**MINISTRY OF HEALTH OF UKRAINE**
**BOGOMOLETS NATIONAL MEDICAL UNIVERSITY**

# *Introduction to pharmacy*

**(Pharmacy technology of drugs)**

**TEACHING AND METHODOLOGICAL MANUAL**

**for classroom work**

**for the second master's level of higher education**

**in the specialty 226 "Pharmacy, industrial pharmacy"**

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The textbook "Introduction to Pharmacy" is recommended for teachers and students of pharmaceutical and medical schools, pharmacists of pharmacies.

The textbook covers the requirements of regulatory and technical documents on the sanitary and anti-epidemic regime of pharmacies and the rules for the manufacture of medicines in pharmacies, the structure and functions of a pharmacy, general requirements for the manufacture of sterile and non- sterile medicines in pharmacies.

To control the level of mastery of the material, situational tasks and sample computer tests are provided.

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**Contents**

## List of abbreviations

| | |
|---|---|
| VDD | higher daily dose |
| BP | manual scales |
| VRD | higher single dose |
| SFSU | State Pharmacopoeia of Ukraine |
| DRUGS | medicinal product |
| PHARMACIES | health care facility |
| MINISTRY OF HEALTH | Ministry of Health |
| NTD | regulatory and technical documentation |
| PPC | passport of written control |
| TFS | temporary pharmacopoeial article |
| FS | pharmacopoeial article |
| GMP | (Good Manufacturing Practice - a system of norms, rules and guidelines for production |
| GPP | (Good pharmacy practice) - a guarantor of the quality of medicines |

## Introduction

Introduction to Pharmacy as an academic discipline lays the foundation for students' knowledge of the general requirements for the practical work of a pharmacist and is one of the links between theoretical disciplines that form the profile of a pharmacist, and is intended to improve the professional and theoretical training of highly qualified specialists in the field of pharmacy.

**The task of the discipline is to** teach students:

- To understand the importance of the requirements of regulatory documents on the sanitary and epidemiological regime of pharmacies and the rules for the manufacture of medicines in a pharmacy, know and comply with them;
- To work with weighing instruments and other small mechanization equipment;
- To dose and package medicinal and excipients of different consistencies;
- To pack and prepare for dispensing various types of dosage forms prepared by a pharmacist.

# SANITARY AND ANTI-EPIDEMIC REGIME OF THE PHARMACY AND PHARMACEUTICAL PROCEDURE. PRODUCTION FACILITIES OF THE PHARMACY, THEIR CLEANING. PERSONAL HYGIENE OF THE STAFF

The main requirements for the sanitary regime of pharmacies are regulated by Order No. 275 of 15.05.06 "Instruction on the sanitary and anti-epidemic regime of pharmacies" [14].

The sanitary condition of the premises and equipment of the pharmacy shall comply with the requirements of the sanitary and anti-epidemic regime of pharmacies. Premises and equipment shall be subject to cleaning, disinfection, and deratization in accordance with written instructions approved by the licensee.

Disinfectants registered in Ukraine and authorized by the Ministry of Health of Ukraine are used to treat the premises and maintain the equipment.

The floor is cleaned at least once per shift, and walls and doors are cleaned at least once a week with disinfectants. The ceiling is cleaned from dust once a month using the wet method [14].

Window panes, frames and the space between them are cleaned at least once a month. At the same time, windows are cleaned from the outside only in the warm season.

The equipment of pharmacy facilities is cleaned from the outside every day, and the cabinets for medicines in the storage rooms for medicines (material rooms) are cleaned from the inside as needed, but at least once a week [14].

Hand washing sinks and sanitary facilities are cleaned and disinfected every day.

If necessary, the premises and equipment are cleaned more frequently.

To perform wet cleaning or disinfection, you must have two containers labeled "1" and "2". Container "1" is filled with a cleaning or disinfectant solution, and container "2" with clean tap water.

The rags and napkins are moistened with the solution contained in the container "1" and thoroughly wipe the area (2+1) $m^2$ of the previously washed surface. Then they are rinsed in container "2", squeezed out, saturated again with the solution from container

"1" and new surface areas are washed.

Change the detergent or disinfectant according to the instructions for use, change the water in the container "2" as it becomes contaminated, but not less than after treating 60 m of$^2$ surface.

Separate equipment (buckets, basins, brushes, rags, etc.) is allocated for cleaning different areas (customer service hall, production facilities, sanitary facilities), which is labeled and used strictly for its intended purpose. It is stored in a specially designated place (room, closet, etc.) separately.

After disinfection and drying, wipes intended for cleaning production equipment are stored in clean, labeled, tightly closed containers.

A sanitary day is held once a month. In addition to a thorough cleaning, minor repairs, disinfestation and deratization measures may be carried out on sanitation days.

