;
- D. fluidized bed mixers;
- E. centrifugal mixers.

**7. Knowing which value allows you to predict the standard sizes of tablets, to correctly choose the amount of pressing pressure for obtaining tablets.**



- A Flowability of the substance;
- B Bulk density,
- C Fractional composition,
- D Porosity,
- E -.

**8. The shape, size and nature of the surface of the powder particles are determined using...**

- A Microscope,
- B Dandruff,
- C Telescope,
- D Without devices,
- E -.

**9. The true density of the powder is determined using ....**

- A Volume meter,
- B Microscope,
- C pH meter,
- D spectrophotometer,
- E –

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

### 3.1. Tasks for fixing the material

<b>№№ c.e.</b>	<b>Mein Tasks</b>	<b>Instructions</b>	<b>Answers</b>
1	2	3	4
1.	What is shredding?	your answer	
2.	Name the main requirements when grinding a substance.	your answer	
3.	What equipment is used for the grinding process?	your answer	
4.	Describe the sieving process.	your answer	
5.	Name the main types and principle of operation of industrial sieves.	your answer	
6.	Describe the mixing process.	your answer	

7.	Name the main technological characteristics used in the mixing process.	your answer	
8.	Name the equipment used in the mixing process.	your answer	
9.	Describe the granulation process and stages	your answer	
10.	Name the main stages of pressing.	your answer	

### 3.2. Questions for self-control:

1. Methods of determining the size of particles of solid bodies.
2. Mechanical processes.
3. Shredding of solid materials.
4. Classification and sorting of materials.
5. Mixing solid materials.
6. Drum, screw and blade mixers.
7. Theoretical foundations of pressing.
8. Features of pressing and main stages.

### 4. Summing up.

### 5. List of recommended literature (main, additional, electronic information resources):

#### Basic literature:

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

#### Additional

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.

3. State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 1. -1128 p.
4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
5. History of medicine and pharmacy: teaching. manual for pharmacy students. education closing and pharmacy Faculty of Higher Education of the Ministry of Health of Ukraine / A. A. Kotvitska, V. V. Gorbanev, O. O. Surikov and others. – Kharkiv: National Institute of Economics and Technology: Golden Pages, 2016. – 168 p.
6. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N MOZU42 – 4.5: 2015 //Edited by Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. -109 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).

### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>
3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine <https://library.gov.ua/>
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbu.gov.ua/>
7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine](http://State%20Expert%20Center%20of%20the%20Ministry%20of%20Health%20of%20Ukraine) <https://www.dec.gov.ua/index.php/ua/>
8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen.

## Practical lesson No. 6

### Theme № 6 «Criteria and methods of evaluation of surfactants»

**Goal.** The formation of students' theoretical ideas about the use of surfactants in various industries and the production of medicinal forms. And also to form the skills of working with solutions of surfactants and the ability to obtain and analyze some physical and chemical characteristics of these solutions.

**Basic concepts.** *Surface-active substances (surfactants)* – are a huge group of substances that cause a decrease in surface tension at the interface of the phases of substances that do not dissolve in each other. Simply put, dirt is washed off thanks to surface-active substances.

*Cationic surfactants* - as detergents, are weaker than anionic surfactants and do not foam well. As active substances in the composition of foaming agents, they are practically not used, but the introduction of small amounts has a softening, antistatic and disinfecting effect. Used mainly in shampoos and shower gels.

*Amphoteric surfactants* - depending on the pH of the medium, manifest themselves either as cationic or anionic surfactants.

*Nonionic* - surfactants are the second most popular group of surfactants after anionic surfactants.

*Amphoteric surfactants* - depending on the pH of the medium, manifest themselves either as cationic or anionic surfactants.

**Equipment:** computer, multimedia equipment.

#### **Plan:**

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

Surface-active substances (surfactants) are a huge group of substances that cause a decrease in surface tension at the interface of the phases of substances that do not dissolve in each other. Simply put, dirt is washed off thanks to surface-active substances.

Classification of surfactants and their features

Anionic surfactants are the most widely used surfactants.

- o Advantages:
- o o low cost;
- o o good washing effect;
- o Disadvantages:
- o o the most aggressive towards the human body;
- o o sensitive to water hardness.

*Cationic surfactants* - as detergents, are weaker than anionic surfactants and do not foam well. As active substances in the composition of foaming agents, they are practically not used, but the introduction of small amounts has a softening, antistatic and disinfecting effect. Used mainly in shampoos and shower gels.

- o Advantages:
- o o have bactericidal properties;
- o o have a conditioning effect;
- o Disadvantages:
- o low functional properties.

*Nonionic surfactants* are the second most popular group of surfactants after anionic surfactants.

- o Advantages:
- o o good effect on fabric;
- o o positive effect on hair structure;
- o o high cleaning effect;
- o o stabilize the foam.
- o Disadvantages:
- o high cost.

*Amphoteric surfactants* - depending on the pH of the medium, manifest themselves either as cationic or anionic surfactants.

- o Advantages:
- o o the safest of surfactants.
- o Disadvantages:
- o o high cost;
- o stability in hard water

## ***2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).***

*- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);*

*- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.*

### **Tests**

#### **1. A characteristic feature of the structure of the surfactant molecule is:**

- A presence of hydrophilic and oleophilic parts,
- B the presence of two hydrophilic parts,
- C the presence of three oleophilic parts,
- D the presence of four carbon atoms.
- E -.

#### **2. Anionic surfactants dissociate in water with the formation of surface-active...**

- A anion,
- B cation,
- C of the hydrophilic part,

D of the oleophilic part.

**3. Cationic surfactants dissociate in water with the formation of surface-active...**

A cation,

B anion,

C carboxyl group,

D amino group.

E -.

**4. Which surfactant does not dissociate into ions in solutions:**

A non-ionic,

B ampholyte,

C cationic,

D anionic.

**5. A heterogeneous mixture of substances consisting of at least two phases that have a highly developed separation surface, chemically do not interact with each other and differ in almost complete mutual insolubility is called....**

A dispersed system,

B emulsion,

C solution,

D suspension.

E-.

