MINISTRY OF HEALTH OF UKRAINE
ZAPORIZHZHIA STATE MEDICAL AND PHARMACEUTICAL UNIVERSITY
DEPARTMENT OF MEDICINES TECHNOLOGY

THE TECHNOLOGY OF MEDICATIONS

GENERAL ISSUES OF MEDICINES MANUFACTURING. PRODUCTION OF WATER SOLUTIONS AND GALENICALS

Manual to practical classes
for pharmaceutical students 4-d year study
specialty 226 “Pharmacy”

Second edition, revised and enlarged

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P56

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P56 General issues of medicines manufacturing. Production of water solutions and galenicals: Manual to practical classes in technology of medications for pharmaceutical students 4-d year study speciality 226 “Pharmacy”. Second edition, revised and enlarged / Burlaka B.S., Gladyshev V.V., Nagorniy V.V., Puchkan L.O.,Gladysheva S.A. – Zaporizhzhia, 2024. – 107 p.

Based on the requirements of the Technology of Medications Work Program, this book presents the main theoretical issues and provides practical tasks for compounding of medicines – galenical, extracts, syrups and etc. The book contributes to the students comprehension and visualization of Pharmaceutical Compounding and is designed in a clear scheme.

Заснований на вимогах робочої програми з технології ліків, цей посібник представляє основні теоретичні питання та практичні завдання стосовно промислового виготовлення сиропів, настоянок, особливостей екстракції. Складений за прозорою схемою, посібник сприяє розумінню та уявленню студентами промислового виготовлення ліків.

SAFETY RULES

• Laboratory coats and caps provide an important barrier for your clothes and, more important, your skin from chemicals. The laboratory coat should fit comfortably, have long sleeves, and should be clean.

• The coats, backpacks, etc., should not be left on the lab benches and table.

• Eating, drinking, and smoking are strictly prohibited in the laboratory.

• Long hair must be tied back when using open flames.

• Learn where the safety and first-aid equipment is located. This includes fire extinguishers, fire blankets, and eye-wash stations.

• Always wash your hands before leaving the lab.

• Inform the teacher immediately in case of an accident.

ORGANIZATION AND METHODOLOGY OF PRACTICAL TRAINING

Practical sessions are conducted within the educational laboratories of the pharmaceutical technology and industrial medicine course. These labs are equipped with apparatus for simulating the manufacturing process of medicines closely mirroring real-world industrial conditions. Students are required to wear white lab coats, along with hats or headscarves, and appropriate footwear. Each student is assigned an individual workstation. Adhering to strict personal hygiene and safety rules is imperative when working in the laboratory. Student protocols are designated to oversee orderliness and ensure compliance with safety protocols.

Methods for conducting practical exercises involve assessing students' initial knowledge levels through technical instructional objectives and testing. The teacher engages the entire academic group in discussing key lesson topics both from their seats and at the blackboard, incorporating visual aids like graphs, tables, diagrams, and slides. The lessons delves into common equipment and potential challenges that may arise during the technological process of producing dosage forms. Practical tasks are executed based on the teacher's instructions.

Progress reports on the work conducted are presented to the teacher in the form of structured protocols (lab reports) and manufactured medications. The testing methodology encompasses several steps. Following the provided prescription, the student drafts a technological plan for drug production and rationalizes the appropriate equipment for the process. Utilizing the technological parameters furnished by the teacher, the student calculates the working formulation of the drug. If needed, the formulation is standardized, accounting for the quality parameters specified by the teacher.

Lesson No1

Topic: Manufacturing process. Material balance. Crushing, grinding. Machines and apparatus

Didactic goals and motivation of the lesson: to become familiar with the methodology of conducting laboratory sessions in the pharmaceutical manufacturing course, to comprehend safety instructions, to grasp the layout of technological production protocols, to acquire proficiency in creating material balances, and to tackle contextual challenges. Gain an understanding of the composition of machinery and equipment used for grinding and sieving.

THEORETICAL QUESTIONS

1. General technological concepts in the factory production of finished medicines.
2. Technological regulations and its components.
3. Material balance, types, characteristics. Material losses.
5. Basic concepts about machines, apparatuses, mechanisms.
6. Heat exchangers.
7. Physical and mechanical bases of mixing. Grinding hypothesis. Grinding work. Crushing rules.
8. Classification of machines and mechanisms. Requirements for them.
9. Machines for medium and fine grinding. Device, principle of operation.
10. Impact shredders - hammer mills, disintegrators, dismembrators.
11. Cutting machines. Grass and root cutters.
12. Shock-abrasive shredders. Vibratory Mills, Ball Mills.
13. Fine grinding machines. Device, principle of operation. Jet mills. Colloidal mills.
14. Sieve separation of materials. Types of sieves, design, principle of operation.

METHODOLOGY OF PRACTICAL WORK

Students and teacher discuss the methodology of conducting laboratory classes on the course, studying safety instructions, an example of a stage-by-stage material balance, situational tasks N 1-5 and corresponding educational drawings are considered. Consideration of educational issues No. 5 and No. 6 is carried out on the basis of samples of machines, assemblies and apparatuses of educational laboratories, diagrams, drawings, photo albums and slides.

Then teams of students conduct a technological analysis of medicinal plant materials, using 100 g of material. The following parameters are defined:

a) Characteristics of external signs of plant materials: Make a conclusion about their compliance with the standards.

b) Fractional composition: A sample of medicinal plant raw materials (100.0 g) is crushed on a grinding machine and sifted through a set of five sequentially assembled sieves (hole diameter 10, 7, 4.5, 1, 0.5 mm).

A sample of crushed material is placed on the largest (upper) sieve and the entire set of sieves is shaken by hand for 5 minutes. Each sieve is then shaken over a sheet of smooth paper. The rest of the material on the sieve is weighed. The results of the sieve analysis are entered into the table, and the "+" sign indicates the fraction remaining on this sieve, and the "-" sign passed through the sieve. The content of fractions of different sizes is expressed as a percentage of the mass of the material.

Name of medicinal plant (raw materials)	Material fraction, %						
	+ 10	-10+7	-7+4.5	-4,5+1	-1+0.5	-0,5	V
							100%

Next, students make a stage-by-stage material balance. Methods and results of research are drawn up in the student's protocols.

PRACTICAL TASKS

1. Calculate K_{cons}. for the production of 5% powder with amikazole (amikazole - 5 hours, talcum powder - 95 hours). 202 kg of raw materials were used to manufacture 200 kg of the product.

Answer: 1.01

2. Find a way out, waste and K_{cons}. for the industrial production of Karlovy Vary salt (sodium sulfate anhydrous - 44 parts, sodium bicarbonate - 36 parts, sodium chloride - 18 parts, potassium sulfate - 2 parts). The amount of raw materials was 30 kg, 29.96 kg were obtained after sieving, and 29.6 kg after mixing.

Answer: 98.67%; 1,33%; 1,014

3. Make a final material balance, find a way out, waste and K_{cons}. For the production of powder "Galmanin" (salicylic acid - 2 parts, zinc oxide - 10 parts, starch and talc equally 44 parts). The amount of raw materials is 50 kg. Losses after 1st mixing - 0.1 kg, after sieving - 0.45 kg and after final mixing, the losses were 0.08 kg.

Answer: 98.74%; 1,26%; 1,013

4. For the production of 108 kg of boric acid tablets of 1.0 g each, 110 kg of boric acid was consumed. Calculate output, spending, and K_{cons}.

Answer: 98.18%; 1,82%; 1,018

5. For manufacturing 100 kg of 1% salicylic alcohol (70% alcohol - 99 parts, salicylic acid - 1 part), 99.9 kg of alcohol (70%) and salicylic acid - 1.01 kg were consumed.

Answer: 99.09%; 0,91%; 1,009

AN EXAMPLE OF SOLVING TASK NO. 3

1. What is the total material loss?

$G_5 = 0,1+0,45+0,08 = 0,63$

2. How many kg of finished product is obtained?

$G_2=G_1-G_5=50-0.63=49.37$ kg

3. What is the yield of the finished product?

$\eta = G_2 : G_1 \bullet 100 = 49,37 : 50 \bullet 100 = 98,74\%$

4. What is the cost of spending?

$E = G_5 : G_1 \bullet 100 = 0,63 : 50 \bullet 100 = 1,26\%$

5. What is K_{cons} equal to?

$K_{cons} = G_1 : G_2 = 50 : 49,37 = 1,01$

SOME THEORETICAL ISSUES

Pharmaceutical technology encompasses the theoretical principles and processes involved in transforming medicinal substances into pharmaceuticals. It constitutes a segment of pharmaceutical science, a comprehensive system of scientific knowledge that encompasses drug properties, production, and analysis.

Industrial production is characterized by large-scale mechanized operations. Pharmaceuticals produced on an industrial scale must demonstrate stability and durability to ensure prolonged storage. The principal objectives of pharmaceutical technology include:

- Formulating the foundational techniques and methodologies for manufacturing novel medicinal substances.
- Enhancing existing medications.
- Exploring, researching, and integrating new additives in pharmaceutical production.
- Investigating the stability and determining the shelf life of drugs, preparations, intermediates, and other products.
- Evaluating the efficacy of the technological processes.

Pharmaceutical companies(drug-producing): 1) are organized on a modular basis; 2) the division of labor is widely used.

The technological process is a sequential chain of its individual stages, which, in turn, consist of separate operations.

All processes within pharmaceutical technology can be categorized into the following groups:

Mechanical Processes: This group encompasses actions such as substance movement, dosing, pressing, and other related activities.

Hydromechanical Processes: These processes occur during the manipulation of liquids, gases, emulsions, and suspensions. Examples include liquid sedimentation, centrifugation, and the removal of dust from gases.

Thermal Processes: These processes involve the transfer of heat between different bodies. They include actions like heating, cooling, and transformations associated with changes in the substance's state of aggregation, such as evaporation, condensation, and drying.

Mass Transfer Processes (Diffusion Processes): This category covers procedures like extraction, rectification, and distillation that involve the movement of mass or substances.

Chemical Processes: These processes pertain to the chemical alterations of materials being processed, following the principles of chemical interaction. This involves the creation of new compounds through chemical reactions such as oxidation, reduction, and neutralization. According to the method of organization, the main processes are divided into:

1) periodic;
2) continuous;
3) combined.

Technological regulation is a governing document that outlines the methods, technical tools, norms, and standards for the preparation of pharmaceuticals.

*A technological nor*m establishes the permissible upper and/or lower limits for technologically relevant parameters in the production process. Deviations from these norms can result in reduced yield or lower product quality (defects).

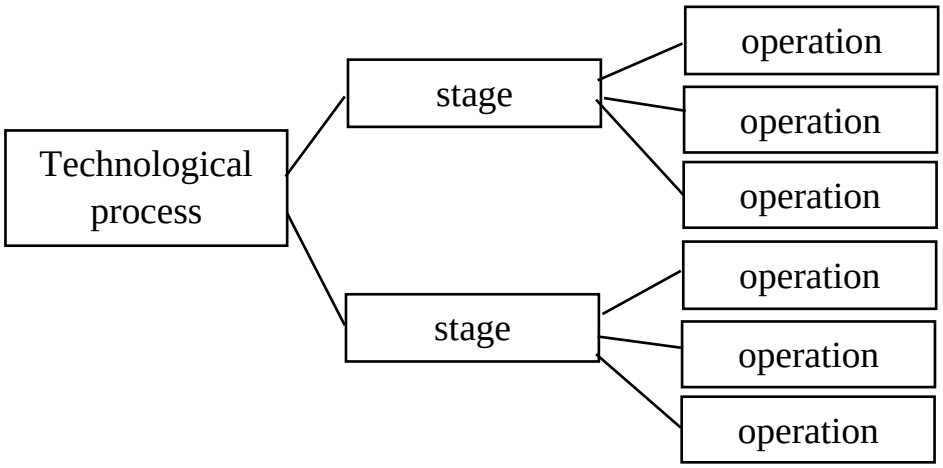
Technical means refer to the collection of production equipment required for executing the technological process.

A technological operation constitutes a segment within a technological process stage. It is necessary to carry out specific tasks and/or maintain particular types of equipment, such as condensation, filtration, drying, packaging, and more.

A stage in the technological process denotes a grouping of technological operations or a portion of the overall process that leads to the creation of an intermediate or final product.

The technological process entails deliberate actions aimed at altering and/or defining the state of the work subject.

Regulated time signifies the duration required for an operation or an element of an operation. This time is dictated by the technological process and must be strictly adhered to. It remains consistent regardless of the production scale; for instance, it applies to the duration of exposure at a specific temperature.



Img 1. Structure of technological process, stages and operations

Material balance — the ratio between the amount of raw materials, materials, intermediates and intermediates used in production, and the quantity of actually obtained finished products, by-products, waste and losses, that is, the ratio of theoretically possible and practically obtained yield of finished products.

This ratio is illustrated by the material balance equation, which has the form:

$$G1 = (G2 + G3 + G4) + G5,$$

where: G1 is the amount of feedstock; G2 — quantity of finished products; G3 – number of co-products; G4 — amount of waste; G5 — number of losses.

The material balance serves as the foundation for production regulations and facilitates the assessment of the organization level of the technological process. It enables the comparison of the process effectiveness across various industries producing identical products. The material balance reflects the refinement of the technological process, making it of significant practical importance.

The material balance is constructed based on experiments conducted per unit of output, production flow, or the overall production capacity. In the case of new productions, it's established according to the project, while for existing industries, it's derived from performance indicators achieved in the year preceding the approval of the regulations. Revision occurs only when operations or stages impacting raw material consumption or waste are introduced or excluded from the technological process.

Material balance can take the form of either an algebraic equation or tables depicting material receipts and expenditures. This approach is characteristic of technological regulations for production. The income section of the balance specifies the quantity of materials introduced into production, while the expenditure portion details the quantity of materials obtained and any losses incurred. Consequently, the income and expenditure components of the balance should be equal.

Through the material balance, crucial technical and economic production indicators are computed, including the regulated rates of raw material, material, intermediate, and energy resource consumption per unit of pharmaceutical product.

Product Yield (η) refers to the percentage comparison between the quantity of the finalized product and the quantity of initial materials used, expressed as a percentage.:

$$\eta = \frac{G_2}{G_1} * 100\%$$

where:

G_2 – quantity of the finished product

G_1 - the amount of starting materials

Technological consumption(waste) (E) is defined as the proportion of irrecoverable losses divided by the quantity of raw materials, expressed as a percentage.

$$E = \frac{G_5}{G_1} * 100\%$$

Where:

G5 – irrecoverable losses

G_1 - the amount of starting materials

If there is waste in production:

$$E = \frac{G_5}{G_1 - (G_3 + G_4)} * 100\%$$

Where:

G5 – irrecoverable losses

G_1 - the amount of starting materials

G3 – number of co-products

G4 — amount of waste

The consumption coefficient (K_{cons}) is determined by dividing the mass of the raw materials used by the mass of the obtained finished product. The consumption coefficient is always greater than one and is calculated with a precision of 0.001.

$$\text{Kcons} = \frac{G_1}{G_2}$$

or

$$\text{Kcons} = \frac{G_1 - (G_3 + G_4)}{G_2}$$

Where:

G_1 - the amount of starting materials

G_2 – quantity of the finished product

G3 – number of co-products

G4 — amount of waste

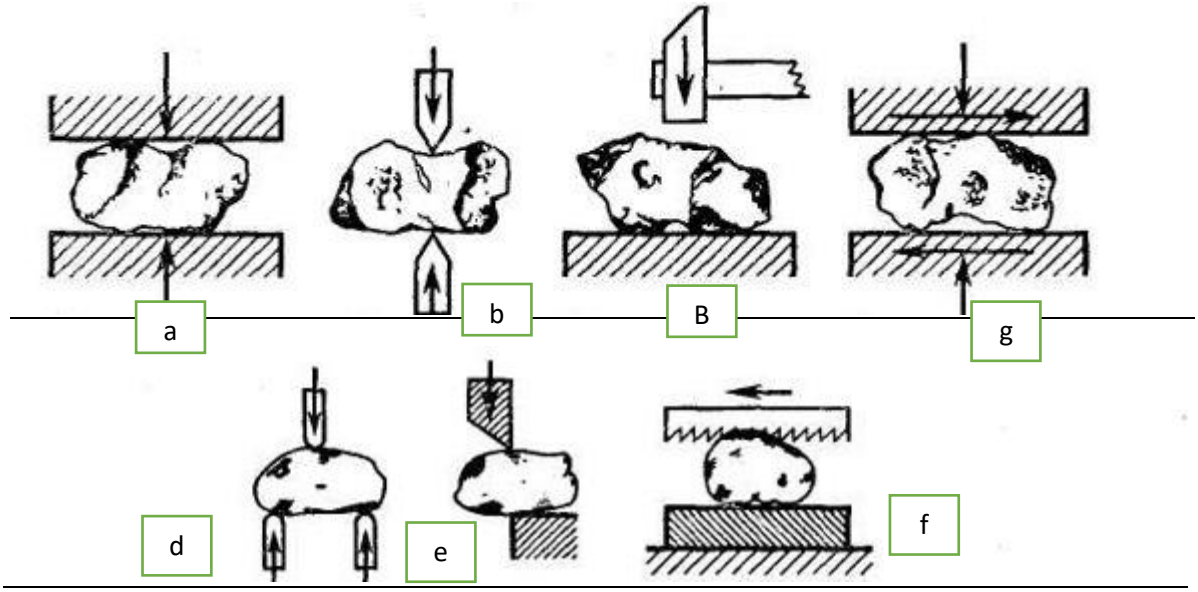
$$N_{cons.} = K_{cons.} * n$$

Consumption norm is consumption coefficient on the number of parts according to the composition.