Pharmacy staff must adhere to the following rules:

- When you come to work, take off your outerwear and shoes in a separate dressing room;
- Before starting work in the second dressing room, remove personal belongings, hang them in individual closets and wash your hands;
- put on technological clothing (gown, cap, apron) and special shoes, which are stored in separate cabinets under bactericidal irradiation (gowns in a hanging state), wash and disinfect hands.
- hand treatment should be carried out before and during work, but no more than 3 times per shift.
- take off your robe before going to the restroom, and wash and sanitize your hands thoroughly after using the toilet;
- do not leave the pharmacy in technological clothing and footwear.

The objects of bacteriological control in pharmacies are:

- purified water and water for injections;
- medicines;
- pharmacy utensils, corks, and other auxiliary materials;
- inventory, equipment;

- hands and clothes of the staff;
- air environment.

Sterilization, disinfection and antisepsis are central to the system of measures aimed at maintaining the sanitary and anti-epidemic regime in pharmacies and pharmaceutical enterprises.

The objects of sterilization are injectable solutions, powders, primary packaging materials and auxiliary materials, culture media for controlling the microbiological purity and sterility of medicines, membrane filters, etc. The most commonly used methods are physical (thermal, radiation, ultrasonic, high and ultra-high frequency currents, laser and electronic UV radiation), less commonly chemical (solutions of substances or gases) and mechanical (filtration).

When disinfecting an object (room surfaces, technological and sanitary equipment, communications, cleaning equipment, etc.), chemicals are most often used, and less often physical and mechanical means. Antiseptic agents should ensure the destruction of pathogenic and saprophytic microorganisms on the skin of the hands of personnel. For this purpose, 76% ethyl alcohol, 2.4% solution of C-4 formulation (a mixture of hydrogen peroxide and formic acid solutions), 1% iodopyrone, octenisept, and others are used.

Disinfectants and antiseptics should be alternated every 1-3 months to prevent the emergence of resistant variants of germs and their spread.

The effectiveness of disinfection measures is monitored using bacteriological (flush method), physical and chemical methods. The latter is based on the change in color of the indicator substance when it interacts with the disinfectant or the color and aggregate state when exposed to temperature.

## Requirements for the pharmacy premises

**For pharmacies engaged in the production (manufacturing) of medicinal products, the** pharmacy premises include all the premises necessary for the retail sale of medicinal products, as determined by the Rules for the manufacture of medicinal products in a pharmacy, approved by the Order of the Ministry of Health of Ukraine No. 441 dated July 1, 2014 [13].

The location of the production facilities must comply with the sequence of

operations of the production process and the requirements for cleanliness, and prevent the intersection of technological, material and human flows. Measures must be taken to prevent unauthorized persons from entering the premises. Areas of production (manufacturing), storage and quality control of raw materials and finished medicinal products should not be used as passageways for personnel who do not work there.

The business entity shall take measures to validate the technological processes carried out in the production facilities and methods of quality control of raw materials and manufactured medicinal products. The business entity shall ensure the mandatory composition and area of the production and auxiliary premises of the pharmacy:

- a pharmacy manufacturing non-sterile medicinal products must have such separate production facilities [13]:

assistant's room - at least 20 square meters; at least 8 square meters to produce purified water; for washing and sterilizing dishes - at least 8 square meters;

a separate room - an office of a pharmacist-analyst or a separate workplace of a pharmacist-analyst in the assistant's room;

- a pharmacy manufacturing sterile medicinal products under aseptic conditions shall have all the above mentioned premises and additionally equipped with such production facilities:

for the production of water for injection - with an area of . square meters or more (can be combined with a room for the production of purified water);

aseptic assistant room with a gateway - from 13 (10 + 3) square meters; for sterilization of manufactured medicines - from 10 square meters; premises for control labeling and hermetic sealing of medicinal products - from . mkv10 .

For pharmacies that manufacture only eye drops under aseptic conditions, it is not mandatory to have separate rooms for sterilization of manufactured medicinal products and for control labeling and hermetic sealing of medicinal products in the aseptic unit.

- office and amenity facilities for staff (staff room, dressing room (staff room and dressing room can be combined), restroom), a separate room or closet for storing household and other equipment;

- rooms/areas for storing raw materials, in-pharmacy preparations (concentrates,

semi-finished products), finished medicines, auxiliary materials, containers, etc;

In the customer service area, non-prescription medicinal products may be placed in display cases, glass and open cabinets, etc. Prescription medicinal products shall be stored in separate cabinets (which are not accessible to consumers) with the obligatory marking "Prescription". Related products shall be placed on display cases, in cabinets, separately from medicinal products. Advertising (in any form) of prescription medicinal products is prohibited.