**6. Lyophilic systems are characterized by:**

A The equilibrium distribution of particles by size,

B Equilibrium concentration,

C Relative density,

D Raw material moisture,

E Fractional composition.

**7. The ability of some compounds to exhibit both hydrophilic and hydrophobic properties due to the presence of charged or polar and non-polar parts in their molecules is called...**

A Amphiphilicity;

B Density,

C Lipophilicity,

D Porosity,

E -.

**8. Disadvantages of neurogenic surfactants include...**

A decomposition due to the presence of an aromatic radical in their composition,

B long-term storage,

C canning,

D destruction within the first two hours,

E -.

**9. The main distinguishing feature of colloidal surfactants is the ability to....**

A to form thermodynamically stable (lyophilic) heterogeneous dispersed systems,

B form non-stable dispersed systems,

**C** to form insoluble complexes,

**D** change for a long time.

**E** -

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

**3.1. Tasks for fixing the material**

<b>№№ п.п.</b>	<b>Mein Tasks</b>	<b>Instructions</b>	<b>Answers</b>
1	2	3	4
1.	Why surface energy and surface tension arise..	your answer	
2.	What is the structure of surfactant molecules?	your answer	
3.	How to explain that surface tension decreases with increasing temperature?	your answer	
4.	Give the classification of surfactants.	your answer	
5.	Give qualitative reactions to the main types of surfactants.	your answer	
6.	What substances are classified as anionic surfactants?	your answer	
7.	What substances are classified as cationic surfactants?	your answer	
8.	What substances are classified as amphoteric surfactants?	your answer	
9.	What substances are classified as nonionic surfactants?	your answer	

**3.2. Questions for self-control:**

1. Lyophilic and lyophobic dispersed systems.
2. Criterion for the formation of lyophilic dispersed systems.
3. Amphiphilic properties of surfactant molecules (surfactants).

4. Principles of classification of South Africa. Surface tension and adsorption of surfactants at different interphase boundaries.
5. Self-organizing structures based on surfactants: surface films, micelles, liquid crystal structures.
6. The role of surfactants in improving or worsening wetting and spreading.
7. Impact of surfactants on the environment and people.
8. Environmental protection as an incentive to search for new safe surfactants.

#### **4. Summing up.**

#### **5. List of recommended literature (main, additional, electronic information resources):**

##### **Basic literature:**

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
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##### **Additional**

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
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4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
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7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/](http://StateExpertCenteroftheMinistryofHealthofUkrainehttps://www.dec.gov.ua/index.php/ua/)
8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen.

## Practical lesson No. 7

### Theme № 7. "Classification of emulsifiers. Properties of surfactants (surfactants). Classification of surfatants and their purpose."

**Goal.** The formation of students' theoretical knowledge about the physicochemical properties of emulsifiers, their structural formulas, the main requirements that emulsifiers must meet and their classification. To learn the physical and chemical properties of emulsifiers, their classification and main characteristics.

**Basic concepts.** *Surface-active substances (surfactants)* – are a huge group of substances that cause a decrease in surface tension at the interface of the phases of substances that do not dissolve in each other. Simply put, dirt is washed off thanks to surface-active substances.

*Solubilization* - is the improvement of solubility with the help of surfactants, which are able to convert poorly soluble or completely insoluble substances into transparent or, in extreme cases, into opalescent solutions without changing their chemical structure.

*Cationic emulsifiers* – are surfactants that form organic cations in an aqueous solution.

*Anionic emulsifiers* – are surfactants that are dissociated in an aqueous solution.

*Nonionic emulsifiers* – are surfactants that do not form ions in an aqueous environment, so they have certain advantages over ionic emulsifiers.

**Equipment:** computer, multimedia equipment.

#### Plan:

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

One of the most important components of dispersed systems of medicinal products are surfactants (surfactants). Due to their wide use, these means have remarkable preventive and curative properties and are in great demand among the population. Most of the creams for external use are created on the basis of emulsions. The use of emulsion forms is due to their specific properties, such as the ability to combine oil and water phases, the possibility of introducing various active components, as well as good consumer properties, such as moisturizing ability, easy absorption and easy application to the skin.

One of the most important components of dispersed systems of cosmetic preparations is surfactants (surfactants). They are unevenly distributed in the solution, and due to their amphiphilic (hydrophilic-hydrophobic) character, they are concentrated (adsorbed) on the surfaces of phase separation, forming adsorption layers. The result of this process is a decrease in interfacial tension. Surfactant molecules contain lipophilic (hydrophobic) and hydrophilic functional groups.

In principle, all emulsifiers can be considered surfactants.

Surfactants are emulsifiers that are used in the manufacture of pharmaceutical products and perform special tasks, therefore they must meet the following specific requirements:

- - toxicological safety;
  - - high biological degradation;
  - - confirmed compatibility with human skin and mucous membranes;
- guaranteed status of admission to use: having a passport and inclusion in the pharmacopoeia or registration in INCI and the like.

It is also advisable to fulfill a number of other conditions, such as multifunctionality (for example, obtaining an additional cosmetic effect), as well as to achieve such important advantages as the possibility of using an emulsifier in a low concentration, which leads to energy savings.

### ***Physico-chemical properties of surfactants and emulsifiers***

*Aggregation.* After reaching a certain concentration, surfactant molecules are able to form relatively large molecular aggregates - micelles. This concentration characteristic of each surfactant is called the critical micelle formation concentration (CMC). This process is reversed: when the solution is diluted with a solvent below the CCM, the surfactant micelles again break down into individual molecules (monomers). Thermodynamic equilibrium is established between monomers and micelles, and it does not matter where the surfactant monomer molecules are located - at the boundary of the phase separation or in the volume of the solution.