Grinding is the procedure of diminishing the particle size of a substance through mechanical means. Grinding is performed to attain powders, including plant powders, which are directly used in pharmaceutical formulations. In such cases, this process (grinding + sieve classification + mixing) constitutes a pivotal step.

Grinding is also undertaken to enhance the efficiency of various technological processes like extraction, dissolution, and granulation. Enhanced grinding of materials facilitates the acceleration of these technological procedures.

The grinding of materials involves techniques such as crushing, splitting, breaking, sawing, rubbing, impacting, and cutting.



Img 2. Type of grinding of materials (images.google.com)

a - crush; b - splitting; B - blow; g - abrasion; d - breaking; e - cutting; f - sawing.

Grinding is executed by the application of external forces.

Crushed materials can be categorized into three major groups:

1. Amorphous materials (such as resins, solid fats, and polymeric substances).
2. Crystalline substances.
3. Materials with a cellular structure (including plant and animal raw materials).

Classification of machines is based on the extent of grinding:

1. Machines for coarse (2-6 degree of dispersion) and intermediate (6-10 degree of dispersion) grinding.
2. Machines for intermediate and fine crushing (10-50 degree of grinding).
3. Fine grinding machines (50-100 degrees of grinding).
4. Machines for ultra-fine grinding (100-10000 degree of grinding).

There are three primary methods for classifying (sifting) crushed products:

1. *Sieve Classification***:** Involves the use of sieves and sieve mechanisms to separate particles based on size.
2. *Pneumatic Classification***:** Utilizes air separation, capitalizing on the varying settling rates of particles of different sizes in air due to centrifugal forces and gravity.
3. *Hydraulic Classification***:** Involves processes like silting and settling.

In the pharmaceutical industry, the first two methods are commonly employed: sieve classification and pneumatic classification.

Sieves can be categorized into three major groups:

1. Woven or mesh sieves.
2. Stamped sieves.
3. Perforated grate or slotted sieves.

Img. 3 Example of Sieves (images.google.com)

Sieve efficiency is measured in terms of the quantity of material (in tons/hour or kg/hour) obtained from 1 m2 of the sieve's working surface. This metric is influenced by several factors that impact the effectiveness and productivity of sifting materials through sieves:

1. *Shape and Size of Holes:* The shape and size of the holes on the sieve's working surface are crucial. They must be chosen to match the shape and size of the particles of the specific material being sifted.

2. *Thickness of Sifted Layer:* The thickness of the layer being sifted is significant. In cases of a thick layer, small particles at the top may not pass through the holes because of the layer's thickness.

3. *Path Length:* A longer path along the sieve's working surface increases the likelihood of small particles entering the holes, leading to a more effective screening process.

4. *Material Advancement Speed:* The speed at which the material advances is important. If the movement is too fast, particles might pass over the holes. It's crucial to determine the optimal pace for maximum sieve performance.

5. *Material Agitation:* Gentle and controlled sliding of material on the working surface can cause small particles to accumulate in upper layers and miss contact with the holes, leading them to be discarded as waste. Periodic agitation is necessary to ensure that upper layers shift to the lower ones.

6. *Moisture Content:* Wet material with small particles can adhere to larger particles, forming lumps that aren't screened out and remain on the sieve. Excessively wet powder can also block the holes on the sieve's working surface, preventing finer particles from passing through.

TEST QUESTIONS

Questions contain five answers and only one correct answer (example with an asterisk).

1. Which of the following best describes the primary objective of pharmaceutical technology?

a) To increase drug sales and marketing

b) To develop new chemical entities

c) To formulate techniques for manufacturing novel medicinal substances*

d) To conduct clinical trials

e) To regulate drug pricing

2. In the context of pharmaceutical manufacturing processes, which category encompasses procedures such as extraction, rectification, and distillation?

a) Mechanical processes

b) Hydromechanical processes

c) Thermal processes

d) Mass transfer processes*

e) Chemical processes

3. What does the term "technological norm" refer to in pharmaceutical production?

a) The average production output

b) The permissible limits for technologically relevant parameters*

c) The standard operating procedures

d) The quality control guidelines

e) The regulatory compliance standards

4. How is the material balance equation represented in pharmaceutical technology?

a) G1 = (G2 + G3 + G4) + G5

b) G1 = (G2 + G3 + G4) - G5

c) G1 = (G2 - G3 - G4) + G5

d) G1 = (G2 × G3 × G4) ÷ G5

e) G1 = (G2 + G3) - (G4 + G5)

5. Which of the following correctly defines the product yield (η) in pharmaceutical production?

a) The ratio of finished product to raw materials, expressed as a percentage

b) The ratio of raw materials to finished product, expressed as a percentage

c) The difference between raw materials and finished product

d) The sum of finished product and raw materials

e) The product of finished product and raw materials, divided by 100

6. What is the primary purpose of grinding in pharmaceutical technology?

a) To increase the particle size of substances

b) To enhance the chemical reactivity of materials

c) To diminish the particle size of substances through mechanical means

d) To improve the color of pharmaceutical products

e) To increase the moisture content of materials

7. Which of the following is NOT a method for classifying crushed products in pharmaceutical technology?

a) Sieve classification

b) Pneumatic classification

c) Hydraulic classification

d) Magnetic classification

e) All of the above are methods for classifying crushed products

8. How is the consumption coefficient (Kcons) calculated in pharmaceutical production?

a) By dividing the mass of the finished product by the mass of the raw materials used

b) By dividing the mass of the raw materials used by the mass of the obtained finished product

c) By multiplying the mass of the raw materials by the mass of the finished product

d) By subtracting the mass of the finished product from the mass of the raw materials

e) By adding the mass of the raw materials to the mass of the finished product

9. Which factor does NOT influence the efficiency of sieve classification in pharmaceutical grinding processes?

a) Shape and size of sieve holes

b) Thickness of sifted layer

c) Material advancement speed

d) Material agitation

e) Particle density*

10. What is the primary purpose of the material balance in pharmaceutical production?

a) To calculate the profit margin of the product

b) To determine the environmental impact of production

c) To serve as the foundation for production regulations and assess process effectiveness

d) To establish the marketing strategy for the product

e) To determine the shelf life of the finished product

Lesson No2

Topic: Water solutions. Syrups. Aromatic waters. Production and standardization

Didactic goals and motivation of the lesson: The objectives of this lesson are to gain a theoretical understanding of the topic and to become familiar with the structure and operation principles of machinery and equipment used for dissolving substances and separating solid and liquid phases. Additionally, we will learn how to prepare aqueous solutions, including liquids, flavoring and medicinal syrups, and standardize them. We will also study the technological production process, the impact of technological factors on the quality of water, alcohol, glycerin, oil solutions, syrups, and aromatic waters. Understanding their nomenclature, composition, properties, and applications will also be a key focus, as well as the ability to solve situational problems.

THEORETICAL QUESTIONS

1. Solutions as a dosage form, theoretical features of dissolution. Technological factors influencing dissolution. Nomenclature, characterization and standardization of aqueous, alcoholic, glycerin and oil solutions.

2. Definition, characterization and classification of syrups.

3. Methods of mixing liquids (mechanical, pneumatic, gravitational, acoustic, circulation). Types of agitators.

4. Separation of liquid heterogeneous systems (sedimentation, decantation, centrifugation). Factors influencing the process. Apparatus.

5. Filtering. Requirements for filter partitions. Groups of filter partitions and their characteristics. Materials and mechanisms: nutsch, druk and frame filter presses.

6. Centrifugation. Types of centrifuges, devices and rules of operation.

7. Pressing. Types of presses. Device, factors that determine the force of pressing.

8. Features of the technology of preparation, analysis and storage of corrective syrups.

9. Features of the technology of preparation, analysis and storage of medicinal syrups (licorice, marshmallow, holosas, pertussine, bronholitin, etc.)

10. Aromatic waters. Methods of production, equipment used.

11. Solving situational problems.

METHODOLOGY OF PRACTICAL WORK

After reviewing the study questions, students prepare sugar syrup. Using refractometric analysis, the sugar concentration is adjusted to 64±1.0%, filtered through cheesecloth and packaged in vials. One of the medicinal syrups is prepared on this syrup. Independent work of students involves the compilation of a nomenclature list of aqueous, alcoholic, glycerin and oil solutions, medicinal syrups and aromatic waters, using NSPh 1 ed. and reference literature: solving situational problems on the topic: analysis of equipment for mixing, centrifugation, pressing on slides, drawings and photographs; individual interview on the theoretical material of independently studied topics and the solution of situational problems.

PRACTICAL TASKS

1. When diluting 25.2% hydrochloric acid, an excess of water was mistakenly added, resulting in 33.8 litres of a 7.1% solution. How many litres of concentrated acid should be added to obtain diluted hydrochloric acid (8.3%) and how much of the product will be obtained?

Answer: 2.4 l; 36.2 litres

2. Calculate the number of kg of ammonia solution with a density of 0.9229 and water required to obtain 50 kg of pharmacopoeial solution (10%).

Answer: 25.0 kg + 25.0 kg

3. How many liters of water will need to be added to 30 kg of glycerin with a density of 1.2559 to obtain a drug of pharmacopoeial dignity (90%) with a density of 1.2347?

Answer: 2,667

4. In what weight quantities should solutions of syrup be mixed with densities ρa - 1.4450 and ρc - 1.1250 to obtain 50 kg of the drug with a density ρv - 1.2300?

Answer: 19.27 kg; 30.73 kg

5. What amount of Burov's liquid (ρ - 1.0480) will be obtained by mixing 12 liters of basic aluminum acetate, the density of which ρc is 1.0300, with a similar solution with a density ρa -1.0560?

Answer: 39.0

6. What is the concentration of ammonia if the hydrometer reading at a temperature of + 18 ° C is 0.915? Answer: 22.745%

7. The pharmacy prepared 15 liters of calcium chloride solution 9.5%. To bring the concentration to 10.0%, it is necessary to use a 93% solution. How much of it will be required and how much product will be obtained?

Answer: 0.09 l; 15.09

8. 62.4 liters of sugar syrup ρ = 1.342 were prepared. How much water should be added to bring it to the standard (ρ=1.312).

Answer: 6.0 L

9. There are two semi-finished products of sugar syrup - 20 liters with ρ = 1.331 and 10 liters with ρ = 1.300. How much finished product will be obtained by combining these semi-finished products and bringing the mixture to the standard (ρ = 1.311). How much water will be used?

Answer: 30,932 liters; 0,932 l

10. 50 kg of 61% sugar syrup was obtained. How many kg of sugar should be added to bring the concentration to 64% and how many kg of syrup will be obtained in the end (Krash.. - 1,000)?

Answer: 4,167 kg; 54,167 kg

11. As a result of production, 50 kg of sugar syrup with ρ= 1.325 was obtained. How many kg will the pharmacopeial product be obtained after bringing it to the standard (ρ-1.311)?

Answer: 51,699 kg

12. Refractometric analysis showed a sugar content of 65.6% in the syrup. How much water should be added to 32 kg of such syrup to bring it to 64%?

Answer: 0.8 L

13. How much sugar should be taken to make raspberry syrup from 19 kg of juice prepared for this purpose? Answer: 31.0 kg

14. What amount (kg) of 96% alcohol should be added to the mixture 61.5 kg of sugar syrup, 9 kg of liquid thyme extract in the production of perptussine. How many kg of product should be obtained provided that there are no material losses?

Answer: 3.75 kg; 75 kg

An example of solving problem No. 4.

1. Drawing up a "mixing rule" and converting volumetric units into weight units:

ρ_a 1,445 — 0,105 L ● 1,445 = 0,15172 kg

$\rho_в$1,230

ρ_c 1,125 — 0,215 L ● 1,125 = 0,24188 kg

0,320 L ● 1,230 = 0,39360 kg

2. How much syrup of high density will be required to obtain 50 kg of a standard product?

0,15172 – 0,39360 kg

x - 50,0 kg — *x* = 19,27 kg

3. How many kg of a solution of syrup with a low density will be required to prepare a given amount of product?

0,24188 – 0,39360

y - 50,0 кг — *y* = 30,73 kg

An example of solving problem No. 5.

1. Drawing up a "confusion rule":

ρ_a 1,056		V_a 0,018 L
	$\rho_в$1,048	
ρ_c 1,030		V_c 0,008 L
		V_b 0,026 L

2. How much of the finished product will be obtained as a result of "strengthening" 12 litres of "weak" solution?

0,008 L - 0,026 L

12 L - x,

x=(12 ● 0,026):0,008 = 39,0 L

An example of solving the problem 6.

1. Determine the correction factor of the density of the solution (a) by interpolation.

ρ_t	ά
0,9200	0,00050
0,915	$ά_1$
0,9100	0,0056

$ά_1$ = 0,00053

2. What is the density of the test solution at +20°C? $\rho_{20}= \rho_t + a ● (t-20)$;

ρ_{20}=0,915+0,00053 ● (18-20)=0,91384

3. What is the nominal concentration of ammonia solution (interpolation method)?

ρ_{20}	C, %
ρ_1 =0,9164	C1= 0,00050
ρ_x = 0,91394	C_x
ρ_2 = 0,9131	C2= 0,0056

$$Cx = \frac{C2(\rho_x - \rho_1) - C1(\rho_x - \rho_2)}{\rho_2 - \rho_1}$$

0,0033 - - 1%

0,00084 - x1 = -0,255

x = 23 + (-0,255) = 22,745%

SOME THEORETICAL ISSUES

The primary step in the creation of solutions, drops, and syrups involves dissolving medicinal and excipient substances in a solvent. This process takes place in reactors equipped with continuous agitation. Dosage forms containing a liquid dispersion medium are generally prepared using the mass volumetric method, unless the solvents used have a higher specific gravity, are viscous, or are volatile.

Liquid dosage forms are categorized as dispersed systems, wherein substances (solid, liquid, or gaseous) are distributed within a liquid dispersion phase. Depending on the dispersed phase, liquid dosage forms can be classified into:

- Homogeneous forms (true solutions, high-molecular substance solutions).
- Heterogeneous forms (colloidal solutions, suspensions, emulsions).
- Combined systems in the form of aqueous, alcohol-water, or other extracts derived from medicinal raw materials of plant, animal, and mineral origin.