**Requirements for the premises and equipment of a pharmacy engaged in the production (manufacturing) of sterile medicinal products:**

- manufacturing (production) of sterile medicinal products should be carried out in clean areas (premises) under aseptic conditions;
- The aseptic unit consists of an airlock, an aseptic assistant room, a room for obtaining water for injection, packaging, capping and sterilization of medicines. It is possible to combine the assistant and packaging rooms;
- the premises of the aseptic unit should be isolated from other premises of the pharmacy as much as possible, rationally interconnected to ensure work processes and reduce the flow of medicines during their production (manufacturing); equipped with gateways that protect the air of the aseptic room from contamination from the outside;
- windows in the aseptic assistant's room must be hermetically sealed;
- the aseptic unit is equipped with supply and exhaust ventilation with a predominance of air inflow over exhaust, which provides at least 10 times the air exchange per hour. The air ventilation system should take into account the size of the room, equipment and personnel in it, and have appropriate filters;
- only designated pharmacy personnel should have access to the aseptic unit.

**Requirements for pharmacy equipment**

Pharmacy production facilities must be equipped with equipment to ensure proper storage of medicinal products (cabinets, racks, refrigerators, safes, etc.) and means to control the temperature and relative humidity of the air.

The devices and apparatus available in the pharmacy must have technical passports

and be subject to timely maintenance and inspection.

Measuring instruments used must be metrologically certified, have a state verification stamp and be verified in accordance with the established procedure.

To ensure appropriate storage of medicinal products during sale, the public service hall should be equipped with equipment (facilities) to ensure the appropriate temperature regime at all times and means for temperature control. Workplaces of employees should be equipped with devices to protect employees from direct drip infection.

The production facilities of a pharmacy manufacturing medicinal products must be provided with the necessary equipment and facilities for the proper manufacture and storage of medicinal products (production equipment, laboratory equipment,

Measuring devices, cabinets, racks, refrigerators, safes, etc.) and technical means for constant temperature and humidity control. It is forbidden to place equipment and facilities in the production premises that are not related to the work performed in them.

Equipment should be positioned and operated in such a way as to minimize the risk of error and to ensure efficient cleaning and operation to avoid contamination and any adverse effect on the quality of the medicinal product.

The production facilities of a pharmacy engaged in the production (manufacturing) of medicinal products should be equipped with mechanical supply and exhaust ventilation to achieve appropriate air purification.

The cloakroom shall be appropriately equipped to ensure the maintenance and safety of personal and work clothes of the staff in accordance with the requirements of the sanitary and anti-epidemic regime of pharmacies.

**TESTS**

1 In accordance with the requirements of the GMP, a set of measures aimed at preventing microbial contamination of medicinal products must be followed in the manufacture of medicinal products. What is this set of measures called?

a Disinfection.
b Antiseptic.
c Asepsis.
d Sterilization.
e Deratization.

2 According to modern concepts, the most complete release of the object from microorganisms is achieved:

a During sterilization.
b With antiseptic.
c For disinfection.

d When washing
e When wiping with a damp cloth

3 The objects of sterilization are:
a Primary packaging materials.
b Injectable solutions.
c The hands of the staff.
d Technological clothing.
e Culture media.

4 The objects of disinfection are:
a Equipment surfaces.
b Pharmacy utensils.
c The hands of the staff.
d Indoor air.
e Technological clothing.

5 The objects of hygienic antisepsis are:
a Indoor air.
b Pharmacy utensils.
c Medicines.
d The hands of the staff.

6 There are requirements for chemical disinfectants:
a Selectivity of antimicrobial action.
b Wide range of antimicrobial action.
c Stability during storage.
d Microbial type of action
e Microbicidal type of action.

7 Sterilization is aimed at releasing an object from microorganisms:
a Pathogenic.
b Conditionally pathogenic.
c Saprophytic.
d Of all kinds.
e No.

8 Violation of the sanitary and epidemiological regime in the production of injectable solutions may be the cause of their pyrogenicity. Specify the sign of a pyrogenic reaction:
a Hypertension.
b Hypothermia.
c Hyperthermia.
d Hypotension.
e No signs of the disease

9 Select the method of sterilization of pharmacy personnel's technological clothing.
a Steam under pressure.
b Dry heat.
c The steam is fluid.
d Tindalization.
e Membrane filtration.

## SITUATIONAL TASKS

Task 1.

It is necessary to carry out preventive disinfection of the pharmacy's production facilities. Specify the disinfectants, disinfection regimens (solution concentration, exposure), and processing method.