*Monomers* in the micelle are placed so that their hydrophobic groups are inside, they are not in direct contact with the solvent, and hydrophilic groups are distributed on the surface of the micelle and ensure their stability in solution

Micelles can have different shapes and sizes. The number of monomers in the micelle fluctuates around the average value characteristic of each surfactant. Nonionic, low molecular weight surfactants have an aggregation number of the order of 50–1000; and in anionic, cationic - charged ones, it is about 50. This is explained by the fact that the electrostatic repulsion between equally charged groups does not create conditions for further aggregation. In addition to spherical, thermodynamically stable forms of aggregation can also be called ellipsoids, paliceta, disk-shaped micelles. The macroscopic properties of solutions containing surfactants, especially their viscosity, depend on the size and shape of the aggregates. For many applications, especially in cosmetics, this is as important as the fact that molecules dispersed in solution have only a slight solubility or even no solubility at all. They can only be mounted inside the micelle and thereby transferred into the solution. This process is called solubilization, or colloidal solubility.

Solubilization should be understood as the improvement of solubility with the help of surfactants, which are able to convert poorly soluble or completely insoluble substances into transparent or, in the extreme case, into opalescent solutions without changing their chemical structure. For solubilization, mainly surfactants with a low value of CCM and so that they are indifferent to chemical interactions are used.

Emulsifiers with two long hydrocarbon chains in the process of their aggregation form another structure that distinguishes them from emulsifiers with one hydrocarbon radical. They spontaneously form multi-layered empty balls - vesicles.

Liposomes are spherical vesicles (25–5000 nm in diameter), the membranes of which consist of one or more double layers of amphiphilic lecithin molecules. At the same time, the lipophilic (hydrophobic) parts of the surfactant are always directed towards the middle of the double layer. If the vesicles form nonionic emulsifiers, they

are called niosomes. Thus, the inner core of liposomes and niosomes always forms a water phase.

Due to their characteristic structure, vesicles are potential delivery systems for hydrophilic systems and water in the stratum corneum or are carriers of lipophilic and amphiphilic molecules (in lipophilic membranes).

Classification of emulsifiers:

**Anionic** emulsifiers are dissociated in aqueous solution. The anion is responsible for the emulsifying effect, but the counterion also determines the technological properties. Fatty acid soap (C12–C18) is an important emulsifier in cosmetic products. Clarification: only water-soluble or colloiddally dispersed sodium, potassium, ammonium, or amine salts are called soaps, while water-insoluble calcium, magnesium, zinc, and aluminum salts are called metal soaps."

From a chemical point of view, soaps mean alkali metal salts of fatty acids, which are formed after the neutralization of fatty acids with alkali. The chemical structures of fatty acid soaps and sodium stearyl sulfate are shown in Fig. 17.

The use of sodium hydroxide solution gives mainly solid soaps, potassium hydroxide - from liquid to pasty. Due to their low viscosity, they are also called liquid soaps.

The cleansing action of amphiphilic salts of fatty acids consists in the fact that their solutions wet the surface of the skin, disperse, emulsify or solubilize particles of pollution stuck to the surface, and then transfer them into a solution.

**Cationic emulsifiers** form organic cations in an aqueous solution.

Due to their ionic character, they are very hydrophilic. Unlike anionic emulsifiers, they have strong preservative properties, so special attention should be paid to dermatological compatibility.

The use of cationic emulsifiers in emulsions is limited by their possible interaction with anionic compounds, and this can reduce their emulsifying ability. Emulsions based on cationic emulsifiers are easily destroyed on the skin, which is explained by a strong interaction with the skin surface. The high adsorption capacity is due to the electrostatic attraction between the opposite charges of the skin surface and the cation of the emulsifier. In this case, the hydrophobic residues of their molecule are directed to the outer side of the skin. As a result, a hydrophobized skin surface is formed; it seems elastic and soft.

**Ampholyte** emulsifiers combine both types of ions in one molecule. Their most important representatives are lecithins and phospholipids. Both of them belong to the group of phosphatides, because they consist of residues of phosphoric acid, fatty acids, alcohol and a nitrogenous component.

Lecithin is produced from egg yolks or from plants - soybeans. The composition of fatty acids it contains greatly affects its technological properties. Phospholipids as natural surfactants are able to stabilize emulsions of various types and can be auxiliary dispersants in suspensions. They are able to form vesicles in the form of liposomes, and in higher concentrations - lamellar liquid crystal phases. These phases are very stable and have sufficient variation in water and fat content. Recipes with lecithin differ from others in their special stability.

This makes it possible to formulate formulations of emulsions and creams, which, depending on the amount of water, will have a lipophilic or hydrophilic character. In

addition, phospholipids are non-toxic, do not cause allergies and irritation. The ability to bind and hold water can make them humectants.

*Nonionic emulsifiers* do not form ions in an aqueous environment, so they have certain advantages over ionic emulsifiers. Electrolytes do not affect their properties, and they behave too indifferently to chemical interactions in recipes. The simplest representatives of substances of this class are higher fatty alcohols, stearins and incomplete esters of fatty acids and polyatomic alcohols. All these substances have in common that the share of their hydrophilic groups in their molecules is very small (one or more hydroxyls), so they are lipophilic fat-soluble substances.

They have minor emulsifying properties and "work" as stabilizers and structure formers. They are used to improve the consistency of cosmetic products. Common commercial unsaturated glycerides are a mixture of mono- and diesters. Their interfacial activity depends on the length of the chain and the degree of saturation of the fatty acid. Unsaturated monoglycerides emulsify better than saturated ones.

## **2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).**

- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);

- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.

### **Tests**

#### **1. All surface-active substances are concentrated on the surfaces of phase separation, forming adsorption layers. What is it connected with?**

- A due to amphiphilic properties,
- B due to hydrophilic properties,
- C due to hydrophobic properties,
- D due to the absence of a lipophilic group,
- E -.

#### **2. Molecules of surface-active substances contain in their composition...**

- A lipophilic and hydrophilic functional groups.
- B exclusively only a lipophilic group.
- C exclusively hydrophilic group.
- D ten hydrophobic groups.

#### **3. Macroscopic properties of solutions containing surfactants, especially their viscosity, depends on the size and shape of the aggregates, their molecules are distributed in the solution, have only a slight solubility or even do not dissolve at all. This process is called...**

- A solubilization,
- B hydrophilicity,
- C lipophilicity,
- D amphiphilic properties.
- E -.