The nature of the bond between dispersed phase particles leads to the distinction between lyophilic dispersed systems, marked by intense interaction with developed solvate layers, and lyophobic systems, where such interaction is weak or absent.

The rate of dissolution can be manipulated by adjusting different process parameters. For instance, to enhance the dissolution rate, we can modify the temperature, increase the concentration gradient, decrease viscosity and boundary diffusion layer thickness by altering hydrodynamic conditions, and increase the contact surface area by grinding the feedstock, among other methods.

As defined by the National Standard of Pharmacy (NSPh), liquid dosage forms contains:

- Oral liquid medications (pharmaceutical solutions, syrups, suspensions, emulsions).
- Parenteral medications (injectables, infusions, concentrates).
- Ocular dosage forms (eye drops, sprays, lotions, contact lens liquids).
- Nasal agents (nasal washes, drops, liquid aerosols).
- Ear products (ear washes, drops, aerosols).
- Pressure-based formulations (aerosols, sprays).
- Medical foams.
- Liquid extraction preparations (tinctures, liquid extracts).

Dissolution is an inherent diffusion-kinetic process that occurs spontaneously when a solute comes into contact with a solvent. The solubility of a substance is the maximum amount of it that can saturate 100 grams of the solvent, expressed in grams.

Solvents can be categorized as:

- Polar solvents: water, acids, lower alcohols, glycols, amines.
- Non-polar solvents: hydrocarbons, haloalkanes.

Various methods are employed for mixing substances:

- *Mechanical Mixing:* Achieved through mixers of various designs, suitable for liquid and bulk mixtures. They are categorized based on rotation speed: low-speed (0.2-1.5 rpm) and high-speed (2.0-30 rpm) mixers.
- *Circulating Mixing:* Involves repeated pumping of liquid through apparatus using pumps or nozzles.
- *Pneumatic Mixing:* Utilizes compressed air or gas with pulsators or bubblers, often in pipelines.
- *Acoustic Mixing:* Employs ultrasonic generators, causing cavitation and mechanical impact on the solid phase, expediting dissolution.

Blade types differentiate mixers:

- *Paddle Mixers***:** Suitable for low-viscosity liquids (up to 0.1 Pa•s).
- *Anchor Mixers:* Used for thick and viscous liquids.
- *Planetary Mixers:* Feature central and side blades connected to a main transmission system. Side blades rotate around their axis while orbiting the central blade, suitable for thorough mixing of viscous liquids.
- *Propeller Mixers:* Equipped with helical curved blades that start with an angle of inclination around 45° at the shaft hub and gradually increase to around 90° at the blade end.

Filtration involves using porous partitions to allow liquid passage while retaining solid particles. Filter devices are categorized as either periodic or continuous.

- *Nutsch Filters:* Convenient when obtaining impurity-free precipitates. Unsuitable for mucous sediments and ether/alcohol extracts due to rapid evaporation under high vacuum.
- *Druk Filters:* Suitable for low-boiling organic solvents like alcohol and ether. Also effective for filtering viscous liquids.
- *Filter Presses:* Offer high filtering capacity and performance, producing well-clarified liquids and washed sediments.

Centrifugation is the separation or filtration process using centrifugal forces, which surpass gravity and pressure in effectiveness.

The removal of mechanical impurities from homogeneous systems typically involves filtration using porous barriers that enable the passage of liquid while capturing solid particles. The pressure differential on either side of the filter barrier drives the filtration process, corresponding to the resistance faced by the filtrate flow as it navigates the resulting sludge layer and the filter barrier.

Syrups are dense, transparent liquids that contain one or more active ingredients dissolved in concentrated aqueous solutions of sucrose or other sugars. Depending on their composition, syrups have a distinctive taste and aroma.

Syrups are classified into two types: flavoring and medicinal. Flavouring syrups serve to improve the taste of active ingredients. This category includes sugar syrup, along with all fruit and berry syrups. Sugar syrup is also utilized in tablet production as a binding agent for granulate preparation.

Img. 4. Sirup Sugar mixing equipment (images.google.com)

The high sugar concentration (about 64%) creates high osmotic pressure in syrups, preventing the growth of microorganisms, causing them to dehydrate and die.

For individuals with diabetes, syrups are formulated without sucrose and instead contain ingredients such as sodium cyclamate, sorbitol, xylitol, and other substitutes. In terms of appearance and taste, a 70% aqueous solution of D-sorbitol closely resembles sugar syrup.

The production of sugar syrup involves several specific steps. To produce 100 kg of syrup, 64 kg of sugar is placed into a reactor and lightly dampened with water. After 30 minutes, the sugar becomes less compact and dissolves more readily. The remaining water (36 liters for 64 kg of sugar) is then added, and steam is introduced to raise the mixture's temperature to 60-70 °C while continuously stirring. Once the sugar is fully dissolved, the syrup is boiled twice, and any resulting foam (composed of protein and mucous substances) is carefully removed. The syrup cooking process is relatively short, typically taking around 35-40 minutes for the sugar to completely dissolve and 20-25 minutes for the two boilings. This method helps to prevent sugar from caramelizing, which could change the syrup's colour and increase the amount of reducing substances, ultimately affecting the syrup's stability during storage. Sugar syrup appears as a clear, colourless, or slightly yellow thick liquid with a sweet taste, no discernible odour, and neutral pH. Its density typically falls within the range of 1.308-1.315, and its refractive index ranges from 1.451-1.454.

The method of extracting essential oils is contingent on two primary factors: the quantity of ether oils present and the susceptibility of those oils to heat (thermolability).

If a plant contains a substantial amount of oil, a mechanical approach, known as the pressing method, is employed.

When there is a sizable amount of oil, and it is resistant to heat, distillation techniques are used, such as:

- Distillation with water.
- Steam distillation.

- Distillation with water vapor under elevated pressure.
- Distillation with water vapor under reduced pressure.

For oils containing thermolabile components that are prone to degradation, the following methods are used:

a) Extraction with low-boiling solvents (e.g., ethyl ether, methylene chloride, petroleum ether, acetone).

b) Extraction with liquefied gases (propane, butane, carbon dioxide).

c) Extraction with fats (maceration of flower raw materials with fatty oils, with or without heating).

Thermolabile oils can also be extracted using absorption methods, which encompass:

- Enfleurage: Essential oil is absorbed by solid high-quality fats from freshly harvested raw materials, primarily flowers.
- Dynamic Sorption: Oils are absorbed by sorbents like activated carbon and silica gel.

The outcomes of these extraction processes are referred to as:

- Essential Oils (for methods like distillation and pressing).
- Extraction Essential Oils (for the extraction method using solvents or gases).
- Floral Lipsticks (for the extraction method using fats).

Medicinal syrups

Marshmallow syrup, also known as Sirupus Althaea, is a thick, transparent liquid with a yellowish color, a faint specific smell, and a sweet taste. It is used as an expectorant. Each 100 ml of the syrup contains 0.15 g of dry marshmallow root (4:1) in terms of polysaccharides, along with nipagin, nipazole, ethyl alcohol, sugar, and purified water as excipients.

The technology for preparing marshmallow syrup involves infusing 4 parts of crushed root in 50 parts of water and 1 part of 90% alcohol for 4 hours to preserve it. The extract is then filtered without squeezing the stem. Next, 36 parts of the filtrate are heated, and 64 parts of sugar are dissolved in it. The solution is boiled,

the foam is skimmed off, and then it's evaporated until 95 parts of syrup are obtained. Finally, 5 parts of alcohol are added to the cooled syrup as a preservative.

TEST QUESTIONS

Questions contain five answers and only one correct answer (example with an asterisk).

1. Which of the following is not a category of liquid dosage forms according to the nature of their dispersed system?

a) Homogeneous forms

b) Heterogeneous forms

c) Combined systems

d) Emulsified forms*

e) True solutions

2. What is the primary factor that prevents microbial growth in syrups?

a) Low pH

b) High osmotic pressure*

c) Presence of alcohol

d) Low temperature

e) Addition of preservatives

3. In the production of sugar syrup, what is the approximate sugar concentration used to create high osmotic pressure?

a) 45%

b) 54%

c) 64%*

d) 74%

e) 84%

4. Which of the following methods is not mentioned as a technique for extracting essential oils from plants?

a) Pressing method

b) Distillation with water

c) Extraction with low-boiling solvents

d) Enfleurage

e) Hydrolysis

5. What is the primary purpose of boiling sugar syrup twice during its production?

a) To increase sugar concentration

b) To remove protein and mucous substances

c) To caramelize the sugar

d) To increase the syrup's density

e) To adjust the pH

6. Which of the following is not listed as a type of mixer used in pharmaceutical liquid preparations?

a) Paddle mixers

b) Anchor mixers

c) Planetary mixers

d) Propeller mixers

e) Ribbon mixers*

7. What is the density range typically observed for sugar syrup according to the text?

a) 1.108-1.115

b) 1.208-1.215

c) 1.308-1.315

d) 1.408-1.415

e) 1.508-1.515

8. In the context of liquid dosage forms, what does the term "lyophilic dispersed systems" refer to?

a) Systems with weak interaction between dispersed phase and solvent

b) Systems with intense interaction and developed solvate layers

c) Systems with no interaction between dispersed phase and solvent

d) Systems with only gaseous dispersed phases

e) Systems with only solid dispersed phases

9. What is the primary active ingredient in Marshmallow syrup (Sirupus Althaea)?

a) Sucrose

b) Ethyl alcohol

c) Nipagin

d) Polysaccharides from marshmallow root

e) Nipazole

10. Which of the following methods is not mentioned as a way to enhance the dissolution rate of substances in liquid preparations?

a) Increasing temperature

b) Decreasing viscosity

c) Increasing the contact surface area by grinding

d) Increasing the concentration gradient

e) Adding surfactants

Lesson No3

Topic: Subtest. Seminar

Didactic goals and motivation of the lesson:

consolidate theoretical knowledge on the topic. Be able to perform calculations for the dilution and strengthening of aqueous solutions, acids, bases, glycerol using density tables, equations and using the mixing rule ("asterisks"). 3 Nomenclature of alcohol, oil and glycerin solutions of factory production.

THEORETICAL QUESTIONS

1.Classification of solutions. Dissolution as a diffuse-kinetic process. Ways to intensify the dissolution process.

2. Mixing. Types of mixers. Methods of mixing. Apparatus.

3. Separation of liquid heterogeneous systems.

3.1. Settling and decanting; factors influencing the process. Apparatus.

3.2. Filtering. Materials and mechanisms. Filters operating under the pressure of a liquid column; filters operating under vacuum; Pressurized filters.

4. Centrifugation. Types of centrifuges, device and rules of operation.

5. Pressing. Types of presses. Device, factors that determine the force of pressing.

6. Clarification. Adsorbents. Device for settling liquids.

7. Features of the technology of solutions of water, alcohol and oil.

8. Standardization of solutions. Dilution by weight, by volume, by density. Strengthening solutions.

9. Syrups. Classification, composition and features of the preparation of corrective medicinal syrups.

10. Essential oils. Methods of production, equipment. Obtaining aromatic waters by dissolving essential oils and by distillation with water vapor.

11. Solving situational problems.

PRACTICAL TASKS

1. How much solution of hydrochloric acid A% and water will be required to obtain M kg of acid B%?

A%	M	B%	Responses:
25	4		1,33 kg; 2,7 kg
28	7	15	3,75 kg: ,1.25 kg

2. How much hydrochloric acid A% and C% will be required to obtain M kg of acid B%?

A%	C%	M	B%	Responses:
20	3	5	10	2,059 kg; 2,941 kg
25	2	2	18	1,39 kg; 0.61 kg

3. How much hydrochloric acid A% and C% will be required to obtain M kg of acid B%?

B%	M	A%	Responses:
25	4	37	5,92 kg
12	7	22	12,83 kg

4. How much A% hydrochloric acid will be required to strengthen V L of hydrochloric acid C% to get B% acid?

A%	V	C%	B%	Responses:
20	1	5	8	0,256 kg
24	1,5	11	16	0,987 kg

5. How much solution of hydrochloric acid A% and water will be required to obtain V L of hydrochloric acid B%?

A%	B%	V	Responses:
18	8	1	0,461 kg; 0,576 L
25	10	3	1,257 kg; 1,885 kg

6. How much water and solution A will be required, the density of which is ρ at temperature T, to prepare M kg of B% solution?

p	T°	M	B%	Responses:
A - NaOH				
1,400	21	3	12	0,92 kg; 2,028 kg
A - KOH				
1,350	25	25	25	36,14%; 7,71 kg; 17,29 kg
A - HNO,				
1,250	17	12	10	40,12%; 9,01 kg; 2,99 kg
A - NH_3,				
0,910	18	3	15	24,39%; 1,845 kg; 1,155 kg

7. How much water should be added to V l of solution A, the density of which is ρ at a temperature of T°, in order to prepare a B% solution?

V	ρ	T°	B%	Responses:
A- CH_3COOH				
2	1, 030	19	20	22,53%; 0,2605 kg
A- NaOH				
0,2	1,300	23	20	27.58%: 0,987 kg
A - HNO_3,				
3	1,320	19	40	51.47%: 1,134 kg
A - NH_3,				
7	0,910	22	20	23,66%; 1,1671 kg

8. How much water should be added to M kg of solution A, the density of which is ρ at T ° , in order to prepare a B% solution?

M	ρ	T°	B%	Responses:
A- CH_3COOH				
5	1,060	22	30	55.771%; ; 4,295 kg
A - -NaOH				
4	1,420	19	20	38,92%; 3,784 kg
A - NH_3,				
10	0,900	21	15	27,13%; 8.087 kg
A - HNO_3,				
40	1,300	19	20	48.21%; 56,47 kg

9. How much water and glycerol with a density of ρ1 will be required to obtain an M kg of glycerol with a density of ρ2?

ρ_1	M	ρ_2	Responses:
1,2025	5	1,0780	2,949 kg; 2,051 kg
1,1533	4	1,0995	1,333 kg; 2,667 kg

10. How much glycerol with a density of ρ1 and glycerol with a density of ρ3 is required to obtain M kg of glycerol with a density of ρ2?

ρ_1	ρ_2	M	ρ_3,	Responses:
1,2508	1,0221	3	1,0995	1,046 kg; 1,95 kg
1,1944	1,0125	4	1,1263	2,551 kg; 1,449 kg

11. How much water will be required to dilute M kg of A% sugar syrup to a standard concentration of 64%?

M	A %	Responses:
1,7	67	0,0796 kg
3,0	66,5	0,117 kg

Lesson No4

Topic: Tinctures. Production and standardization

Didactic goals and motivation of the lesson:

To successfully complete this lesson, students must demonstrate a comprehensive understanding of the theoretical foundations of the extraction process. This involves expanding their knowledge of nomenclature, composition, types of packaging, methods of storage and use of tinctures, as well as understanding the structure and operating principles of relevant machinery and apparatus. Furthermore, students will need to adeptly solve situational problems related to tincture production and solidify their grasp of the physicochemical and technological properties of ethanol.

THEORETICAL QUESTIONS

1. Characteristics of tinctures. Requirements of the State Pharmacopoeia of Ukraine for tinctures.

2. Theoretical foundations of extraction. Molecular and convective diffusion, their quantitative characteristics

3. Physics and mechanics of the process of extracting active substances from the cell (swelling, desorption, dissolution, diffusion, dialysis, osmosis). Factors influencing the process of extraction of plant raw materials (concentration difference, time, temperature, surfactant, etc.).

4. Stages of the extraction process and their characteristics (capillary impregnation, formation of primary juice, mass transfer).

5. Extraction methods (maceration and its modifications; turboextraction, extraction with RPA, extraction with ultrasound, extraction with electric discharges; remaceration, percolation, dissolution. Comparative characteristics of methods in the production of tinctures.