Sample answer

When disinfecting an object (room surfaces, technological and sanitary equipment, communications, cleaning equipment, etc.), chemicals are most often used. Antiseptic agents should ensure the destruction of pathogenic and saprophytic microorganisms on the skin of the hands of

personnel. For this purpose, 76% ethyl alcohol, 2.4% solution of C-4 formulation (a mixture of hydrogen peroxide and formic acid solutions), degmine, 1% iodopyrone, 0.1% octeniderm, octenisept, and others are used.

The floor is cleaned at least once per shift, and the walls and doors are cleaned at least once a week with disinfectants. The ceiling is cleaned from dust once a month using a wet method. Window panes, frames and the space between them are cleaned at least once a month. At the same time, windows are cleaned from the outside only in the warm season.

Task 2.

It is necessary to disinfect rubber and plastic products in a pharmacy. Specify the disinfectants, disinfection regimen (solution concentration, exposure), and processing method.

Task 3.

Disinfect cleaning equipment in a pharmacy. Specify the disinfectants, disinfection modes (solution concentration, exposure), and processing method.

Task 4.

It is necessary to disinfect metal and glass products in a pharmacy. Specify the disinfectants, disinfection regimens (solution concentration, exposure), and processing method.

Task 5.

It is necessary to disinfect sanitary equipment (sinks, toilets, etc.) in the pharmacy. Specify the disinfectants, disinfection regimens (solution concentration, exposure), and processing method.

Task 6.

It is necessary to disinfect the technological footwear of pharmacy personnel. Specify the disinfectants, disinfection regimens (solution concentration, exposure), and processing method.

Task 7.

It is necessary to sterilize pharmacy glassware. Suggest methods, modes, equipment, and conditions for sterilization, as well as methods for monitoring its effectiveness.

Task 8.

It is necessary to sterilize filter paper and parchment in a pharmacy. Suggest the method, mode, equipment, and conditions of sterilization, as well as methods for monitoring its effectiveness.

Task 9.

In a pharmacy, it is necessary to sterilize products made of polymeric materials. Suggest methods, modes and conditions of sterilization, methods of monitoring its effectiveness.

Task 10. It is necessary to carry out preventive antiseptic treatment of hands of pharmacy staff. Suggest antiseptic agents, their concentration, method of treatment.

# TYPES OF CONTAINERS AND PACKAGING; REQUIREMENTS FOR PROCESSING, WASHING AND DRYING OF PHARMACY UTENSILS. PRODUCTION OF PURIFIED WATER, QUALITY CONTROL AND STORAGE CONDITIONS

Medicinal products, as well as prepared medicinal products, depending on their aggregate state and properties, are stored and released from pharmacies in appropriate containers.

Containers are used to protect medicinal products and drugs from external factors: light, temperature, oxygen, carbon dioxide, air and moisture. It should also be borne in mind that the properties of the packaging used affect the shelf life and quality of medicines, as the material from which it is made can interact with medicines [1-4].

Containers and closures must meet the requirements for cleanliness, protective properties, environmental resistance, appearance, and adhesion properties.

*The purity of the material* includes the absence of carcinogenic, toxic substances and foreign odors that can be adsorbed by medicinal substances. All materials must pass sanitary and toxicological tests, and the Ministry of Healthcare of Ukraine must authorize their use in contact with medicinal products.

*Indicators of the material's protective properties* include permeability to water vapor, volatile substances, gases (atmospheric and those released by medicines), water, alcohol, oils, fats, organic substances, etc., as well as the material's adsorption of those ingredients of medicines that tend to penetrate the material.

Environmental *resistance indicators of materials* include resistance to atmospheric factors (light, temperature, relative humidity) and mechanical stress (punctures, compression, shock, vibration), the effects of drugs, mold, microorganisms, and the absence of chemical adsorption and diffusion interactions with the packaged drug.

*Appearance indicators* include color and uniformity of color, surface smoothness and cleanliness (absence of grease and mechanical contamination, mold, corrosion, etc.).

*Adhesion properties* characterize the ability of materials to be joined with adhesives or by thermal welding.

Depending on the type of materials, they are subjected to verification requirements

for a particular group of indicators.

Depending on the purpose, containers can be: prescription, stationary, and material.

**Prescription** - for dispensing medicines to patients, often in small volumes, cheap and easy to use. Various liquids are dispensed in vials without ground (ground) stoppers with a capacity of 5 to 500 g. Injectable solutions are available in neutral glass vials with rubber stoppers and metal caps. Medicinal products of thick and ointment-like consistencies are sold in jars made of glass, porcelain, plastic and other materials with a capacity of 5 to 500 g [1].

**Stationary - the** so-called "vials" - is intended for storing medicines in the assistant's room. It is made of glass and porcelain with lapped stoppers. Its volume is from 0.5 to 2 kg. Bulk, liquid, thick, and ointment-like substances are stored in such containers [2].