**4. For solubilization, mainly surfactants are used, indicators of the critical concentration of micelle formation, which have...**

- A low values,
- B high values,
- C presence of hygroscopicity and homogeneity of particles,
- D presence of good solubility and wettability.

**5. Which emulsifiers in the process of their aggregation form multi-layered empty balls - vesicles?**

- A with two long hydrocarbon chains,
- B with three short hydrocarbon chains,
- C with one long hydrocarbon chain,
- D with four short hydrocarbon chains.
- E-.

**6. Liposomes are spherical vesicles whose membranes consist of...**

- A of several double layers of amphiphilic lecithin molecules,
- B of several double layers of hydrophobic structures,
- C of one layer of lecithin,
- D three layers of fat,
- E fractional sklaud.

**7. What are the vesicles that form nonionic emulsifiers called?**

- A by niosomes;
- B polysomes,
- C trichosomes,
- D sometimes
- E -.

**8. The most important representatives of ampholytic emulsifiers are...**

- A lecithins and phospholipids,
- B fatty alcohols,
- C stearins and unsaturated fatty acid esters,
- D polyhydric alcohols,
- E -.

**9. Cationic emulsifiers form in an aqueous solution...**

- A organic cations,
- B organic anions,
- C salts,
- D alcohols,
- E -

**10. The use of cationic emulsifiers in emulsions is limited by their possible interaction with anionic compounds, and this can lead to ....**

- A decrease in their emulsifying ability,
- B increasing their emulsifying ability,
- C neutralization of their emulsifying ability,

D formation of salts.

E –

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

**3.1. Tasks for fixing the material**

№№ с.е.	Mein tasks	Instructions	Answers
1	2	3	4
1.	Define the concept of emulsifiers?	your answer	
2.	The main criteria of emulsifiers?	your answer	
3.	Physico-chemical properties of surfactants and emulsifiers.	your answer	
4.	Anionic emulsifiers.	your answer	
5.	Cationic emulsifiers.	your answer	
6.	Ampholytic emulsifiers.	your answer	
7.	Nonionic emulsifiers.	your answer	
8.	Polymeric emulsifiers.	your answer	
9.	Emulsions as liquid systems.	your answer	
10.	Surfactants (surfactants)	your answer	

**3.2. Questions for self-control:**

1. Surfactant emulsifiers used in the manufacture of dosage forms. Give examples.
2. Describe the physical and chemical properties of surfactants.
3. What is solubilization?
4. What is the significance of solubilization in the process of dissolving insoluble substances?
4. What are vesicular systems? Mesophases.
5. Name anionic emulsifiers. Examples.
6. Cationic and ampholyte emulsifiers. Lecithin. Appointment.
7. Describe nonionic emulsifiers. What is lanolin?

8. Nonionic emulsifiers based on sugars and polyglycerols. Give examples.
9. System of hydrophilic-lipophilic balance of nonionic surfactants.
10. Polymer emulsifiers. The principle of their action.
11. Surface-active substances in cosmetics, anionic surfactants. Give examples of their use.
12. Nonionic surfactants, amphoteric and cationic surfactants. The principle of their action and use.

#### **4. Summing up.**

#### **5. List of recommended literature (main, additional, electronic information resources):**

##### **Basic literature:**

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

##### **Additional**

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.
3. State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 1. -1128 p.
4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
5. History of medicine and pharmacy: teaching. manual for pharmacy students. education closing and pharmacy Faculty of Higher Education of the Ministry of Health of Ukraine / A. A. Kotvitska, V. V. Gorbanev, O. O. Surikov and others. – Kharkiv: National Institute of Economics and Technology: Golden Pages, 2016. – 168 p.



6. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N MOZU42 – 4.5: 2015 //Edited by Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. -109 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).

### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>
3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine <https://library.gov.ua/>
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbu.gov.ua/>
7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/](http://StateExpertCenteroftheMinistryofHealthofUkrainehttps://www.dec.gov.ua/index.php/ua/)
8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen.

## Practical lesson No. 8

### **Theme № 8. "Influence of HLB emulsifiers and production technology on quality parameters of emulsions. Types of emulsions. Types of instability of emulsions."**

**Goal.** The formation of students' theoretical knowledge about emulsifiers, the influence of the hydrophilic-lipophilic balance of emulsifiers on the technology of obtaining emulsions. Learn the physical and chemical properties of emulsifiers, types of emulsions and types of instability of emulsions.

**Basic concepts.** *Hydrophilic-lipophilic balance (HLB)* – is a number characterizing the effectiveness of the emulsifier. If the HLB number is within 3-6, a w/m emulsion is formed. Emulsifiers with a HLB number of 8-13 give an m/v emulsion. By changing the nature of the emulsifier and its concentration, it is possible to achieve phase reversal of the emulsion.

*Emulsions* – are typically lyophobic dispersed systems. The loss of their aggregative stability can be due to the processes of isothermal distillation or coagulation (coalescence of drops) and is usually accompanied by a loss of sedimentation stability (layering of the system). The time of existence of a certain volume of the emulsion until its complete delamination can be taken as a measure of the stability of the emulsion.

**Equipment:** computer, multimedia equipment.

#### **Plan:**

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

Surface-active substances, due to their wide use, have considerable preventive and curative properties and are in great demand in the manufacture of creams for external use based on emulsions. The use of emulsion forms is due to their specific properties, such as the ability to combine oil and water phases, the possibility of introducing various active components, as well as good consumer properties.

Along with the classification of emulsifiers according to their chemical structure, there were attempts to make a classification according to their technological properties. In practice, we have to decide which emulsifier is most suitable for the emulsion we need. In the so-called system of hydrophilic-lipophilic balance (HLB) according to Griffin, all nonionic surfactants are assigned numerical values from 1 to 20. HLB gives information about the size and strength of hydrophilic and lipophilic groups in an amphiphilic substance. Low numerical values are assigned to lipophilic compounds, and higher numerical values to hydrophilic emulsifiers.

For the HLB system, an equation was later developed, according to which the value of HLB can be approximately calculated based on the molecular weight of their hydrophobic part and the total weight of the emulsifier molecule.