METHODOLOGY OF PRACTICAL WORK

During two lessons, each student will prepare and standardize two tinctures using both maceration and percolation methods. In the first lesson, students will address educational matters, review safety guidelines, determine the initial alcohol concentration, perform necessary calculations, and prepare aqueous-alcoholic solutions of the extractant. It is recommended to begin tincture preparation with the percolation method. Either 5.0 or 10.0 grams of the raw material will be placed in a macerator and poured with 0.5 or 1 times the amount of extractant, then left for 1 hour. The swollen raw material will then be transferred to the percolator, the bottom of which is closed with a gauze napkin, compacted, filled with an extractant, sealed with foil, and left until the next lesson. Following this, tincture preparation by maceration will commence with 5.0 or 10.0 grams of the prepared raw material placed in a macerator and poured with 5 or 10 times the amount of extractant, sealed with a lid, and left until the next lesson.

PRACTICAL TASKS

1. From 100 kg of belladonna leaves with an alkaloid content of 0.4%, 1000 liters of tincture (0.033% alkaloids) were prepared. Make a material balance, find a way out, waste and expenditure coefficient for alkaloids.

Answer: yield of the finished product (η)-82,5% g 1=0,4 kg

cost of spending (E) -17,5 g2=0,33 kg

K_{cons}. -1,212 g5=0,07 kg

2. 350 liters of lily of the valley tincture with a content of 68% alcohol in it were obtained, for which 425 liters of 70% alcohol were consumed. 120 liters of alcohol 32% were recovered from waste raw materials. Make a material balance for absolute alcohol. Find a way out, spending and expense ratio.

Answer: yield of the finished product - 91,856% g1 =297,5 L

cost of spending -8,14% g2=238 L

K_{cons}. - 1,0886 g4=38,4 L

g5=21,l L

3. 250 liters of Strychnos nux-vomica tincture with an alkaloid content of 0.645% were obtained. Bring the tincture to the standard (0.239-0.273%).

Answer: 629.88 L (0.256% tincture), 379.88 L 70% alcohol.

4. 165 liters of belladonna tincture with a content of 0.040% alkaloids were obtained. Bring the tincture to the standard (0.033%). What are the volumes of diluent and finished product?

Answer: 200 liters, 365 liters tincture.

5. 100 liters of belladonna tincture with an alcohol content of 37% was obtained, for which 120 liters of 40% alcohol were consumed. 50 liters of 14.8% alcohol were recovered from waste raw materials. Make a material balance for absolute alcohol. Find a way out, spending, spending coefficient.

Answer: see below.

6. From 100 kg of belladonna leaves with an alkaloid content of 0.36%, 1000 liters of tincture was prepared that meets the requirements of regulatory documents (0.033% alkaloids). Make a material balance and calculate the consumption coefficient for alkaloids.

Answer: see below.

7. As a result of the production of St. John's wort tincture, 28 liters of recuperate with an alcohol content of 12% (vol.) were obtained. How many liters of 96% alcohol will be required for the sale of the recuperate and the preparation of a total of 90 liters of extractant?

Answer: 14 + 20 liters of 96% alcohol.

An example of solving a problem 4.

According to the rule of mixing:

0,040 — 0,033 — 0

0,033 x 1000 = 33

0,007 x 1000 = 7

0,040 x 1000 = 40g

calculate:

33 - 7
165 - x_1,.
x_1 = 35 l 40% add alcohol to 165 liters of the resulting semi-finished product.
x_2 = 165+35=200 l or

33 - 40
165 - x_2 x_2 = 200 l tincture

Calculate:
33 - 7 1
65 - x1,.
x1 = 35 liters of 40% alcohol added to 165 liters of the resulting semi-finished product.

x2 = 165 + 35 = 200 l or
33 - 40
165 - x2, x2 = 200 liters of tincture

An example of solving problem 5.

1. Absolute alcohol consumed: x = 120 ● (12 : 100) = 48 liters.

2. Obtained absolute alcohol in the finished product: x = 100 ● (37 : 100) = 37 L

3. Recovered absolute alcohol: x = 50 ● (14.8 : 100) = 7.4 liters.

Absolute alcohol balance: 48 = 37 + 7.4 + (3.6 = g5).

yield of the finished product η = 37 : (48 – 7.4) ● 100 = 91.13% 6.

Expenditure E = (3.6 : 40.6) ● 100 = 8.87%

7. $K_{cons.}$ = (48 – 7,4) : 37 = 1,097

An example of solving the problem 6.

1. Taken alkaloids (in leaves):

100 - 0,36

100 - x, x = 0.36 kg of alkaloids.

2. Obtained alkaloids in the finished product: 100 - 0,033 1000 - x, x = 0.33 kg of alkaloids.

3. Alkaloid balance: 0.36 = 0.33 + (0.03 = g5).

4. yield of the finished product η = (0.33 : 0.36) ● 100 = 91.67% 5.

Expenditure ἐ = (0.03 : 0.36) ● 100 = 8.33%

6. $K_{cons.}$ =0,36 : 0,33 = 1,091

SOME THEORETICAL ISSUES

The extraction of medicinal raw materials involves a complex mass transfer process governed by fundamental laws of mass transfer and encompassing various intertwined processes: diffusion, osmosis, dialysis, dissolution, and desorption of substances.

Molecular Diffusion: This process entails the transfer of a distributed substance due to the random movement of molecules within a stationary medium.

Convective Diffusion: Characterized by the coefficient of convective diffusion (β), this process measures the amount of substance transferred through 1 m2 of phase contact surface into the medium per second with a concentration difference of one between the layers.

The extraction of dried plant material commences with the extractant's penetration into the material, followed by wetting substances within cells, dissolution, desorption, diffusion through cell membrane pores, and culminates in the transfer of substances from the material's surface to the solution.

Factors influencing extraction's completeness and speed include:

- Hydrodynamic conditions.
- Phase interface.
- Leaching coefficient.
- Concentration difference.
- Extraction time (duration).
- Anatomical structure of raw materials.
- Chemical structure of extractives.
- Raw material porosity.
- Temperature and pressure.

- Extractant application method.
- Exposure to electric pulse discharges.

The maceration or infusion method involves soaking crushed raw material with a calculated amount of extractant in a maceration container, maintaining it at 15-20°C, and stirring periodically. Typically, the infusion lasts up to 7 days, unless otherwise specified. The infusion period for each raw material type is presently determined through kinetic extraction studies. After infusion, the solution is drained, and the residual material is squeezed. The spent raw material is washed, re-squeezed, added to the original extract, and then the combined extract is settled and brought to the desired volume with more extractant.

Img. 5. Maceration tank equipment
(images.google.com)

Percolation refers to filtering the extractant through plant material to extract substances soluble in it. This process is conducted in variously designed containers known as percolator-extractors.

Img 6. Percolation in laboratory
(https://joanmorais.com/percolation-herbal-alcohol-extract/)

TINCTURES

Tinctures are liquid extracts made from dried or fresh plant or animal materials using alcohol or a mixture of alcohol and water, without the application of

heat to the extraction process. These extracts are transparent and possess the flavors and aromas of the original plant materials.

Tinctures come in two main types: simple, which are derived from a single raw material, and complex, which are a blend of extracts from multiple plants, often with the addition of medicinal substances.

Most tinctures are made using 70% ethanol, although some, such as tincture of barberry and St. John's wort, are made with 40% ethanol. Other concentrations, like 90% for mint and capsicum tinctures or 95% for lemongrass tincture, are extremely rare.

When creating tinctures, a mass-volume ratio is applied, resulting in 5 volumetric parts of the finished product from one weight part of plant raw materials, or 10 parts of potent raw materials. Some tinctures are prepared in other ratios, such as arnica tincture at 1:5, and calendula, hawthorn, and peony tinctures at 1:10. Mint tincture is prepared at a ratio of 1:20, while sophora tincture is prepared at a ratio of 1:2.

The production of tinctures involves several techniques, including extraction methods such as:

- maceration and percolation;
- dissolution of concentrated and desiccated extracts.

The latter method is utilized for a limited number of tinctures, such as Strýchnos nux-vómica tincture, which is made from a dry extract. This approach is particularly suitable for seeds that are difficult to powder and contain poison due to their extreme hardness. Likewise, a potent or dry licorice extract is employed in the production of a breast elixir. In this process, a calculated amount of dry or concentrated extract is dissolved in alcohol of the required strength in a reactor with an agitator, followed by filtration. While this method significantly reduces the time required to obtain tinctures, slight variations in composition may occur. However, the majority of tinctures are obtained through the extraction of plants.

To obtain simple tinctures, it is common to use the percolation method. When extracting tinctures at a ratio of 1:5 to ensure the complete extraction of the raw

materials, the process involves circulating mixing using centrifugal pumps, vibration, or other similar methods.

When extracting medicinal plant raw materials, the resulting extracts are often cloudy liquids containing a substantial amount of suspended particles. It is necessary to allow the extracts to settle for a minimum of 2 days at a temperature not exceeding 10°C to purify them.

Different pharmacopoeias offer varying recommendations for the settling time of tinctures. According to the Japanese pharmacopoeia, settling should take 2 days, while the Romanian pharmacopoeia recommends 6 days, and the Italian pharmacopoeia suggests 12 hours. When using vortex extraction, settling for 3 days at a low temperature is necessary until a clear liquid is obtained. It's important to note that at this temperature, the solubility of impurities such as proteins and mucus decreases, leading to their precipitation. Therefore, when storing tinctures at 15°C, the likelihood of sedimentation is minimal.

After settling, filtration is carried out in combination with decantation.

Some example of tinctures

№	**The name of tinctures**	**Raw materials, alcohol, ratio, Method of obtaining**	**The Ingredients, application**
1	Oplopanax tincture	Rhizomes and roots, 70%,1:5, percolation	Steroid saponins. Tonic application
2	Hyperucium tincture	Grass, 40%, 1:5, percolation	Anthracene derivatives. In the treatment of gingvitis and stomatitis
3	Ginseng tincture	Roots, 70%, 1:10, maceration	Tetracyclic saponins. Stimulator of the central nervous system

4	Hawthorn tincture	fruits, 70%, 1:10, percolation	Flavonoids. With functional disorders of cardiac activity
5	Calendula tincture	Marigold flowers, 70%, 1:10, Percolation	Vitamins. For cuts, purulent wounds and ulcers. Choleretic
6	Tinctura Belladonnae	Leaves, 40%, 1:10, percolation	Alkaloids 0.027-0.033%. Antispasmodic. List B Belladonna tincture Tinctura belladonnae Leaves, 40%, 1:10, percolation of alkaloids 0.027-0.033%. Antispasmodic
7	Lily of the valley tincture	leaves, 40%, 1:10, percolation	cardenolides, 10-13 Frog units. Cardiotonic
8	Peppermint tincture Tinctura	eaves and essential oil, 90%, 1:20 + 5% oil, percolation and repercolation	Essential oil (menthol). With nausea and to improve digestion. It is part of the potions as corrigents

Standardization of tinctures involves ensuring their consistency and quality. Common methods for testing tinctures encompass:

1. *Organoleptic Characteristics:* This involves sensory analysis to assess attributes like color, odour, taste, and overall appearance.

2. *Quantitative Determination of Alcohol:* Measuring the alcohol content to ensure it adheres to the specified concentration.

3. *Quantitative Determination of Extractives:* Analyzing the quantity of active compounds present in the tincture.

4. *Heavy Metals Testing:* Ensuring the absence of harmful heavy metal contaminants.

5. *Density Measurement:* Determining the density of the tincture to ensure it aligns with established standards.

6. *Microbiological Purity:* Ensuring the absence of harmful microorganisms.

7. *Accuracy of Dosing:* Verifying that the dosing of the tincture corresponds to the specified amount.

These methods collectively contribute to the quality assurance and consistent production of tinctures.

In the spent plant raw materials - meal (material) is retained from 2 to 3 volumes of extractant in relation to the mass of raw materials. This extractant is recuperated (Recuperatio) - extracted by various methods and returned to production.

TEST QUESTIONS

Questions contain five answers and only one correct answer (example with an asterisk).

1. Which of the following is NOT mentioned as a factor influencing the completeness and speed of extraction?

a) Hydrodynamic conditions

b) Phase interface

c) Extraction time

d) Raw material porosity

e) pH of the extractant*

2. What is the typical alcohol concentration used for most tinctures?

a) 40%

b) 70%*

c) 90%

d) 95%

e) 100%

3. Which method is described as filtering the extractant through plant material to extract soluble substances?

a) Maceration

b) Percolation*

c) Decoction

d) Infusion

e) Distillation

4. What is the recommended settling time for tinctures according to the Japanese pharmacopoeia?

a) 12 hours

b) 2 days

c) 3 days

d) 6 days

e) 12 days

5. Which of the following tinctures is prepared at a ratio of 1:20?

a) Arnica tincture

b) Calendula tincture

c) Hawthorn tincture

d) Mint tincture

e) Sophora tincture

6. What is the primary reason for settling tinctures at a temperature not exceeding 10°C?

a) To increase the alcohol concentration

b) To enhance the extraction of active compounds

c) To decrease the solubility of impurities like proteins and mucus

d) To improve the color of the tincture

e) To increase the shelf life of the product

7. Which of the following is NOT mentioned as a method for standardizing tinctures?

a) Organoleptic characteristics

b) Quantitative determination of alcohol

c) Heavy metals testing

d) Microbiological purity

e) Spectrophotometric analysis

8. What is the process of extracting and returning the retained extractant from spent plant raw materials to production called?

a) Recycling

b) Recuperation

c) Repercolation

d) Regeneration

e) Rectification

9. Which type of diffusion is characterized by the coefficient of convective diffusion (β)?

a) Molecular diffusion

b) Convective diffusion*

c) Osmotic diffusion

d) Dialysis

e) Desorption

10. What is the ratio of raw material to finished product for most tinctures, unless otherwise specified?

a) 1:2

b) 1:5

c) 1:10

d) 1:15

e) 1:20

Lesson No5

Topic: Tinctures -2. Rectification and recovery of ethyl alcohol

Didactic goals and motivation of the lesson: Students are expected to demonstrate a comprehensive understanding of the physicochemical and technological properties of ethanol. This encompasses proficiency in production methods, rectification, and dehydration, as well as a sound comprehension of the functioning and principles of operation of both periodic and continuous action distillation plants. Additionally, proficiency in recovering alcohol through steam distillation and water displacement is required.

THEORETICAL QUESTIONS

1. Mass transfer of substances from plant material to extractant. Mass transfer equation. Mass transfer coefficient under different extraction conditions.
2. Recovery of extractant from waste raw materials. Methods, their evaluation.
3. Nomenclature of tinctures. The technology of preparation of tinctures of valerian, lily of the valley, motherwort, hawthorn, mint, bitter.
4. Physicochemical and technological properties of ethanol.
5. Methods of expression and methods for determining the concentration of alcohol in aqueous-alcoholic solutions and pharmaceuticals.
6. Comparative characteristics of alcohol meters and the rules for using them.
7. Rectification of alcohol. Theoretical foundations of rectification, distillation installations of periodic and continuous action. Device. Principle of operation.

METHODOLOGY OF PRACTICAL WORK

The lesson begins with the implementation of the percolation process. Percolation is carried out at a rate of 20 drops per minute. Then the meal (cake) is pressed and transferred to alcohol recovery. The tincture is filtered, standardized,

packaged. During percolation, test control is carried out and training issues are considered. In the course of work, students prepare tinctures by maceration. For this purpose, the extraction is separated from the solid phase by squeezing on the filter and its volume is measured. With the missing volume of extractant up to 50 ml, the meal is washed and re-squeezed. Both extracts are combined, the resulting tinctures are defended, filtered and standardized. In the same lesson, alcohol recovery is carried out. At the same time, depleted medicinal plant raw materials are transferred to a flask, filled with water and distilled. The volume of distillation and its concentration are measured, the material balance for anhydrous alcohol is compiled.