For storage of viscous liquids (castor oil, syrups, ichthyol, etc.), special "collar" vials are used, in which there is a rim around the outer neck surface, on the inner surface of which a recess is made for the viscous liquid to drain. For storing substances that emit caustic vapor (fuming nitric acid, mustard oil, concentrated ammonia), vials with a lapped stopper and a lapped cap are used.

**Material** - designed for transportation and storage of medicines in basements and material rooms of pharmacies [1].

Pharmacy containers are made of the following materials: glass, polymers, porcelain, metals, cardboard and paper. The main materials for closures are cork, rubber, polymers, paper, and glass.

## Washing and disinfecting dishes

The quality of medicines and their shelf life largely depend on the cleanliness of the utensils. Regardless of the source of supply, all utensils should be thoroughly cleaned, degreased, washed and disinfected. It is washed in the washing room, where sinks for washing dishes intended for injection solutions and eye drops, internal and external dosage forms should be separated and labeled. Cylinders, measuring cylinders, watering cans, mortars, etc. used in the preparation of dosage forms are washed in them. Do not

wash your hands in these sinks. Warm aqueous mustard suspension (1:20) and sodium bicarbonate solution of 0.5-2% with soap chips may be used as detergents for manual dishwashing. Detergents may be used for automatic and manual washing of pharmacy tableware.

After soaking in the detergent solution, the dishes are washed in the same solution using a ruff or a washing machine. To ensure complete rinsing of detergents containing surfactants, rinse the dishes 5 times with running tap water and 3 times with purified water, filling the bottles and vials completely. With automatic rinsing, depending on the type of washing machine, the exposure time in the rinsing mode is from 5 to 10 minutes.

After treatment with mustard or sodium bicarbonate detergent solutions with soap and water, five times washing with water (2 times with tap water and 3 times with purified water) is sufficient.

Glass containers intended for packaging of eye drops, eye ointments used for the treatment of wounds and mucous membranes, after processing as described above, should be sterilized with hot air in dry heat sterilizers (drying cabinets) at 180°C for 60 minutes.

The pharmacy may also receive tableware from infectious disease departments of hospitals, which must be disinfected with appropriate solutions: 1% activated chloramine solution; freshly prepared 3% hydrogen peroxide solution containing 0.5% detergents, etc.

When working with perhydrole and chloramine, follow the safety rules: wear gloves, goggles and a four-layer gauze bandage. If perhydrol and chloramine come into contact with the skin, rinse them off immediately with water. After disinfection, the utensils are rinsed with tap water and then purified water and dried at a temperature of at least 80°C. Reuse of the same disinfectant solution is not allowed.

**Quality control of washed dishes.** The degree of cleanliness of the washed dishes is checked visually for the absence of foreign inclusions and the uniformity of water flowing from the walls of the vials after rinsing.

After rinsing the corks, the rinse water should also be free of mechanical inclusions in the form of fibers or droplet inclusions visible to the naked eye. To determine the mechanical inclusions in the rinse water after rinsing the plugs, a 200 ml

wash is taken into a 250 ml conical flask with a lapped stopper, shaken for 5 seconds and, after the end of the release of air bubbles, brought into the viewing area and viewed for 30 seconds.

The complete rinsing of synthetic detergents and detergent-disinfectants is determined by the pH value using the potentiometric method. After the last rinsing of dishes or corks, the pH of the rinsing water should correspond to the pH of the source water.

Plastic containers are also subjected to sanitization. Canisters, jars, vials, dropper bottles, vials, test tubes are washed for 2-3 minutes in a 0.5% solution of laundry or bath soap, detergent solution, or mustard solution heated to 60±5°C. The washed products are rinsed 4-5 times with tap water to remove detergents, then kept for 20 minutes in tap water heated to 60±5°C or for 2-3 hours in tap water at room temperature, and then rinsed 2-3 times with purified or desalted water. It is allowed to use brushes when washing products. Do not soak the products in detergent solution and do not use abrasives (sand) and other water-insoluble substances. Detergents must not have a perfume odor.

Products made of low-density polyethylene (LDPE) and its compositions with polyisobutylene (PIB) intended for packaging of medicinal products containing fats are dried at a temperature not exceeding 40°C; polystyrene products for the same purpose are dried in air at room temperature.

Disinfection of plastic containers is carried out in cases stipulated by the regulations for the production of medicinal products. Plastic products are preliminarily subjected to sanitary and hygienic treatment (drying may be excluded), then placed in a special vessel, where they are kept in a 6% hydrogen peroxide solution for 40 minutes at room temperature, rinsed 4-5 times with freshly prepared purified or desalted water, and then stored in the same vessel, closed with a lid, but not more than 24 hours before use. It is allowed to fill containers with a volume of 0.5 liters or more instead of processing in a special vessel with a 6% solution of hydrogen peroxide to the top.