HLB values are calculated based on the stoichiometric ratio of the lyophilic and hydrophilic parts of the molecule.

The relationship between the HLB value of some nonionic emulsifiers and their purpose is approximately as follows:

HLB 1–3 – as defoamers; HLB 3–8 – water-in-oil emulsifiers (cholesterol, cetaryl alcohol, lanolin alcohol, stearet-2, glyceryl stearate, sorbitan stearate);

HLB 7–9 – as winders; HLB 8–15 – as emulsifiers of the "oil in water" type (polysorbate-65, stearate-10, sucrose stearate, laureate-4, REG-8-stearate, sorbitan laurate);

HLB 13–15 – as part of detergents;

HLB 15–20 – solubilizers (polysorbate-80, PEG-150 laurate, PEG-30 glyceryl laurate, PEG-40 – hydrogenated castor oil).

But nonionic surfactants do not obey the above laws, so it is better to determine their HLB values experimentally; they can significantly exceed the upper limit (20) of the HLB scale.

The advantage of the HLB system for the mixture of emulsifiers is that the value of the mixture of emulsifiers is additively composed of the fractions of the components:

$HLB_{zag} = HLB_1x_1 + HLB_2x_2 + HLB_3x_3 + \dots$ , where  $x_1, x_2, x_3$  are mass fractions of individual components.

This additivity also applies to the required HLB values, which are determined only experimentally. The required value of HLB is understood as the numerical value that an emulsifier or a mixture of emulsifiers should have, so that the dispersed oil phase has both optimal distribution and optimal stability. Thus, the value of HLB is attributed not only to emulsifiers, but also to substances that are emulsified.

In general, the value of HLB is only an aid for evaluating the possibilities of using emulsifiers. The use of only one HLB concept sometimes does not apply to cases of incompatibility of formulation components with the emulsifying base.

The temperature of rotation is a feature of emulsions obtained with the help of nonionic emulsifiers. The conversion of a lipophilic emulsion (water-in-oil type) into a hydrophilic one (oil-in-water type) or vice versa is called phase rotation. Such a rotation is possible when the temperature changes. This is explained by the fact that ethoxylated nonionic emulsifiers change their hydrophilic-lipophilic properties, namely, the HLB value, depending on the temperature.

It can be said that the ability of hydrophilic nonionic surfactants to stabilize direct emulsions (o/w) decreases with increasing temperature, and at the end, at a certain temperature, the emulsion turns into the opposite type (w/o). This temperature is called the phase rotation temperature. In ethoxylates, the TOF correlates with the cloud point. The latter refers to the temperature above which an aqueous solution of nonionic surfactants becomes cloudy, loses solubility and separates into two non-viscous isotropic phases.

Phase inversion occurs when the water-soluble hydrate of the emulsifier splits off so much of its water of hydration that an oil-soluble emulsifier or oil-soluble hydrate is formed. Or vice versa, phase rotation occurs when an emulsifier dissolved in a non-aqueous medium forms a sufficiently water-soluble hydrate when water is added, and then the "water-in-oil" emulsion turns into an emulsion (o/w).

When the phases rotate, the interphase tension reaches a minimum, while the electrical conductivity also decreases sharply.

Emulsions are typically lyophobic dispersion systems. The loss of their aggregative stability can be due to the processes of isothermal distillation or coagulation (coalescence of drops) and is usually accompanied by a loss of sedimentation stability (layering of the system). The time of existence of a certain volume of the emulsion until its complete delamination can be taken as a measure of the stability of the emulsion.

The stability of the emulsion is increased by introducing a stabilizer (emulsifier) into the system, as electrolytes, surfactants, and high-molecular compounds can be used. Aggregative stability of emulsions is determined by the same factors that cause resistance to coagulation of other lyophobic dispersed systems.

Dilute emulsions can be quite stable in the presence of such weak emulsifiers as electrolytes. The stability of these emulsions is mainly due to the presence of a double electric layer on the particles of the dispersed phase. The stability of concentrated and highly concentrated emulsions in most cases is determined by the action of the structural-mechanical barrier during the formation of adsorption layers of the emulsifier. The formed interphase adsorption layers cause a smooth change in the properties of the transition zone at the boundary of the separation of two liquid phases, increasing the lyophilicity of the particles of the dispersed phase. The strongest stabilizing effect is created by high-molecular compounds and colloidal surfactants (soaps, nonionic surfactants), the adsorption layers of which have a gel structure and are highly hydrated.

The type of emulsion formed during mechanical dispersion largely depends on the ratio of the volumes of the phases. A liquid contained in a larger volume usually becomes a dispersion medium. When dispersing equal volumes of two liquids, emulsions of both types appear, and the one with higher aggregative stability is preserved and is determined by the nature of the emulsifier. A special case is the stabilization of emulsions with highly dispersed powders. Such stabilization is possible with limited selective wetting of powders (at the edge angle  $\theta$  is greater than  $0^\circ$ , but less than  $180^\circ$ ). At the same time, the powders better stabilize the phase that is less wet. Thus, hydrophilic chalk "armors" the oil phase and prevents oil droplets from coalescing in an aqueous dispersion medium.

## ***2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).***

*- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);*

*- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.*

## **Tests**

### **Tests**

#### **1. Which of the emulsifiers is the most optimal for the production of a direct emulsion?**

**A** potassium palmitate.

**B** In Kaolin.

**C** With Gelatin.

**D** Butanol.

**E** Plumbum oleate.

**2. What is the name of the process of spontaneous clumping of droplets in emulsions?**

- A Coalescence.
- B In Flocculation.
- C Sedimentation.
- D Flotation.
- E Coagulation.

**3. All surface-active substances are concentrated on the surfaces of phase separation, forming adsorption layers. What is it connected with?**

- A due to amphiphilic properties,
- B due to hydrophilic properties,
- C due to hydrophobic properties,
- D due to the absence of a lipophilic group,
- E -.

**4. For solubilization, mainly surfactants are used, indicators of the critical concentration of micelle formation, which have...**

- A low values,
- B high values,
- C presence of hygroscopicity and homogeneity of particles,
- D presence of good solubility and wettability.