SOME THEORETICAL ISSUES

Tinctures are liquid extracts obtained from dried or fresh plant or animal raw materials using alcohol or hydroalcoholic solutions. These extracts are prepared without heat and without removing the extractant. Tinctures appear as transparent, coloured liquids that carry the taste and aroma of the plants they are derived from. Tinctures can be categorized as simple or complex, which may consist of a combination of extracts from multiple plants, sometimes including medicinal substances.

To create tinctures, the following methods are utilized:

1. *Extraction Methods:* These include maceration and its variations, as well as percolation.

2. *Dissolution of Thick and Dry Extracts***:** In this method, concentrated extracts are dissolved in alcohol.

Ethyl alcohol, also known as *Spiritus aethylicus*, is a clear, colorless, and mobile liquid with a distinctive odor and burning taste. It has a boiling point of 78°C. Ethyl alcohol (C_2H_5OH) is utilized in pharmaceutical production and is obtained through the fermentation of starch-containing raw materials, primarily potatoes and grains.

Ethyl alcohol can be categorized as a non-aqueous solvent with a degree of conventionality, as it is typically used in the form of water-alcohol solutions of various concentrations as opposed to absolute ethanol. Alcohol is capable of mixing

with water, glycerin, ether, and chloroform in any proportion. It is chemically neutral, does not undergo oxidation in the presence of air, and possesses bacteriostatic and bactericidal properties.

Alcohol has non-indifferent properties, and a lethal dose of 96% ethyl alcohol is about 200-300 ml. Ethyl alcohol serves as a widely used solvent in pharmaceutical production. The production typically involves supplying 96.2-96.7% ethanol, which is then diluted with water or weak alcohol to achieve the required concentration.

The concentration of ethanol is typically expressed in volume percent (%) or in percent by weight [% (m)]. Unless otherwise specified, a volume percentage is implied. The ethanol concentration in volume percent (Cv) indicates the amount of milliliters of anhydrous ethanol present in 100 milliliters of aqueous alcoholic solution at 20 °C. On the other hand, the ethanol concentration as a percentage by weight (Cm) indicates the amount of grams of anhydrous ethanol in 100 grams of aqueous alcoholic solution.

The ethanol content in aqueous-alcoholic solutions can be measured using glass and metal alcohol meters, as well as by density using a densimeter (hydrometer) or pycnometer.

Img. 7. Recuperation ethanol equipment
(images.google.com)

There are two ways to recover ethanol from meal: leaching with water and distillation with water vapor.

Water Leaching Method:

- *Purpose*: The water leaching method is used to recover residual ethanol from the pressed meal and to extract additional substances from the raw material.
- *Process*: The process involves pouring the pressed meal into a container filled with water and allowing it to infuse for 1.5 hours.
- *Ethanol Diffusion*: During infusion, ethanol diffuses from the raw material into the water, resulting in a mixture of water and ethanol.
- *Wash Water*: The mixture of water and ethanol obtained after infusion is referred to as "wash water."
- *Ethanol Recovery*: The amount of wash water obtained depends on the concentration of the original extractant (ethanol). For example, for 70% ethanol, about 5 volumes of wash water are obtained per volume of raw material. For 40% ethanol, about 3 volumes of wash water are obtained.
- *Composition*: Wash water contains a percentage of ethanol (5-30%) and a significant amount of ballast substances extracted from the raw material.
- *Characteristics*: Wash water is typically cloudy and retains the volatile aroma of plant material. However, this aroma may deteriorate during storage.

Recovery of Extractant by Distillation with Steam:

1. *Preparation of Meal:* After the initial extraction process, the plant material is usually left with a significant amount of the extractant, such as ethanol. This meal contains both the extracted substances and the solvent.
2. *Distillation Setup:* The recovery process begins with setting up a distillation apparatus. This typically involves a distillation flask containing the mixture of meal and extractant, a condenser to cool and condense the vapor, and a collection vessel to collect the distillate.

3. *Steam Generation:* Steam is generated using an external source of heat. The steam is then passed into the distillation flask containing the meal and extractant.
4. *Steam Distillation:* The steam passes through the mixture and interacts with the extractant, causing it to vaporize. The vaporized extractant and steam rise together through the distillation flask.
5. *Condensation***:** As the vaporized mixture moves into the condenser, it is cooled down by the cold water circulating around the condenser. This causes the vapor to condense back into a liquid phase.
6. *Collection of Distillate:* The condensed liquid, which consists of the extractant and a small amount of water, is collected in the receiving vessel. This liquid is known as the distillate.
7. *Separation of Extractant:* The distillate contains the recovered extractant, which is now separated from the plant material and other impurities that might have been present in the meal.
8. *Further Processing:* Depending on the intended use, the recovered extractant may undergo further processing to separate it from any remaining water or impurities. This could involve additional distillation or purification steps.
9. *Recovery and Reuse:* The recovered extractant, such as ethanol, can be purified and reused in subsequent extraction processes. This reduces the need for additional solvent and is more environmentally friendly.

By using steam distillation to recover the extractant, the process efficiently separates the solvent from the plant material while preserving the valuable compounds extracted during the initial process. It's a sustainable approach that allows for the efficient reuse of solvents and reduces waste.

Rectification is a crucial process in the field of distillation, particularly when dealing with mixtures of liquids that have similar boiling points. The goal of rectification is to achieve a higher degree of separation and purity of the individual components within the mixture. This process is particularly important in industries

such as chemical, pharmaceutical, and beverage production. Here's a more detailed explanation:

Principle of Rectification:

Rectification is based on the principle that when a mixture of liquids with close boiling points is repeatedly vaporized and condensed, it allows for the separation of the components based on their different vapor pressures and affinities for the vapor and liquid phases. This repeated vaporization and condensation enhances the separation of the components.

Distillation Units for Rectification:

Continuous Distillation Columns: Continuous rectification is often carried out using distillation columns. These columns consist of a series of trays or packing materials that provide surfaces for vaporization and condensation. As the vapor rises through the column, it comes into contact with the descending liquid. The repeated contact and vaporization-condensation cycles help in achieving greater separation.

Fractionating Columns: Fractionating columns are specialized types of distillation columns used for rectification. They are designed to maximize the separation of components with similar boiling points. These columns typically have multiple trays or structured packing materials to facilitate the separation process.

Azeotropic Distillation Columns: In some cases, azeotropic mixtures (mixtures that have boiling points lower or higher than those of their individual components) require special techniques. Azeotropic distillation columns are designed to break azeotropes by altering the composition of the vapour and liquid phases using additional agents or entrainers.

Batch vs. Continuous Rectification:

Rectification can be carried out using both batch and continuous methods:

Batch Rectification: In batch rectification, the mixture is loaded into a distillation apparatus, heated, and the vapour is condensed to obtain separate components. This process is repeated in several batches to enhance the degree of separation.

Continuous Rectification: In continuous rectification, a continuous flow of the mixture is fed into the rectification column, and the separated components are continuously collected as distillate or bottoms.

Applications of Rectification:

Rectification is used in various industries, including:

Chemical Industry: To purify chemicals, separate reaction products, and obtain high-purity solvents.

Pharmaceutical Industry: To separate and purify active pharmaceutical ingredients (APIs) from reaction mixtures.

Beverage Industry: To produce high-proof alcohol, separate ethanol from fermentation mixtures, and purify essential oils.

Overall, rectification plays a crucial role in achieving high-purity components from complex mixtures and is an essential technique in various industrial processes.

TEST QUESTIONS

Questions contain five answers and only one correct answer (example with an asterisk).

1. **What is the primary purpose of rectification in distillation processes?**

A) To increase the yield of distillate

B) To achieve a higher degree of separation and purity of components *

C) To reduce the boiling point of the mixture

D) To enhance the color of the final product

E) To minimize the use of solvents

2. **Which method is commonly used to measure the ethanol content in aqueous-alcoholic solutions?**

A) Thermometer

B) Barometer

C) Alcohol meter *

D) Refractometer

E) Spectrometer

3. What is the typical concentration of ethanol used in pharmaceutical production?

A) 40-45%

B) 50-55%

C) 60-65%

D) 70-75%

E) 96.2-96.7% *

4. In the recovery of ethanol by water leaching, what is the 'wash water'?

A) Pure ethanol recovered from the raw material

B) A mixture of water and ethanol obtained after infusion

C) A byproduct of ethanol fermentation

D) Ethanol solution used for sterilization

E) Water used to clean equipment

5. Why is steam distillation used in the recovery of extractants like ethanol?

A) It enhances the flavor of the final product

B) It allows for the efficient separation of solvents from plant material

C) It is faster than other extraction methods

D) It requires less equipment

E) It reduces the boiling point of the solvent

6. What are the two main methods used to create tinctures?

A) Percolation and sublimation

B) Maceration and percolation

C) Filtration and crystallization

D) Extraction and distillation

E) Leaching and boiling

7. What characteristic of ethyl alcohol makes it a widely used solvent in pharmaceutical production?

A) Its ability to oxidize quickly

B) Its high boiling point

C) Its capability to mix with water, glycerin, ether, and chloroform in any proportion

D) Its solid state at room temperature

E) Its low toxicity

8. What is the primary difference between the volume percent (Cv) and percent by weight (Cm) when expressing ethanol concentration?

A) Cv indicates the amount of ethanol in grams; Cm indicates the amount in milliliters

B) Cv indicates the amount of ethanol in a mixture at 30°C; Cm at 20°C

C) Cv indicates milliliters of ethanol in 100 ml solution; Cm indicates grams of ethanol in 100 grams solution

D) Cv measures ethanol purity; Cm measures ethanol density

E) Cv is used for solid mixtures; Cm is for liquid mixtures

9. Which method is used to recover ethanol by directly separating it from the meal using steam?

A) Water leaching

B) Refluxing

C) Steam distillation

D) Fermentation

E) Sublimation

10. What is a primary use of fractionating columns in the context of rectification?

A) To enhance the color of the distillate

B) To extract medicinal compounds

C) To maximize the separation of components with similar boiling points

D) To add aroma to the final product

E) To cool down the vapors before condensation

Lesson No6

Topic: Liquid extracts. Production and standardization

Didactic goals and motivation of the lesson: students should thoroughly review the theoretical material related to the topic. This includes understanding extraction methods, nomenclature, properties, applications, and storage conditions of liquid extracts. They should also learn how to prepare liquid extracts using percolation and repercolation methods, standardize the prepared preparations, become familiar with the extraction equipment, and be able to solve situational problems.

THEORETICAL QUESTIONS

1. Extracts. Classification. Characteristics of liquid extracts, requirements for them of the State Pharmacopoeia of Ukraine 1. Assortment, properties, standardization, application and storage conditions of liquid extracts. Examples.
2. Classification of methods for obtaining liquid extracts.
3. Percolation method and its characteristics.
4. Preparation of liquid extracts by repercolation with unfinished and finished cycle with evaporation.
5. The essence and characteristics of the repercolation method with a complete cycle without evaporation and separation of raw materials into unequal purities.
6. Circulating extraction.
7. Countercurrent extraction, instrument.
8. Ultrasonication extraction, extraction in a battery of extractors.
9. Electroplasmolysis, electrodialysis. Extraction with liquefied CO_2.
10. Features of the production of liquid standardized extracts-concentrates (1: 2), their nomenclature.

METHODOLOGY OF PRACTICAL WORK

For the manufacture of liquid extract by percolation, 20 g of plant raw materials are moistened with 10 (20) ml of extractant for 3-4 hours, half an hour before the end of the lesson, the raw material is loaded into the percolator, poured with the amount of extractant allocated for 1 lesson and left until the next lesson.

PRACTICAL TASKS

1. The container contains 100 liters of 95.6% alcohol (temperature + 20 ° C). How much thyme herb extractor can be prepared from it?

Answer: 318.7 liters.

2. It is necessary to prepare 200 liters of extractant for the production of liquid nettle extract. How much 96.3% alcohol should be measured at temperature:

a) +20 ° C, b) + 25 ° C and c) -2.5 ° C?

Answer: 103.84 L; 104.7L ; 101.26 L.

3. What amount of extractant for the preparation of liquid extract of a shepherd's purse will be obtained by using 120 liters of recuperate (alcohol concentration 46%, liquid temperature + 24 ° C) and a sufficient amount of 96% alcohol of the same temperature?

Answer: 222.94 L.

4. Buckthorn bark contains anthracene derivatives 4.5%. How much liquid extract can be obtained from 100 kg of this raw material, provided that the active ingredients yield is 100% and the content of the latter in the finished extract is 1.5%?

Answer: 300 L.

5. Viburnum bark, containing 7% tannins, is used to produce liquid extract. How much of the finished product with a 5% tannin content can be prepared from 100 kg of medicinal plant materials?

Answer: 140 L.

6. For the production of 50 liters of liquid standardized extract-concentrate (1: 2) containing 0.5% alkaloids, 25 kg of thermopsis herb with an alkaloid content of 1.3% was consumed. Calculate the output and spending.

Answer: 76.92%; 23,08%.

7. How much diluent (50% alcohol) will be required to normalize 50 liters of extract containing 6% tannins, and how much pharmacopeial extract (4% tannins) will be obtained?

Answer: 25 L and 75 L.

An example of solving problem No. 2.

1. How much liters of 96.3% alcohol should be measured at + 20 ° C to prepare 200 liters of a 50% solution?

Xa = P ● (b : a) = (200 ● 50) : 96.3 = 103.84 L

2. How much liters of anhydrous alcohol are contained in 200 liters of a 50% solution?

50 liters - in 100 liters of solution

X - 200 l, X = 100 L

3. What is the multiplier for 96.3% alcohol at a temperature of + 25 ° C? Using the horizontal interpolation method in table No. 5 of Standart, a multiplier of 0.9550 is found.

4. How much 96.3% alcohol should be measured at +25°C to contain 100 litres of anhydrous alcohol?

0.9550 L without water alcohol contain in 1 litres 96.3% (T = + 25 ° C)

100 litres without water alcohol in X_b 96.3% (T = + 25 ° C),

X_b = (100 ● 1) : 0.9550 = 104.712 L

5. What is the multiplier for 96.3% alcohol having a temperature of -2.5 ° C. Using double interpolation, find a multiplier of 0.98754.

6. What is the volume of 96.3% alcohol should be measured at a temperature of -2.5 ° C? 0,9875 - 1L 100.0 - Hv X_b = (100 ● 1) : 0.98754 = 101.26 L

SOME THEORETICAL ISSUES

Liquid Extracts:

- Definition**:** Liquid extracts are concentrated aqueous-alcoholic extracts obtained from medicinal plant materials.
- Extraction Ratio: They are prepared in a ratio of 1:1, meaning that 1 kg of liquid extract is obtained from 1 kg of raw materials.
- Preparation Method**:** Liquid extracts are typically prepared by weight, ensuring a consistent ratio of raw material to final extract.
- Solvent**:** Liquid extracts are obtained using a mixture of water and alcohol (alcoholic extractant).
- Consistency**:** Liquid extracts maintain the same consistency as the mixture of water and alcohol used during the extraction process.
- Concentration**:** The final product is highly concentrated due to the 1:1 extraction ratio.

Liquid Extracts Benefits:

1) the same ratios between the active substances contained in the medicinal raw materials and in the finished product;

2) convenience in measuring in pharmacies;

3) the possibility of obtaining without the use of evaporation makes it possible to obtain liquid extracts containing volatile substances (essential oils).

Disadvantages of liquid extracts:

1) their saturation with concomitant substances extracted from plant materials;

2) the appearance of precipitation with a slight decrease in temperature or partial evaporation of alcohol;

3) the need for hermetic closure and storage at a temperature of 15-20 ° C;

4) Large volumes of extractant are used to obtain liquid extracts, which are then evaporated.

To obtain liquid extracts, the calculation of the amount of extractant (X):

$$X = n \cdot V + m \cdot K$$

Where is:

n is the number of extractant volumes required for the complete depletion of raw materials;

V is the required amount of extract, kg

m – number of medicinal plant raw materials, kg

K is the coefficient of alcohol absorption by raw materials, showing the amount of alcohol retained by 1 g of raw materials.