Products made of heat-resistant plastics (polypropylene, high-density polyethylene, polyethylene blend) may be disinfected by boiling them in water or by treating them with flowing steam for 1 hour. They must be disassembled and immersed in water completely.

Autoclaving of these products is allowed after preliminary checking of a part of the products from the specified batch for the absence of deformation after autoclaving.

Plastic products should be stored indoors away from heating systems and heating appliances in tightly closed dustproof cabinets painted with light oil paint inside. Exposure to direct sunlight and bactericidal radiation is not allowed. The room where polymeric products are stored should be free of ammonia vapors, phenol, formaldehyde, chloral hydrate, hydrogen chloride, essential oils and other volatile substances with a strong odor, unpleasant taste or high chemical activity.

Finished medicinal products placed in appropriate pharmacy containers, depending on their aggregate state and properties, are sealed with stoppers (cork, rubber, plastic, glass), lids and caps.

Today, plastic products are widely used as a closure material: screw-on and pull-on lids, caps, and gasket stoppers. They are intended for sealing vials, jars, test tubes, vials, etc. Products manufactured in accordance with OST 64-2-87-72 and approved by the Ministry of Health for use in pharmacy should be used for sealing medicines.

High and low density polyethylene, a mixture of low density polyethylene with polyisobutylene (PIB), polypropylene, polystyrene, aminoplastic, cardboard with a double-sided film coating of low density polyethylene, etc. are used to make closures. The type of material used is specified in the accompanying documents.

## Obtaining purified water (Aqua purificata)

**Purified water can be produced by various methods, namely:**

- by distillation;
- ion exchange;
- electrolysis;
- reverse osmosis.

***Of all the methods, the most common is the production of purified water by distillation (distillation), for which special distillation apparatus, aqua-distillers, are used*** [4]**.**

The essence of the distillation method is that water is heated to turn into steam,

which condenses, and the resulting condensate is collected in appropriate receivers.

According to the design, distillation apparatus used to produce purified water are batch and circulating (continuous) distillation apparatus. Distillation stills consist of three main parts: evaporator, condenser and collector. Electric distillers - DE-25, DE-10, etc., and fire distillers - DT-10, DTVS-4 (Fig. 1).