**5. Which emulsifiers in the process of their aggregation form multi-layered empty balls - vesicles?**

- A with two long hydrocarbon chains,
- B with three short hydrocarbon chains,
- C with one long hydrocarbon chain,
- D with four short hydrocarbon chains.
- E-.

**6. Liposomes are spherical vesicles whose membranes consist of...**

- A of several double layers of amphiphilic lecithin molecules,
- B of several double layers of hydrophobic structures,
- C of one layer of lecithin,
- D three layers of fat,
- E fractional sklaud.

**7. What are the vesicles that form nonionic emulsifiers called?**

- A by niosomes;
- B polysomes,
- C trichosomes,
- D sometimes
- E -.

**8. The most important representatives of ampholytic emulsifiers are...**

- A lecithins and phospholipids,

- B fatty alcohols,
- C stearins and unsaturated fatty acid esters,
- D polyhydric alcohols,
- E -.

**9. Choose a substance that will optimally stabilize the type emulsion "oil-water":**

- A Casein,
- B Ethanol,
- C Benzene,
- D Potassium chloride.
- E -

**10. What amount (cm<sup>3</sup>) of toluene must be mixed with water containing sodium oleate to obtain 100 cm<sup>3</sup> of a concentrated emulsion?**

- A from 0.1 to 74.0 cm<sup>3</sup>
- B from 10.0 to 75.0 cm<sup>3</sup>
- C is more than 75.0 cm<sup>3</sup>
- D from 74.0 to 90.0 cm<sup>3</sup>
- E to 0.1 cm<sup>3</sup>

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tests, etc. (if necessary).

### 3.1. Tasks for fixing the material

<b>№№ c.e.</b>	<b>Mein Tasks</b>	<b>Instructions</b>	<b>Answers</b>
1	2	3	4
1.	Classification of emulsions.	your answer	
2.	Basic criteria of emulsifiers.	your answer	
3.	Physico-chemical properties of emulsifiers.	your answer	
4.	Application of emulsions.	your answer	
5.	Methods of obtaining emulsions.	your answer	
6.	Surfactants	your answer	
7.	Emulsions as liquid systems	your answer	
8.	Temperature of rotation in emulsions.	your answer	

9.	Types of emulsions.	your answer	
10.	Types of instability of emulsions.	your answer	

### 3.2. Questions for self-control:

1. What dispersed systems are called emulsions?
2. Can any liquids form an emulsion?
3. How are emulsions classified? Their practical application.
4. What substances are called emulsifiers?
5. How do emulsifiers stabilize emulsions?
6. Methods of obtaining emulsions.
7. What is the circulation of phases of emulsions? Under what conditions does it occur?
8. What are the methods of breaking emulsions? What are they based on?
9. Why does water poured into it not flow out of a sieve (diameter of holes 1 mm), covered with a thin layer of paraffin?
10. Nonionic surfactants, amphoteric and cationic surfactants. The principle of their action and use.

### 4. Summing up.

### 5. List of recommended literature (main, additional, electronic information resources):

#### Basic literature:

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

#### Additional

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.
2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.

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4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
5. History of medicine and pharmacy: teaching. manual for pharmacy students. education closing and pharmacy Faculty of Higher Education of the Ministry of Health of Ukraine / A. A. Kotvitska, V. V. Gorbanev, O. O. Surikov and others. – Kharkiv: National Institute of Economics and Technology: Golden Pages, 2016. – 168 p.
6. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N MOZU42 – 4.5: 2015 //Edited by Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. -109 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).

### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>
3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine <https://library.gov.ua/>
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbu.gov.ua/>
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8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen



## Practical lesson No. 9

### Theme № 9 "Rheological properties of ointment bases. Methods of determining rheological properties."

**Goal.** The formation of students of higher education theoretical foundations about the classification of ointment bases, their features in use and combination with pharmacologically active components. Familiarization with rheological methods of research of ointment bases. To learn the physical and chemical properties of active substances in the composition of soft dosage forms; requirements for ointment bases; principles of selection of bases for soft dosage forms.

#### **Basic concepts.**

*Hydrophilic-lipophilic balance (HLB)* – is a number characterizing the effectiveness of the emulsifier. If the HLB number is within 3-6, a w/m emulsion is formed. Emulsifiers with a HLB number of 8-13 give an m/v emulsion. By changing the nature of the emulsifier and its concentration, it is possible to achieve phase reversal of the emulsion.

*Emulsions* – are typically lyophobic dispersed systems. The loss of their aggregative stability can be due to the processes of isothermal distillation or coagulation (coalescence of drops) and is usually accompanied by a loss of sedimentation stability (layering of the system). The time of existence of a certain volume of the emulsion until its complete delamination can be taken as a measure of the stability of the emulsion.

**Equipment:** computer, multimedia equipment.

#### **Plan:**

**1. Organizational measures (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).**

In the production of soft pharmaceutical preparations, a large assortment of ointment bases is used, and to facilitate their selection, it is desirable to have a clear systematization. However, due to their different nature, chemical structure and diversity of influence on the properties of active pharmaceutical ingredients, and, therefore, the pharmacotherapeutic characteristics of drugs, different functional purposes in the production of drugs, as well as the absence of their production at enterprises of a single industry, their clear classification is difficult and is an urgent issue today

Ointment bases can be in the form of individual or a sum of various substances that determine the required volume, appropriate consistency and some specific features of the ointment. Due to its consistency, the base is an excellent lubricant for the skin, which makes it soft, smooth, elastic and protects it from drying out. Under the action of the base, the natural fatty protection of the skin is strengthened, cracks and sores heal faster, water evaporation decreases, due to which the stratum corneum swells and natural heat is retained, which achieves significant protection against humidity and

cold. The last circumstance is of significant importance for swimmers who are in the water during the competition. In addition, the foundations absorb external contamination of the skin well and facilitate its removal.

There are complex relationships between the medicinal substance and the base, which do not allow considering it as an inert carrier that does not take part in the action of the ointment. Ointment must be considered as a unity of form and content. The form must be active in terms of manifestation and disclosure of its content.