If the extraction method does not provide for the concentration of extractions, then n is taken to be equal to 1.

As an extractant in the production of liquid extracts, 50-70% ethanol is usually used, less often other concentrations.

Methods of obtaining. Liquid extracts are obtained by extraction methods of percolation, repercolation (in various versions), remaceration in various modifications, and countercurrent extraction. Liquid extracts can be obtained by dissolving dry or thick extracts.

Concentration: After the initial extraction of plant materials, the resulting extract may contain a mixture of active compounds along with the extraction solvent. To obtain a more concentrated and potent final product, the extract is subjected to concentration. Concentration involves removing a significant portion of the extraction solvent to increase the concentration of the desired compounds.

One common method for concentrating extracts is the use of vacuum evaporators. These devices apply reduced pressure (vacuum) to lower the boiling point of the solvent, allowing it to evaporate at lower temperatures. The extract is heated while under vacuum, causing the solvent to vaporize and leave behind a concentrated extract. Vacuum evaporation is a controlled process that helps preserve the integrity of the active compounds while removing excess solvent.

Cleanup: Extracts obtained from the extraction process often contain impurities such as pigments, waxes, resins, and other unwanted substances that were extracted along with the desired compounds. The cleanup step aims to remove these impurities to improve the quality, stability, and appearance of the final product.

Some common cleanup methods used in the extraction process:

1. **Settling and Filtration:** After extraction, the mixture is allowed to settle over a period of time. Impurities and sedimentation will settle at the bottom, while the clear upper layer can be carefully separated and filtered to remove any remaining particulates.
2. **Adsorption:** Adsorbents like talc, kaolin, or activated carbon can be added to the extract to adsorb impurities. This can improve the clarity and quality of the extract.
3. **Decantation:** This involves carefully pouring off the clear liquid layer from the sediment or precipitate that has settled at the bottom, effectively separating the cleaner liquid from the impurities.
4. **Dehydration:** Sometimes, precipitation of impurities can be achieved by adding water or another suitable solvent to the extract. The impurities form a precipitate that can be separated by filtration or centrifugation.
5. **Salting Out:** Adding salts to the extract can lead to the precipitation of certain impurities or unwanted compounds, allowing them to be easily removed by filtration or centrifugation.

The choice of cleanup method depends on the specific impurities present in the extract and the desired quality of the final product. By removing these unwanted substances, the cleanup process ensures that the extract is purer, more stable, and suitable for further processing or formulation into various pharmaceutical or cosmetic products.

Ethyl alcohol (Spiritus aethylicus) is a transparent, colorless, and mobile liquid characterized by a distinct odor and a burning taste. It has a boiling point of 78°C. Ethyl alcohol is miscible in all proportions with water, glycerin, ether, and chloroform. It is neutral in nature, resistant to oxidation in the presence of oxygen in the air, and possesses bacteriostatic and bactericidal properties.

The concentration of ethanol is expressed in two main ways:

1. *Percentage by Volume (%):* This indicates the volume of anhydrous ethanol present in a given volume of aqueous-alcohol solution. If not otherwise specified, the volume percentage is usually understood. The concentration of ethanol

in volume percent (Cv) signifies the amount of milliliters of anhydrous ethanol in 100 milliliters of the aqueous-alcohol solution at 20°C.

2. *Percentage by Weight (% (m)):* This denotes the weight of anhydrous ethanol contained in 100 grams of the aqueous-alcohol solution.

The concentration of ethanol is typically determined using glass alcohol meters of class 0.1 (with a division of 0.1%) or class 0.5. At a temperature of 20°C, a glass alcohol meter provides the concentration of ethanol in volume percentages. These methods of measurement help accurately assess the ethanol content in various solutions.

Img. 8 glass alcohol meters (images.google.com)

For more precise measurements with an accuracy of 0.1%, the concentration of alcohol is determined using a metal alcohol meter. This instrument consists of a hollow ball with a soldered scale on its upper portion and a conical rod on its bottom to hang weights. The scale is graduated from 0 to 10, with each division further divided into five parts, allowing for precise readings and measurements of alcohol concentration. This metal alcohol meter is a valuable tool in accurately assessing the ethanol content in solutions.

Img.9. metal alcohol meter (images.google.com)

Measurements using the metal alcohol meter are relative and involve both the weight of the attached kettlebell and the scale readings. When the alcohol meter is submerged without the kettlebell, 100 is added to the scale readings. The concentration of ethanol (Cv) based on the metal alcohol meter readings is determined using Table IV provided by the Standards Publisher.

The dilution of aqueous-alcoholic solutions can be performed using two methods:

1. *By Volume:* This involves mixing specific volumes of the original solution and a solvent, often water, to achieve the desired dilution.

2. *By Weight:* In this method, the original solution is mixed with a solvent based on their respective weights to achieve the desired dilution.

These methods of dilution allow for precise adjustments of the concentration of ethanol in aqueous-alcoholic solutions.

$$X \cdot (A-C) = P \cdot (B-C)$$

Where :

X is the amount of strong alcohol;

A is the concentration of strong alcohol;

P the amount of alcohol of the required concentration;

B is the required concentration.

When diluted by volume, the required volume of strong ethanol is calculated. Indeed, determining the exact amount of water needed for dilution can be

challenging due to the phenomenon of "contraction," which refers to the reduction in volume that occurs when water and ethanol are mixed compared to their individual volumes. To simplify this process, it's often more practical not to calculate the precise amount of water required. Instead, you can add water to the calculated quantity of concentrated ethanol until the desired final volume is achieved at a temperature of 20°C. This approach takes into account the contraction effect and ensures that the resulting solution meets the desired concentration accurately.

TEST QUESTIONS

Questions contain five answers and only one correct answer (example with an asterisk).

1. What is the typical extraction ratio used for liquid extracts?

A) 1:2
B) 1:5
C) * 1:1
D) 2:1
E) 5:1

2. Which of the following is a disadvantage of liquid extracts?

A) Their extraction ratio is too low
B) They require the use of high temperatures
C) * They may form precipitates with slight temperature changes
D) They have a very short shelf life
E) They are ineffective in pharmacies

3. What is the primary solvent used in the production of liquid extracts?

A) Ether

B) Water

C) Glycerin

D) * Alcohol

E) Chloroform

4. What role does vacuum evaporation play in the concentration of liquid extracts?

A) It adds essential oils to the extract

B) It lowers the boiling point to evaporate solvents at lower temperatures

C) It increases the boiling point to retain more compounds

D) It removes solid impurities from the extract

E) It enhances the color of the extract

35. Which of the following is NOT a method used to clean up extracts?

A) Adsorption

B) Sublimation

C) Decantation

D) Settling and filtration

E) Salting out

36. What does the concentration of ethanol in volume percent (Cv) indicate?

A) The amount of ethanol by weight in 100 grams of solution

B) The volume of anhydrous ethanol in 100 milliliters of aqueous solution

C) The total volume of the solution

D) The amount of water present in the solution

E) The amount of impurities present in the ethanol

37. What is a common cleanup method that involves pouring off the clear liquid from settled impurities?

A) Adsorption
B) Decantation
C) Filtration
D) Salting out
E) Distillation

38. What tool is used for precise ethanol concentration measurements with an accuracy of 0.1%?

A) Glass alcohol meter
B) Pycnometer
C) Metal alcohol meter
D) Hydrometer
E) Thermometer

39. Which property allows ethyl alcohol to mix with water, glycerin, ether, and chloroform in any proportion?

A) Its low boiling point
B) Its miscibility
C) Its bacteriostatic properties
D) Its high viscosity
E) Its high density

40. What phenomenon causes a reduction in volume when water and ethanol are mixed?

A) Evaporation

B) Contraction

C) Expansion

D) Precipitation

E) Distillation

Lesson No7

Topic: Thick and dry extracts. Oil extracts. Production and standardization

Didactic goals and motivation of the lesson:

the students must acquire and consolidate theoretical knowledge on the topic, know the methods of obtaining and purifying primary extracts, evaporation and drying, study the equipment, know the private technology, nomenclature, properties, application and standardization of thick, dry and oil extracts.

THEORETICAL QUESTIONS

1. Definition and requirement of the State Pharmacopoeia of Ukraine of the first edition for thick, dry and oil extracts.
2. Classification and properties of thick, dry and oil extracts.
3. Methods for removing ballast substances from water and alcohol extracts. Adsorbents.
4. Evaporation. Equipment: film evaporators, tubular vacuum evaporators, centrifugal rotary-film evaporators.
5. Side effects during evaporation and ways to eliminate them. Types of dispersions during evaporation.
6. Oil extracts. Methods of obtaining. Nomenclature.
7. Sea buckthorn oil, rosehip oil. Preparation, standardization.
8. Drying. Forms of connection of moisture with the material. Statics and kinetics of drying.
9. Factors determining the drying speed (characteristics of moist air, aerodynamic conditions, design of dryers, etc.).
10. Drying methods and equipment. Contact and air dryers. Spray dryers, freeze dryers.
11. Roller vacuum dryers, spray drying, freeze drying. Vacuum drying oven.
12. Special drying methods (sorption, ultrasonic, high-frequency currents).

METHODOLOGY OF PRACTICAL WORK

The percolation method involves obtaining a concentrated extract (85%) and 1 "tempering", the latter is evaporated to 15%, combined with concentrated percolate and left in a bottle for settling for a week. Evaporation is carried out in compliance with fire safety and safety precautions when working with gas. The preparation of the extract is completed by filtering it through a paper filter and carrying out according to the following indicators:

1) Appearance - "clear liquid, opalescence and slight sediment are allowed; The smell is characteristic of this raw material;

Color - from green to brown with various shades;

Density, kg / cubic meter - 890-990;

Refractive index - 1.340-1.370; pH-4.0-8.7;

Mass fraction of non-volatile substances,% - not less than 2.0.

Determination of the mass fraction of non-volatile substances. 0.5-1.0 g of the extract is added to the evaporation cup and weighed on a technical balance with an error of no more than +0.02 g. The cup with the extract is placed on a sand bath and dried to a constant mass, when the difference between weighing does not exceed 0.02 g.

The mass fraction of non-volatile substances (X) as a percentage is calculated by the formula:

$X = (M \times 100) : m$,

where M is the mass of the extract after evaporation,

g; m is the weight of the sample of the extract taken for evaporation, g.

At the same time, the manufacture of oil extract from medicinal plant raw materials is carried out. When preparing an oil extract from medicinal plant materials, each student weighs 1.0 g of crushed raw materials, moisturizes it in a container of 1.0 ml of 95% ethyl alcohol and leaves it for 1 hour. After that, the raw materials are transferred to evaporation cups, add 10.0 g of vegetable oil and keep

in a sand bath with stirring for 30 minutes. At the end of the extraction, the extract is filtered into the collector through a double layer of gauze, the raw material is squeezed on a press filter and the resulting spin is added to the main extraction. Standardization of the extract is carried out according to the following indicators:

1) Color – corresponding to the color of this extraction;

2) Appearance and smell - a clear liquid with a characteristic smell for the plant. Turbidity is allowed, disappearing when heated to 50 ° C;

3) Refractive index - 1.462-1.469;

4) Acid number, mg KOH per 1 g of extract - no more than 2.5.

Determination of acid number. A sample of an extract weighing 1.3-1.9 g, weighed with an error of no more than ±0.02 g, is placed in a suspended conical flask. The sample is dissolved in 20 ml of chloroform. The resulting solution is titrated with 0.1 N. alcohol solution of potassium oxide hydrate in the presence of 4 drops of bromothymol blue until the color of the solution changes. At the same time, in similar conditions, a "single" experiment is carried out (only one per group is carried out).

The acid number (X), mg of KOH per 1 g of extract, is calculated by the formula:

$$X = \frac{5,6 \cdot K \cdot (V - V_n)}{m},$$

where:

V is the volume of the titrant spent on titration of a sample of oil extract, ml;

V0 - the volume of the titrant spent on titration in the "idle" experiment, ml; m is the weight of the sample of the extract, g;

5.6 - the amount of KOH contained in 1 ml of 0.1 n. solution of KOH, mg;

K is the correction factor for the KOH solution.

PRACTICAL TASKS

1. How much of the finished product can be obtained from 60 kg of licorice root extract containing 12% glycyrrhizic acid and 35% moisture to prepare a standard preparation (glycyrrhizic acid - 16%, moisture - 20%)?

Answer: 45 kg.

2. Calculate the amount of dry (anhydrous) diluent injected into 40 kg of licorice extract containing glycyrrhizic acid 22% and moisture 25% to obtain a thick extract with 15% glycyrrhizic acid.

Answer: 19.87 kg.

3. 50 kg of thick belladonna extract containing 2.2% alkaloids, moisture - 30% were obtained. How many kg of starch molasses (moisture content 30%) should be added and how much moisture should be evaporated in order to prepare a pharmacopoeia preparation with a tropane alkaloid content of 1.5% and a moisture content of 20%?

Answer: 33.81 kg of molasses, 10.47 liters of moisture.

4. Calculate the amount of finished product, thinner and moisture removed required to standardize 85 kg of semi-finished product of belladonna extract thick, containing alkaloids 1.95%, moisture 22%. As a diluent, dextrin with a moisture content of 6.8% is offered. The finished product should contain 1.5% alkaloids, 18% moisture.

Answer: see below.

5. From 100 kg of dandelion root containing 28% extractives, 33 kg of thick extract with a moisture content of 20% was obtained. Calculate output, spending, and Krash.. on extractives.

Answer: 94.3%, 5.7%, 1.061.

6. 53 kg of thick male fern extract with a 36% phylicin content was prepared. How much petroleum jelly should be added to bring the drug to normal (26.5%)? Answer: 19.0 kg.

7. It is necessary to bring to the standard (6% anthracene derivatives, humidity 4%) 50 kg of intermediate product of dry buckthorn extract containing anthraglycosides 11% and moisture 3%, using dextrin with a moisture content of 1.5%. How many kg of the finished product will be obtained, how much diluent and water should be introduced?

Answer: 91,667 kg, 40,102 kg, 1,565 L.

An example of solving a problem 4.

1. How much anhydrous diluent should be introduced into the semi-finished product.

$$X = \frac{P \bullet (a_o \bullet c_1 - a_1 \bullet c_0)}{100 \bullet c_0} = \frac{85 \bullet (82 \bullet 1,95 - 78 \bullet 1,5)}{100 \bullet 1,5} = 24,31 \text{ kg}$$

2. How much dextrin should I use for this?

93.2 kg of anhydrous water is contained in 100 kg of dextrin 24.31 kg of anhydrous water is contained in X kg

$$X = \frac{24,31 \bullet 100}{9,32} = 26,084 \text{ kg dextrin}$$

3. How much moisture should be introduced together with the diluent to bring the product to the specified moisture content?

$$V = \frac{P \bullet (a_o \bullet c_1 - 100 \bullet c_0 - (a_o \bullet c_1 + a_1 \bullet c_0))}{100 \bullet c_0} =$$

$$= \frac{85 \bullet (100 \bullet 1,95 - 100 \bullet 1,5 - 82 \bullet 1,95 + 78 \bullet 1,5)}{100 \bullet 1,5} = 1,13 \text{ kg}$$

4. How many kg of finished product will be obtained?

85+24,31+1,13=110,5 kg

5. How much moisture should be evaporated?

110,5 - (86+26,084)=-0,584 kg

An example of solving problem 7.