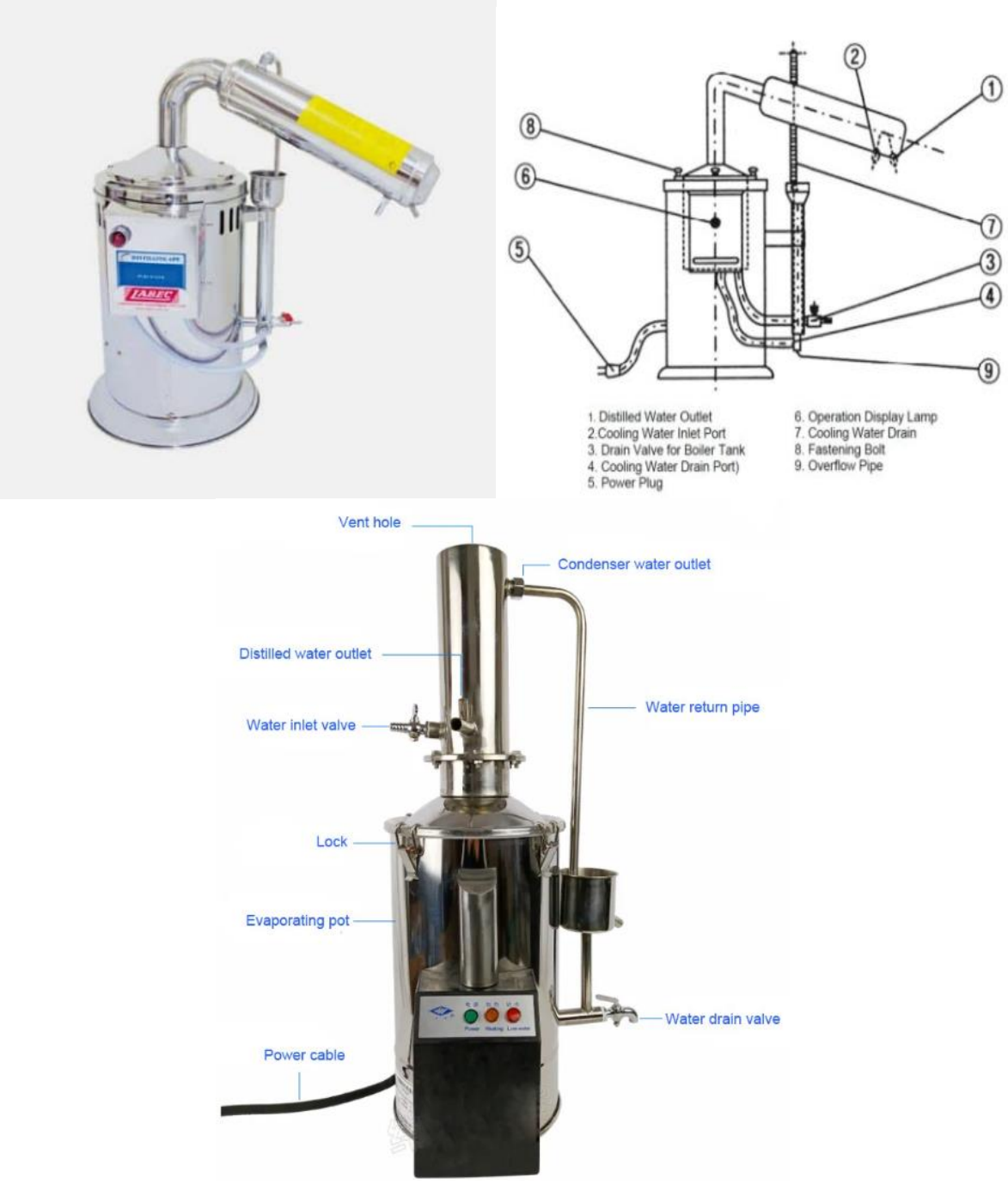


**Fig. 1. Scheme of the D-25 distiller**

Every day in the pharmacy, the water from each cylinder is checked by an analytical chemist for the absence of chlorides, sulfates, calcium salts, etc. in accordance with the

FS. In addition, the quality of the purified water is periodically checked by conducting samples:

- to the control and analytical laboratory for a full chemical analysis once a quarter;
- to the local sanitary and bacteriological laboratory for bacteriological testing - 2 times a quarter.

Purified water is stored under aseptic conditions for no more than 3 days in well-washed, sterilized and sealed chemically resistant glass cylinders in a cool place.

**SITUATIONAL TASKS**

Task 1

A pharmacist measured purified water, ammonium chloride solution, simple syrup, sodium bromide solution, and finally added valerian tincture to a dispensing bottle. Did he violate the rules for preparing the mixture?

Sample answer.

The pharmacist violated the rules for preparing the mixture by mixing the ingredients in the wrong order.

Task 2

When checking the prepared mixture, the pharmacist-technologist found that its volume is 196 ml instead of theoretically calculated 200 ml. Can this medicinal product be released?

Task 3

A pharmacist has labeled a mixture consisting of magnesium sulfate, potassium bromide solution, valerian tincture, and water with the label "Internal" only. Did the pharmacist take into account the physical and chemical properties of the ingredients and the type of dispersion system?

Task 4

The pharmacist measured out solutions of caffeine benzoate, sodium bromide, purified water, and valerian tincture into a stand, mixed well, and poured into a dispensing vial. Evaluate the pharmacist's actions.

Task 5

A pharmacist has measured purified water into a dispensing bottle, dissolved codeine phosphate, added adoniside, sodium bromide solution, and labeled the drug for dispensing with the label "Internal". Point out the mistakes made.

Task 6

A pharmacist measured purified water, valerian tincture, sodium benzoate solution, and sodium bicarbonate solution into a dispensing bottle and mixed them well. Did he do the right thing? The pharmacist aged the stand, weighed 200.0 of water into it and dissolved 4.0 of sodium bromide in it, transferred it to the dispensing bottle. Evaluate the correctness of his actions.

Task 8

A pharmacist dissolved 10.0 magnesium sulfate in 200 mL of water and filtered it into a vial for dispensing. Did he choose the right technology?

Task 9

During the preparation of a tincture mixture, the drug product became cloudy. The pharmacist strained the mixture and prepared it for dispensing. Did he do the right thing?

Task 10

When preparing 200 ml of 10% calcium chloride solution, the pharmacist weighed out 20.0 of the crystalline drug and dissolved it in 180 ml of water. Is the drug preparation correct?

## PHARMACIST'S WORKPLACE. DOSAGE IN PHARMACY PRACTICE. WEIGHING INSTRUMENTS USED IN PHARMACY PRACTICE

The main operations used in the preparation of medicinal products are dosing, which involves measuring the mass of a substance, and measuring it in certain portions (doses). In pharmacy practice, the most commonly used dosing methods are weighing and measuring by volume and drops [1-4].

The pharmacological effect of medicinal products, and thus their therapeutic effect on the body, depends on the accuracy of these operations. Dosing is carried out using special devices that are subject to appropriate requirements, and the metrological system of measures is used, which is generally accepted and mandatory in our country.