It has been proven that the same medicinal substance used in the form of an ointment can act completely differently depending not only on how it is introduced into the ointment, but also on what ointment base it is combined with. So, for example, many antibiotic ointments based on petroleum jelly are weakly active, but the same ointments prepared on a hydrophilized petroleum jelly-lanolin base have a more pronounced antibiotic effect. ;'

The choice of the ointment base depends on the physicochemical properties of the prescribed drugs and the nature of the ointment's action. The base, which would provide the maximum therapeutic effect of the ointment, must meet the following requirements:

- have a lubricating ability, that is, the necessary structural and mechanical (consistent) properties: viscosity, plasticity, fluidity, thixotropic, etc.;
- to perceive medicinal substances well, i.e. to have absorbent capacity;
- do not change under the influence of air, light, temperature fluctuations and do not react with medicinal substances introduced into it, i.e. have chemical resistance;
- to be pharmacologically indifferent, not to have an irritating and sensitizing effect, to help maintain the original pH value of the skin (3-4 units) or mucous membrane;
- not to be inseminated by microorganisms;
- should not stain clothes, not be too sticky, easily washed off with or without soap;
- the properties of the base must correspond to the purpose of the ointment: the bases of protective ointments used for preventive purposes must dry quickly and adhere tightly to the surface of the skin; bases for surface-acting ointments should not be absorbed; bases for ointments with a resorptive effect should, on the contrary, penetrate deeply into the skin, reach the bloodstream and promote the absorption of medicinal substances.

However, there are no ointment bases that fully meet these requirements. Therefore, to obtain the necessary quality of the base, mixtures of different substances are often used (complex ointment bases).

*Classification of bases.* Substances used as bases for ointments differ in their sources of production, chemical composition, physicochemical properties, etc. This is reflected in the classification of bases given in various training manuals, textbooks, reviews and articles. A significant disadvantage of many proposed classifications is that they mix the bases for ointments with their individual components.

Depending on the sources of production, ointment bases and their components are divided into *natural and artificial*. The last group includes bases, which are various synthetic or semi-synthetic substances or their mixtures both with each other and with natural substances.

Based on their chemical composition, bases are divided into *glycerol esters with higher fatty acids, esters of these acids with high molecular weight monoatomic alcohols, high molecular weight hydrocarbons and their amines, inorganic compounds, polysaccharides, etc.*

Classification should be based on the most characteristic feature, which allows combining substances into a single, organically connected group. Such a characteristic feature of all substances or compositions of bases is their ability to interact with water. According to the intensity of interaction with water, all bases are divided into three groups: *hydrophobic, hydrophilic and diphilic*. This classification is considered the most rational.

Classification of methods of measuring rheological characteristics.

The first method - the constant shear rate method - is usually implemented by using an electromechanical or hydraulic drive. At the same time, the resistance of the medium is measured by various dynamometers.

The second method - Constant load method or - Structurally, it is much simpler, since the speed of movement or rotation of the measuring body is easy to measure with an ordinary stopwatch or recorded on a chart tape.

With the third measurement method, the constant load force is due to the constant mass of the moving part of the device. The measurement time is usually constant (180 - 300 s) and is taken slightly longer than the relaxation period. The devices measure the depth of immersion in the material of the indenter of a special shape as the speed decreases, which in the limit reaches zero.

The fourth method allows you to determine the deformation energy based on the area of the diagram obtained in "force - displacement" coordinates, and the ordinate on the diagram shows the effort. In addition, in devices of this group, energy can be calculated by power, if the device is equipped with a self-recorder or shows a wattmeter or counter.

According to M. P. Volarovich's classification, rheological research methods and devices can be divided into integral ones, which make it possible to determine the total effect of the flow, and differential ones, which allow direct observation of the deformation over time at each point of the dispersed system during its course.

Differential methods make it possible to observe changes in the field of stresses and deformations over time when studying complex cases of the course of structured systems. At the same time, observations can be made visually, as well as with the help of fluoroscopy, microcinema, etc. Differential methods allow obtaining only a qualitative characteristic of the phenomenon under study. For example, when studying the flow of a viscoplastic material in the gap between two cylinders, M. P. Volarovich and his colleagues applied aluminum powder to the surface of the material before the study. During deformation (during rotation of the inner cylinder), two zones are clearly defined on the surface of the material: a) Zone of plastic flow; b) Zone of the elastic state.

Integral methods allow observing the total effect of the flow. Depending on the research conditions, the number of independent characteristics of the mechanical properties of the studied system, necessary for solving the task, is determined in each individual case using model analysis. The most advanced are the methods of capillary and rotational viscometry, introduction of a cone, longitudinal displacement of the plate, as well as ball viscometers.

**2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary).**

- requirements for students' theoretical readiness to perform practical classes (knowledge requirements, list of didactic units);
- questions (test tasks, problems, clinical situations) to check basic knowledge on the subject of the lesson.

### **Tests**

**1. Ointments are made on both hydrophobic and hydrophilic bases. Indicate which of the foundations prevents skin contact with air and is difficult to wash off with water:**

- A. Pork fat
- B. Methylcellulose
- C. Propylene glycol
- D. Polyethylene glycol
- E. Glycerin

**2. To make a cream of surface action, you need to take the following ointment base....**

- A. Vaseline
- B. Lanolin
- C. Bason of Kutumova
- D. Gelatin-glycerin base
- E. Polyethylene oxide base

**3. Glycerin is added to the composition of hydrophilic bases for the purpose of:**

- A. Reduction of desiccation
- B. Ensuring microbiological purity
- C. Providing a cooling effect
- D. Increase in viscosity
- E. Ensuring high stability

**4. Glycerin esters with higher fatty acids, esters of these acids with high-molecular monoatomic alcohols, high-molecular hydrocarbons and their amines, inorganic compounds, polysaccharides - these are all classifications of ointment bases according to:**

- A chemical composition,
- B source of receipt,
- C physical and chemical properties,
- D presence of good solubility and wettability.

**5. Depending on the sources of production, ointment bases and their components are divided into:**

- A natural and artificial,
- B synthetic,
- C natural and semi-synthetic,
- D oily.