1. How much anhydrous dextrin is required for production?

$$X = \frac{50 \bullet (96 \bullet 11 - 97 \bullet 6)}{100 \bullet 6} = 39,5 \text{ kg}$$

2. How much dextrin does this correspond to (humidity 1.5%) available?

$$У = \frac{39,5 \bullet 100}{98,5} = 40,102 \text{ kg}$$

3. How much moisture should be introduced together with the diluent to bring the extract to the standard (specified anthracene derivatives content and moisture)?

$$V = \frac{50 \bullet (100 \bullet 11 - 100 \bullet 6 - (96 \bullet 11 - 97 \bullet 6))}{100 \bullet 6} = 2,167 \text{ kg}$$

4. What is the expected yield of the product?

50+39,5+2,167=91,667 кг

5. How much water should be added, taking into account the moisture content of dextrin?

91,667 - (50+40,102)=1,565 kg

Thick extracts are concentrated extracts derived from medicinal raw materials. These extracts are characterized by their viscous consistency and contain a maximum moisture content of 30% (according to European standards) or 25% (according to national Pharmacopeia guidelines). They are obtained through partial evaporation of the extractant used. Thick extracts usually exhibit a non-pourable nature, forming threads that eventually consolidate into a solid mass. They primarily function as intermediates for producing various dosage forms, including tablets, suppositories, ointments, syrups, and more complex combination preparations.

On the other hand, dry extracts are concentrated extracts from medicinal raw materials. They manifest as powdery masses with a moisture content not exceeding 5%, achieved by removing the extractant. Dry extracts are convenient to handle and boast minimal weight. However, their drawback lies in their high hygroscopic nature, which causes them to clump and lose their fluidity when exposed to moisture.

Img. 10. Example dry extract
(images.google.com)

The production process for thick extracts encompasses three main stages:

1. *Extraction:* Obtaining the initial extract.
2. *Purification:* Cleaning the initial extract.
3. *Thickening:* Increasing the concentration of the extract to achieve the desired consistency.

Dry extracts can be produced through two different routes:

- *First Case:* This method involves four stages: 1. Extraction, 2. Purification, 3. Thickening, and 4. Drying of the thickened extract.
- *Second Case:* In this scenario, the thickening stage is bypassed, resulting in a process with three stages: 1. Extraction, 2. Purification, and 3. Drying of either a liquid or slightly condensed extract.

Img. 11. Example of thick extract
(images.google.com)

In the production of thick and dry extracts, various methods are employed to obtain extracts from raw materials:

1. *Remaceration and Variants:* A method involving soaking the raw material in an extractant, such as a solvent, for a period of time to allow for extraction.

2. *Percolation:* A process where the extractant flows through the raw material, extracting soluble components as it passes.

3. *Repercolation*: Repeating the percolation process to ensure thorough extraction.

4. *Circulating Extraction:* The extractant is pumped through the raw material in a loop to enhance extraction efficiency.

5. *Countercurrent Extraction:* This method involves using a series of percolators with circulating stirring to ensure optimal extraction.

6. *Continuous Countercurrent Extraction:* Extraction occurs while continuously moving raw materials and extractant through a system.

Additionally, other methods include grinding raw materials in an extractant medium, vortex extraction, and employing techniques like electromagnetic oscillations, ultrasound, electrical discharges, electroplasmolysis, and electrodialysis.

Cleaning of the obtained extracts involves various techniques based on the nature of impurities and the extractant used:

1. *Settling and Filtration:* Allowing extracts to settle at a low temperature followed by filtration.

2. *Thermal Denaturation:* Boiling water extracts to remove proteins, typically at 100°C for a specified time.

3. *Adsorption*: Utilizing substances like talc, kaolin, bentonite, or cellulose powder to adsorb suspended particles and impurities.

4. *Dehydration and Alcohol Purification:* Precipitating mucus, pectin substances, and proteins using alcohol.

5. *Salting and Precipitation:* Using salts to precipitate proteins and carbohydrates.

6. *Precipitation by Heavy Metal Salts:* Employing heavy metal solutions to form insoluble compounds with proteins.

7. *Isoelectric Point Manipulation:* Adjusting the pH to encourage protein association and precipitation.

8. *Fermentation***:** Adding enzymes to catalyze the hydrolysis of polysaccharides into permissible mono- and oligosaccharides.

9. *Dialysis and Electrodialysis:* Utilizing semipermeable membranes to separate biologically active substances from high-molecular weight compounds based on their size differences.

Cleaning alcohol extracts is an essential step to remove impurities and undesirable substances present in the extracts. Alcohol extracts often contain various resinous compounds, pigments (such as anthocyanins, carotenes, chlorophyll, and flavones), and other ballast substances like waxes, sterols, and fats. To remove these impurities, a process known as alcohol purification is employed. In alcohol purification, the initial alcohol extract is treated with a different solvent to replace the original extractant and selectively remove unwanted components.

After the extract is cleaned, the next step is to thicken it. This involves evaporating the solvent under vacuum conditions to achieve the desired consistency. The temperature during this thickening process typically ranges from 50 to 60 °C, and a vacuum of 80 to 87 kPa (600 to 650 mm Hg) is applied. When thickening alcohol extracts or extracts that have undergone alcohol purification, the alcohol is removed first, often without the application of vacuum.

Once the extract is thickened, the final step is drying. Various types of drying equipment are used in the production of herbal extracts, each classified based on their design features. Some common types of dryers include drum dryers, tunnel dryers, belt dryers, mine dryers, spray dryers, and chamber dryers. These dryers are used to remove residual moisture from the thickened extract, ensuring its stability and preservation.

Oil extracts, also known as medical oils (Olea medicata), are extracts from medicinal plant materials that are obtained using vegetable or mineral oils. There are two main schemes used in the production of oil extracts:

1. *Vegetable Oil Infusion:* In this method, refined and deodorized vegetable oil (such as sunflower, olive, or sesame oil) is used as an extractant. The oil is heated to 60-70°C and then infused (macerated) with finely ground raw materials. This process allows the oil to extract the lipophilic (oil-soluble) compounds from the plant material, resulting in an oil extract.

2. *Solvent Extraction and Blending:* In this approach, volatile organic solvents (such as methylene chloride, dichloroethane, chloroform, ether, or 70% ethanol) or liquefied gases (like carbon dioxide or freons) are used as the extractant. These solvents efficiently extract lipophilic compounds. The obtained concentrate of lipophilic complexes is then blended (mixed) with a suitable vegetable oil to achieve the desired standard indicators.

Img. 12. Example of oil extract
(image.google.com)

Both methods are used to produce oil extracts, each with its advantages and considerations in terms of safety, efficiency, and product quality.

TEST QUESTIONS

Questions contain five answers and only one correct answer (example with an asterisk).

1. What is the maximum moisture content allowed for thick extracts according to European standards?

A) 5%

B) 15%

C) 20%

D) 25%

E) * 30%

2. Which of the following describes the nature of dry extracts?

A) High moisture content, viscous

B) * Powdery, with minimal moisture content

C) Non-pourable, forms solid mass

D) Forms threads, clumps in moisture

E) Oil-soluble, high in fats

3. What is the main difference between the two cases of dry extract production?

A) The use of different solvents

B) The temperature used in extraction

C)* The omission of the thickening stage in the second case

D) The type of medicinal raw material used

E) The use of vacuum in one process

4. Which extraction method involves soaking raw material in a solvent for a period of time?

A) Percolation

B) Remaceration

C) Circulating Extraction

D) Countercurrent Extraction

E) Repercolation

5. Which method is used for cleaning alcohol extracts to remove pigments and resinous compounds?

A) Settling and Filtration

B) Salting and Precipitation

C) Adsorption

D) Alcohol Purification

E) Thermal Denaturation

6. What is the typical temperature range used for thickening extracts under vacuum conditions?

A) 20-30°C

B) 30-40°C

C) 50-60°C

D) 70-80°C

E) 80-90°C

7. In the production of herbal extracts, which type of dryer is NOT often use?

A) Drum dryer
B) Tunnel dryer
C) Spray dryer
D) Freeze dryer
E) Belt dryer

8. What is the primary function of oil extracts in medicinal plant materials?

A) Extracting water-soluble compounds
B) Extracting alcohol-soluble compounds
C) Extracting lipophilic (oil-soluble) compounds
D) Extracting proteins
E) Extracting polysaccharides

9. In the production of oil extracts using vegetable oil infusion, what is the typical temperature to which the oil is heated?

A) 20-30°C
B) 40-50°C
C) 60-70°C
D) 80-90°C
E) 100-110°C

10. Which solvent is NOT used for the extraction of oil extracts?

A) Methylene chloride

B) Ethanol

C) Chloroform

D) Gasoline

E) Ether

Lesson No8

Topic: Suspensions. Emulsions. Medical pencils, ointments, patches, Production. Production. Quality assessment

Didactic goals and motivation of the lesson:

familiarize yourself with the technological process for producing liniments, suspensions, emulsions, medical soaps, plasters, and ointments. You should be able to prepare various types of liniments, introduce medicinal substances, homogenize, and standardize. It's important to know the properties of emulsifiers and stabilizers, as well as the equipment's structure and operation principles. You should also have knowledge about the nomenclature, properties, applications, and storage conditions of these drugs, as well as understanding the structure and operation principles of production equipment.

THEORETICAL QUESTIONS

1. Characteristics and classification of soft dosage forms for external use in accordance with the State Pharmacopoeia of Ukraine, I ed.
2. Classification, assortment of emulsifiers, stabilizers used in the production of soft dosage forms for external use.
3. Methods for the preparation of liniments, creams, gels and ointments, especially the introduction of medicinal substances with different physical and technological properties.
4. The use of ultrasound in the production process of liniments in the factory. Cavitation. Voiced emulsions, suspensions.
5. Characteristics of equipment for obtaining liniments; dispersers, homogenizers, turbine sprayers, colloidal mills. Nomenclature of ointments, creams, liniments, pastes, and gels of factory production. Properties. Application.
6. Plasters. Classification. Characteristic.
7 Simple lead plaster. Composition, methods of production. Drugs of this group.

8. Rubber plasters. Adhesive plaster, bactericidal, pepper, corn plasters. Components and their role. 9. Mustard plasters. Technology.

10. Soaps. Classification. Medical soap, green (potash), medicinal soaps.

METHODOLOGY OF PRACTICAL WORK

Students are divided into 2 groups. Each group prepares 50.0 g of streptocide liniment or synthomycin liniment 1%.

1. Streptocide liniment 5%:

Streptocid	5,0 g
Sunflower oils	34,0 g
Benzoic acid (sorbic acid)	0,2 g
Emulsifier No. 1	5,0 g
Tween-80	2,0
Purified water	Before 100,0

2. Synthomycin liniment 1%

Synthomycin	1,0 g
Sunflower oils	20,0 g
Emulsifier No. 1	5,0 g
Benzoic acid (sorbic acid)	0,2 g
Na-CMC	2,0 g
Purified water	Before 100,0

Manufacturing technology. Emulsifier No. 1 is melted in an evaporation cup in a water bath, purified water is introduced in parts, Na-CMC is mixed. A suspension of streptocide (synthomycin), a preservative, in sunflower oil, is added to the emulsion heated to 60-70 ° C and mixed by hand in a mortar or in a glass of a mechanical stirrer device for 1-2 minutes. One team prepares aloe liniment with homogenization in a mortar, the other at the homogenization stage mixes the

liniment and homogenizes in a glass of a mechanical stirrer for 2-3 minutes. In the manufactured dosage forms, students determine:

- Type of emulsion by mixing with water and dyeing method.
- Thermal stability.

When determining thermal stability, students fill 2/3 of two test tubes - one with aloe liniment homogenized in a mortar, the other in a stirrer glass. The tubes are placed in a water bath for 40-45 minutes, after which the height of the oil layer released from the emulsion (H_1) and the height of the emulsion layer in the test tube (H_2) are measured. The stability coefficient of the emulsion is calculated according to the formula:

$$K = \frac{H_1}{H_2}$$

Comparing: the values of the stability coefficients of emulsions, homogenized manually and using mechanization, conclude that the use of intensive mixing methods is important for the quality of the dosage form. The student hands over the finished preparations, regulations, protocol, analysis results, solution of situational problems to the teacher at the end of the lesson.

PRACTICAL TASKS

1. The liniment of streptocide in the thermostat at 45 ° C exfoliated within 6 hours. Can you draw a conclusion about the quality of liniment?
2. Two liniments of the same composition are obtained in different ways. One is sterile and the other is not. What conclusion can be drawn about the method of preparation of liniments?
3. What liniments can be prepared from the thick extract of capsicum available at the enterprise?
4. Calculate the consumption of streptocide, if 5.05 kg of the drug substance is spent on the production of 100 kg of streptocide liniment 5%?

Answer: 1%.

5. In what cases is homogenization of the ointment in production mandatory?
6. Make a working prescription for obtaining 10,000 hemostatic pencils, given that the weight of the pencil is 10.0 g, and K_{cons}.-1,120.

   Answer: 84.0 kg, 16.8 kg, 11.2 kg.
7. Make up the consumption of materials for the preparation of 20000 alum pencils of 3.3 g each, if K_{cons}. -1,110.

   Answer: See. Example solution.
8. The results of the analysis of the ointment showed the content of the active substance of 40%. The total amount of ointment obtained is 100 kg. How many kg and what component should be added to bring the ointment to the standard (1: 1)?

   Answer: 20 kg of active ingredient.
9. How much Bom-Benge ointment can be prepared from 2.0 kg of menthol, if Krash. is 1,050?

   Answer: 49,523 kg.

An example of solving problem No. 7 1.

How many kg of potassium alum and glycerin are contained in one pencil?

60 г - в 62,5 g

X - 3,3 X=3,168 g Alum

$$У = \frac{3,3 \bullet 2,5}{62,5} = 0,132 \text{ g glycerin or}$$

У = 3,3 – 3,168 = 0,132 g glycerin

What is the material consumption for 20000 pieces of pencils?

Aluminum: 3.168 ● 20000 ● 1.110 = 70.33 kg.

Anhydrous glycerin: 0.13220000 ● 1.110 = 2.93 kg.

SOME THEORETICAL ISSUES

Emulsions are colloidal systems consisting of two immiscible liquids, where one liquid is dispersed in the form of small droplets within the other liquid, forming the continuous phase. Emulsions are widely used in various industries, including the pharmaceutical and cosmetic industries, for the formulation of creams, lotions, ointments, and other products. The properties and stability of emulsions are crucial for their effectiveness and shelf life.

There are two main types of emulsions based on the nature of the liquids involved:

1. *Oil-in-Water Emulsion (1st kind or O/W Emulsion*)**:** In this type of emulsion, oil droplets are dispersed within a continuous phase of water. This is the more common type of emulsion and is often used in skincare products and pharmaceutical formulations. These emulsions are water-washable and are suitable for applications where water is the primary solvent.
2. *Water-in-Oil Emulsion (2nd kind or W/O Emulsion):* In this type of emulsion, water droplets are dispersed within a continuous phase of oil. These emulsions are leave-in with water and are often used in products that need to provide a protective barrier, such as certain moisturizers and sunscreens.

Emulsions can also become more complex with the formation of multiple emulsions, where droplets of one type of emulsion are dispersed within another type of emulsion. For example, water-in-oil-in-water (W/O/W) and oil-in-water-in-oil (O/W/O) multiple emulsions can be created, offering specific properties for certain applications.

Stability of emulsions is a critical factor in their formulation. Emulsions are prone to various forms of instability, such as creaming (settling of droplets), coalescence (merging of droplets), and phase separation. To maintain stability, emulsions are often formulated with surfactants or emulsifying agents. These substances contain both hydrophilic (water-loving) and hydrophobic (water-repelling) parts in their

molecular structure, which allows them to position themselves at the interface between the oil and water phases, effectively preventing droplets from coalescing.

The hydrophilic-lipophilic balance (HLB) is a parameter used to characterize surfactants based on their affinity to water or oil. Surfactants with higher HLB values are more water-soluble and are better suited for forming oil-in-water emulsions, while those with lower HLB values are more oil-soluble and are suitable for water-in-oil emulsions. The balance between the hydrophilic and hydrophobic properties of the surfactant molecule determines its emulsifying ability and the type of emulsion it can form.