E-.

**6. The constant shear rate method is usually implemented by applying:**

- A electromechanical or hydraulic drive,
- B as the speed of movement or rotation of the measuring body,
- C load due to the constant mass of the moving part of the device,
- D slow rotation of the measuring body,
- E -

**7. According to the classification of M. P. Volarovich, integral rheological research methods make it possible to determine...**

- A is the total effect of the flow;
- B Bulk density,
- C Fractional composition,
- D Porosity,
- E -.

**8. Differential rheological methods of research, according to the classification by M. P. Volarovich, allow you to directly observe:**

- A deformation in time at each point of the dispersed system during its course,
- B percentage ratio of humidity to true density,
- C deformation of the density before grinding,
- D is the percentage ratio of bulk density to concentration.
- E –

**3. Formation of professional abilities and skills (mastery of skills, curation, determination of treatment regimen, laboratory research, etc.):**

- content of tasks (tasks, clinical situations, etc.);
- recommendations (instructions) for performing tasks (professional algorithms, orienting maps for the formation of practical skills and abilities, etc.);
- requirements for work results, incl. to registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary).

### 3.1. Tasks for fixing the material

<b>№№ c.e.</b>	<b>Mein tasks</b>	<b>Instructions</b>	<b>Answers</b>
1	2	3	4
1.	Classification of ointment bases.	your answer	
2.	Basic requirements for ointment bases.	your answer	
3.	Natural ointment bases.	your answer	
4.	Artificial ointment bases.	your answer	
5.	<i>Glycerol esters with higher fatty acids.</i>	your answer	

6.	<i>Fatty acid esters with high molecular monoatomic alcohols.</i>	your answer	
7.	<i>High molecular weight hydrocarbons and their amines.</i>	your answer	
8.	<i>Inorganic compounds, polysaccharides.</i>	your answer	
9.	Basic methods of research of rheological characteristics.	your answer	
10.	Differential methods of research of rheological characteristics.	your answer	

### 3.2. Questions for self-control:

1. Classification of bases for ointments and requirements for them.
2. Principles of selection of ointment bases.
3. Characteristics of hydrophobic ointment bases.
4. Characteristics of hydrophilic ointment bases.
5. Name representatives of hydrophobic and hydrophilic ointment bases.
6. Characteristics of diphylous bases for ointments and emulsifiers used for their preparation.
7. Representatives of diphylic bases.
8. Classification of methods for measuring rheological characteristics.

### 4. Summing up.

### 5. List of recommended literature (main, additional, electronic information resources):

#### Basic literature:

1. Gladukh E.V. Theoretical foundations of pharmaceutical technology. Study guide for extracurricular independent work / E.V. Gladukh, I.V. Saiko, A.A. Sichkar, D.P. Soldatov. Kh.: NFaU, 2016. - 202 p.
2. Technology of drugs of industrial production (vol. 2 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2013. - 638 p.
3. Technology of drugs of industrial production (vol. 1 of 2). Chuyeshov V. I., Gladukh E. V., Saiko I. V., Lyapunova O. O., Sichkar A. A., Krutskikh T. V., Ruban O. A. Kh.: National University of Applied Sciences; Golden Pages, 2012. - 694 p.

#### Additional

1. Technological equipment of the pharmaceutical and biotechnological industry: tutorial. for university students education closing III-IV accreditation level / M.V. Stasevych and others; 2nd ed., revision. and added – Lviv: Novy svit-2000, 2018. – 410 p.

2. Yarnykh, T. G. Extemporaneous formulation (technology, analysis, application): method. rec. / T. G. Yarnykh, Fr. I. Tikhonov, I. S. Hryshchenko and others. - Kh., 2015. -379 p.
3. State Pharmacopoeia of Ukraine / State enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products" - 2nd edition. - Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeia Center for the Quality of Medicinal Products", 2015. - Vol. 1. -1128 p.
4. Extraction of plant raw materials: training. Guide / Yu. I. Sidorov, I. I. Gubytska, R. T. Konechna, V. P. Novikov. – Lviv: View of the National Lviv Polytechnic University, 2018. - 336 p.
5. History of medicine and pharmacy: teaching. manual for pharmacy students. education closing and pharmacy Faculty of Higher Education of the Ministry of Health of Ukraine / A. A. Kotvitska, V. V. Gorbaney, O. O. Surikov and others. – Kharkiv: National Institute of Economics and Technology: Golden Pages, 2016. – 168 p.
6. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of non-sterile medicinal products in pharmacies" ST-N MOZU42 – 4.5: 2015 //Edited by Prof. O.I. Tikhonov and Prof. T.G. Jarnih - Kyiv, 2015. -109 p. (Approved by order of the Ministry of Health of Ukraine No. 398 dated 07/01/2015).

### **Electronic information resources**

1. Ministry of Health of Ukraine <http://moz.gov.ua>
2. «State Register of Medicinal Products of Ukraine" - Access mode: <https://moz.gov.ua/derzhavnij-reestr-likarskih-zasobiv-ukraini>
3. State Formulary of Medicinal Products 12th issue, 2020: – Access mode: <https://www.dec.gov.ua/materials/chinnij-vipusk-derzhavnogo-formulyara-likarskih-zasobiv/>
4. State Expert Center of the Ministry of Health of Ukraine <http://https://www.dec.gov.ua/>
5. National Scientific Medical Library of Ukraine [https:// library.gov.ua/](https://library.gov.ua/)
6. National Library of Ukraine named after V.I. Vernadskyi <http://www.nbu.gov.ua/>
7. Legislation of Ukraine [Electronic resource]. - Access mode: [http:// State Expert Center of the Ministry of Health of Ukraine https://www.dec.gov.ua/index.php/ua/](http://StateExpertCenteroftheMinistryofHealthofUkrainehttps://www.dec.gov.ua/index.php/ua/)
8. Compendium online – <https://compendium.com.ua/uk/>
9. News of medicine and pharmacy: Postgraduate education online [Electronic resource]. – Access mode: <http://www.mif-ua.com/education/symposiums> - Name from the screen