In addition to surfactants, other factors that affect emulsion stability include the particle size distribution of droplets, the viscosity of the continuous phase, the presence of electrolytes or other additives, and the manufacturing process used to create the emulsion. Proper formulation and selection of emulsifiers play a crucial role in achieving the desired properties and stability of emulsion systems.

By chemical nature, surface-active substances are divided into two classes: ionic and nonionic according to their ability to dissociate or not dissociate into ions in an aqueous medium. Surfactants play a crucial role in the formulation of various products, including pharmaceuticals, cosmetics, detergents, and more. Here's a summary of the key points you mentioned:

1. Ionic Surfactants:

- Anionic Surfactants: These surfactants dissociate into negatively charged ions (anions) and are often used in detergents and cleaning products.
    - Examples include carboxylic acids (soaps), alkyl sulfates, alkyl sulfonates, olefin sulfonates, etc.
- Cationic Surfactants: These surfactants contain positively charged ions (cations) and are known for their surfactant and bactericidal properties.
    - Examples include long-chain aliphatic primary, secondary, and tertiary amines.

2. Ampholytic Surfactants:

• Ampholytic surfactants contain both acidic and basic functional groups, and their properties (anionic or cationic) depend on the pH of the solution.

• They are versatile and can be used for various purposes, including as foam stabilizers, emulsifiers, wetting agents, and more.

3. Nonionic Surfactants:

• Nonionic surfactants do not dissociate into ions and are less toxic compared to ionic surfactants.

• They are widely used due to their versatility and compatibility with various substances.

• Examples include oxyethylated alcohols, acids, phenols, amines, amides, alkyl sulfates, and esters of polyols and fatty acids.

Each class of surfactants offers unique properties that make them suitable for different applications. The choice of surfactants depends on the desired properties of the final product, such as foaming capacity, stability, compatibility, and toxicity. It's important to consider these factors when formulating pharmaceuticals, cosmetics, and other products to ensure their effectiveness and safety.

Img. 13. Example equipment for ointment manufacturing, filter press (images.google.com)

Key considerations for selecting an appropriate ointment base:

1. Structural and Mechanical Properties: The ointment base should possess the right consistency and texture to allow for easy application and uniform distribution. It should be smooth and easily spreadable on the skin or affected area.

2. Absorbent Capacity: The base should be capable of absorbing and holding the medicinal substances in a stable form. This helps ensure proper delivery and prolonged release of the active ingredients.

3. Chemical Resistance: The base should remain stable and not undergo chemical reactions with the medicinal substances, environmental factors, or other ingredients. This preserves the integrity of both the base and the active ingredients.

4. Pharmacological Neutrality: The chosen base should not induce irritation, sensitization, or adverse reactions when applied to the skin or mucous membranes. It should help maintain a comfortable environment for application.

5. pH Compatibility: The base should have a pH level that is compatible with the intended application area, whether it's the skin (around pH 5.5) or mucous membranes (around pH 3-4). This helps maintain the natural pH of the body and minimizes potential disruptions.

6. Microbial Stability: To prevent contamination and ensure product safety, the base should be resistant to microbial growth. Antimicrobial preservatives might be added to enhance microbial stability.

7. Purpose and Therapeutic Effect: The choice of base should align with the intended purpose of the ointment. Different bases may be suitable for various applications, such as moisturizing, wound healing, anti-inflammatory, or antimicrobial effects.

Common ointment bases include:

- **Hydrophobic Bases:** Made primarily from fats or oils and are water-repellent. Examples include petrolatum, white ointment, and anhydrous lanolin. These are suitable for incorporating lipophilic medicinal substances.
- **Hydrophilic Bases:** Contain water and can absorb aqueous medicinal substances. Examples include hydrophilic ointment, creams, and gels.

- **Absorption Bases:** These are water-in-oil emulsions that can absorb a significant amount of water. They're suitable for incorporating water-soluble substances.
- **Water-Soluble Bases:** Made from water-soluble substances and are designed for easy washability. Examples include polyethylene glycol (PEG) ointments.
- **Emulsion Bases:** Combination of water and oil phases, providing versatility in accommodating different types of medicinal substances.

The selection of the appropriate ointment base involves a balance of the factors mentioned above, ensuring optimal drug delivery, stability, and patient comfort. Different pharmaceutical or cosmetic products may require different bases to achieve the desired therapeutic effect and user experience.

TEST QUESTIONS

Questions contain five answers and only one correct answer (example with an asterisk).

1. What are emulsions?

A) Mixtures of solid particles and liquid
B) Colloidal systems consisting of two immiscible liquids *
C) Homogeneous solutions of two liquids
D) Mixtures of gas and liquid
E) Suspensions of solid particles in a liquid

2. Which type of emulsion is commonly used in skincare products?

A) Water-in-Oil Emulsion
B) Oil-in-Water Emulsion *
C) Water-in-Water Emulsion
D) Gas-in-Water Emulsion
E) Oil-in-Gas Emulsion

3. What is the function of surfactants in emulsions?

A) Increase the temperature of the emulsion
B) Stabilize the emulsion by preventing droplet coalescence *
C) Decrease the viscosity of the emulsion
D) Separate the oil and water phases

E) Remove impurities from the emulsion

4. What is the HLB value used for?

A) Determining the pH of emulsions
B) Measuring the temperature of emulsions
C) Characterizing surfactants based on their affinity to water or oil
D) Determining the particle size in emulsions
E) Measuring the viscosity of emulsions

5. Which type of surfactants do not dissociate into ions?

A) Anionic surfactants
B) Cationic surfactants
C) Ampholytic surfactants
D) Nonionic surfactants
E) Electrolyte surfactants

6. What are the two main types of emulsions?

A) Gas-in-Oil and Oil-in-Gas
B) Oil-in-Water and Water-in-Oil
C) Water-in-Water and Oil-in-Oil
D) Oil-in-Solid and Solid-in-Water
E) Gas-in-Water and Water-in-Gas

7. What causes instability in emulsions?

A) High viscosity
B) Low temperature
C) Phase separation, creaming, and coalescence
D) High pH levels
E) Low particle size

8. Which type of surfactant dissociates into negatively charged ions?

A) Nonionic surfactants
B) Ampholytic surfactants
C) Anionic surfactants
D) Cationic surfactants
E) Zwitterionic surfactants

9. What type of emulsion forms when water droplets are dispersed within a continuous phase of oil?

A) Oil-in-Water Emulsion
B) Water-in-Oil Emulsion
C) Water-in-Water Emulsion
D) Gas-in-Oil Emulsion
E) Oil-in-Gas Emulsion

10. What is the purpose of using an emulsion base in ointment formulations?

A) To reduce the viscosity of the ointment
B) To separate active ingredients
C) To enhance the stability and effectiveness of active ingredients
D) To increase the pH of the ointment
E) To make the ointment non-spreadable

Lesson No9

Topic: Subtest. Seminar

Didactic goals and motivation of the lesson:

ensure familiarity with the fundamental laws and techniques for extracting plant raw materials, as well as the influence of various factors on enhancing the speed and efficiency of extraction processes. It is important to understand how to apply the core principles of extraction theory to actual extraction processes using diverse methods and a variety of equipment. Additionally, expand your knowledge of extraction product nomenclature, and acquaint yourself with the devices and operational principles of extraction, evaporation, drying, rectification, and recovery apparatuses. Develop the ability to address practical extraction standardization tasks. Learn to determine alcohol content in solutions, and to measure the density and strength of alcohol in aqueous-alcoholic solutions at temperatures ranging from +40 °C to -25 °C using hydrometers, glass and metal alcohol meters. Proficiency in the interpolation method and the ability to perform calculations for alcohol solution dilution and strengthening, as well as to calculate contraction and the quantity of anhydrous alcohol in a specified volume or mass of the solution, is essential.

THEORETICAL QUESTIONS

1. Theoretical foundations of extraction. Molecular and convective diffusion. Mass transfer equation, mass transfer coefficient.
2. The main technological factors affecting the completeness and speed of extraction.
3. Ways of intensification of mass transfer.
4. Extraction methods - maceration and its modifications, percolation, repercolation, circulation, countercurrent extraction.
5. Characteristics of extraction with liquefied gases. Apparatus.

6. Equipment for active countercurrent extraction. Device, principle of operation, characteristics.

7. Rectification of alcohol. The structure and principle of operation of distillation plants. Alcohol recovery. Apparatus. Side effects during evaporation. Extractant removal methods (simple, vacuum residue) and equipment (ball, tubular, film, thin-film rotary vacuum evaporators).

8. Theoretical foundations of drying. Types of moisture, drying mechanism, air characteristics (humidity, moisture, heat content). The structure and principle of operation of contact and convective dryers: drying cabinets, roller, belt, spray, jet-spray, acoustic, thermoradiation, freeze dryers, fluidized material and fluidized bed dryers (pneumatic, air-fountain, vortex, etc.).

9. Nomenclature and features of the preparation of tinctures. National pharmacopoeia Requirements, 1st ed.

10. Nomenclature of alcoholic liquid, thick and dry extracts. Standardization on National pharmacopoeia, 1st ed.

11. Nomenclature and features of the production of liquid and dry standardized concentrate extracts.

12. Oil extracts. Methods of obtaining. Quality assessment, nomenclature. Obtaining sea buckthorn oil and rosehip oil.

PRACTICAL TASKS

1. Bring to the standard content of alkaloids (in%) V l tincture of belladonna containing a% alkaloids, if the standard content is 0.033%.

V, L	a, %	Answer
105	0,042	28,6 L
70	0;044	23,33 L
50	0,050	25,76 L
120	0,048	54,55 L
100	0,037	12,12 L

2. How much bleached oil can be obtained from 10 kg of henbane leaves containing 0.07% tropane alkaloids?

Answer: 140 kg with an alkaloid content of 0.05%.

3. How many kg of standard thick belladonna extract (contains 1.6% alkaloids and 75 dense residue) can be obtained from m kg of extract containing A% alkaloids and B% dense residue? How much filler should be added?

m, kg	A,%	B, %	Extract	Excipient
30	2,20	74,5	41,25	11,25
95	2,18	73,0	129,44	34,44
40	2,15	70,0	53,75	13,75
50	2,06	74,0	64,38	14,38
65	1,90	72,0	77,19	12,19

An example of solving a situational problem. How many kg of standard thick extract will be obtained from 120 kg of thick belladonna extract containing 2.2% alkaloids and 80% dense residue (in the standard content of 1.6% alkaloids and 75 dense residue).

1. How many alkaloids are contained in 120 kg of custom extract?

100 - 2,2

120 - x, x=2,64

2. How many kg of standard extract will be obtained from 2.64 kg of alkaloids?

1,6 - 100

2,64 - x, x=165 kg

3. What is the amount of dense residue contained in 120 kg of non-standard extract?

100 - 80

120 - x, x= kg

4. How much solid residue should be contained in 165 kg of standard extract?

75 - 100

X - 165, x=123,75 kg

5. How much anhydrous excipient should be added to the custom extract?

123,75 - 96,0=27,75 kg

6. Total number of excipients:

165 - 120=45 kg

7. Including the amount of water added:

45 - 27,75=17,25 kg

I. Determination of the concentration of alcohol by the density of the solution.

1. What is the concentration of alcohol as a percentage of the volume, if the density of the solution at + 20 ° C is 0.8138?

Answer: 94.38%

2. Determine the strength of alcohol in% by volume, if the hydrometer readings at + 20 ° C are equal to 0.805.

Answer: 96.6%

3. Determine the concentration of alcohol in % by weight in a solution having a temperature of + 20 ° C, if its density is equal to 0.8025.

Answer: 95.595%

4. What % by weight corresponds to the solution, the strength of which in % by volume is equal to 88.04%?

Answer: 83.16%

5. What is the concentration of alcohol in % by volume, if its concentration in % by weight is 85.84%?

Answer: 90.14%

II. Translation of methods for expressing the concentration of alcohol using alcoholometric tables and formulas

1. What is the concentration of alcohol in% by weight of a 40.9% solution (by volume)?

Answer: 34.100% (m)

2. What is the concentration (% by volume) of alcohol in the solution, the strength of which in % by weight is 60.90%, and the density at + 20 ° C is 0.8890?

Answer: 68.59% (vol.).

3. Determine the value of the concentration of alcohol in% by weight, the strength of which in % by volume is 93.6, using alcoholemetric table and the method of interpolation.

Answer: 90.458% (m).

4. What is the concentration in % by weight of 96.65% (by volume) of alcohol?

Answer: 94.79% (m).

5. Using the interpolation method, calculate the % by weight of 60% (by volume) of alcohol.

Answer: 52.09% (m).

III. Dilution of alcohol using alcoholometric tables

1. Determine the mass in kg of 96% alcohol and water to obtain 10 kg of 70% alcohol.

Answer: 6.65 kg, 3.35 kg

2. Calculate the number of liters of water required to dilute 5 liters of 65% alcohol when obtaining a 50% aqueous-alcoholic solution.

Answer: 1,555 liters of water

3. Determine the number of liters of water required to dilute 10 liters of 50% alcohol in the preparation of a 30% solution.

Answer: 6.74 liters

4. Calculate the volumes of 95% alcohol and water required for the preparation of 10 liters of 40% alcohol.

Answer: 4.21 liters and 6.07 liters

5. Calculate the amount of 35% alcohol and water required to prepare 3.5 liters of 30% alcohol.

Answer: 3.0 liters of alcohol 35% and 0.501 liters of water

IV. Dilution and strengthening of aqueous-alcoholic solutions using the "asterisk" rule and dilution formulas

1. How many liters of 96.1% ethanol is required to make 100 liters of 50% alcohol?

Answer: 52,029 l.

2. How many liters of 40% alcohol can be prepared from 30 liters of 95.3% solution?

Answer: 71,475 l.

3. How much 80% and 12.5% alcohol should be taken to prepare 150 liters of 50% alcohol?

Answer: 83.333 L 80% and 66.667 L 12.5%.

4. In what ratios should 90% and 45% alcohols be mixed to obtain 60%?

Answer: 15:30 (1:2).

5. How much 45% alcohol will be obtained from 86 liters of 23% alcohol, using an 88% solution to strengthen it?

Answer: 130 L.

6. The pharmaceutical factory has 15 liters of 15% alcohol, 20 liters of 95% alcohol. A 50% aqueous-alcoholic solution should be prepared from them. How much water should be used in this case, how much volume of solution will be obtained (excluding contraction)?

Answer: 7.5 liters of water, 42.5 liters of 50% alcohol.

7. It is necessary to prepare 15 kg of 40% alcohol. How many kg of alcohol 96.5% will it take?

Answer: 5,282 kg.

8. How many liters of 50% alcohol can be prepared from 21.15 liters of 21% recuperate, using 92.3% alcohol to strengthen?

Answer: 35.65 L.

9. How many kg of 85.92% (by weight) of alcohol can be prepared from 141l of 96.55% (by volume) and a sufficient amount of 20.0% (by volume) of alcohol?

Answer: 15.75 kg.

RECOMMENDED LITERATURE

Regulatory

1. Державна Фармакопея України: у 3 т. Державне підприємство "Український науковий фармакопейний центр якості лікарських засобів". – 2 вид. - Харків: Державне підприємство "Український науковий фармакопейний центр якості лікарських засобів". 2014. - Т.1. - 1128 с.: - Т.2. - 724 с.: - Т.3. - 732
2. European Pharmacopoeia 8.0 [8th edition] / European Directorate for the Quality of Medicines & HealthCare. – Strasbourg, 2013. – 3638 p.
3. Good manufacturing practices for pharmaceutical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-second report. Geneva, World Health Organization, 2022, Annex 1 (WHO Technical Report Series, No. 823).

Basic

1. Pharmaceutical Formulation. The Science and Technology of Dosage Forms. e-book / ed. by Geoffrey D. Tovey. – The Royal Society of Chemistry, 2019. 409 p.
2. Loyd V. Allen Jr. The Art, Science, and Technology of Pharmaceutical Compounding, 6th edition. – Washington, D.C. : APhA, 2020. – 699 p.

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