## DOSAGE BY WEIGHT

**Types of scales.** One of the most common methods of dosing is weighing, which is performed using a balance [1].

A balance is a device designed to determine the weight of medicines by comparing it with mass standards (conventionally accepted units - weights) [1].

From the point of view of metrological characteristics (stability, stability of readings, accuracy and sensitivity), scales are distinguished:

- metrological scales are designed to compare the mass of working standards with the state standard. These are scales of the highest accuracy, of a special design, and their oscillations are monitored from the next room using special optical devices;
- sample weights - for checking and verifying weights;
- analytical - for weighing in precise chemical analyzes;
- technical - 1st, 2nd and 3rd classes [1].

For the preparation of medicinal products in pharmacy practice, equal-shouldered scales of the 2nd class are used: technical pharmacy (container) and hand-held pharmacy scales. In the material room, ordinary tabletop cup scales are used, and for large masses - decimal and hundredth scales.

Pharmacy manual balances (BP) (GOST 7328-61) are designed for dosing by weight of dry medicinal substances in amounts from 0.02 to 100.0 g, as well as for technical analyzes. Depending on the permissible maximum load, BPs are available in several

standard sizes: BP-1, BP-5, BP-20 and BP-100.

RTs consist of a rocker arm that carries the arrow and rests its support prism on a ring-shaped cushion pressed into a ring cage. The cheeks protect the prism from slipping off the cage. At the ends of the rocker arm are load-lifting prisms, on which earrings are worn. Flat massive cups are suspended from the latter by silk cords.

For sanitary and hygienic reasons, it is advisable to use thin threads made of synthetic materials or a stainless steel chain to hang the scale cups. Manual scales do not have a reading scale. The moment of equilibrium is determined by the coincidence of the pointer with the cage.

## Kettlebells and weights

A scale is a set of weights. Weights are measures of a clearly defined mass (weight) that are used in weighing. For calibration and verification of scales [2].

When weighing a body, we compare its mass with the value accepted as a unit in the international metrological system of measures. The unit of mass is the kilogram. In everyday pharmacy practice, the basic unit of measurement for the mass of a drug is the gram, a thousandth of a kilogram. The names of lower units of gram fractions are formed using the Latin prefixes "deci" (0.1), "centi" (0.01), "milli" (0.001). In a recipe, the word "gram" or its symbol "g" is omitted. Any number in a recipe that is indicated by decimal digits, whole or fractional, is taken to be an expression of the amount of a substance in grams, unless otherwise indicated.

Depending on the purpose, there are different types of kettlebells;

- exemplary, made of gold, platinum and copper alloys;
- analytical, made of copper alloys and steel with a carefully polished surface coated with gold, platinum, nickel, or chrome;
- technical kettlebells of the 1st, 2nd and 3rd classes.

In pharmacy practice, technical weights of the 2nd class are used in the form of special sets (weights): large (gram), containing weights from 1.0 g to 500.0 g, and small (milligram), containing weights from 0.01 g to 0.500 g. Gram weights are made of brass or carbon steel with a nickel or chrome coating to prevent oxidation. The surface of the

weights must be smooth, without cracks, scratches, etc. Weights have the shape of straight cylinders with heads. Milligram weights are made of melchior or aluminum in the form of various plate shapes: triangles, squares, hexagons.

To protect them from external influences and damage, the weights are stored in special boxes with nests.

**Fig. 2. A set of kettlebells and weights**

Kettlebells must be kept clean, for which they are periodically cleaned of dust and grease by washing them in soapy warm water or in organic solvents (alcohol, gasoline), and then thoroughly wiped dry with a soft cloth. They should be picked up only with tweezers; it is strictly forbidden to clean the kettlebells with various polishing agents.

**Rules for weighing on technical and manual balance scales**

Before working, wash your hands thoroughly (Fig. 3), inspect the balance, wipe it with a gauze cloth moistened with an alcohol-ether mixture, and make sure it is in balance in an unloaded state. As a rule (for convenience), the weights are placed on the left cup of the balance, and the medicinal product to be weighed - on the right (Fig. 4.)

**Fig. 3. Washing hands before weighing**

When weighing powdery substances on a hand balance, place them directly on a cup, and thick substances on a circle of parchment or filter paper (previously aged).


**Fig. 4. Rules for weighing medicinal substances**

Weighing any substances directly on the balance is not allowed; use appropriate containers (vials, cans, capsules, etc.). To avoid errors, we do not recommend using

weights for taring.

Bulk substances are weighed directly from the caliper by lightly tapping it with the index finger of the right hand. The substance is added in small portions so that the balance threads are not contaminated. As the moment of equilibrium is approached, the portions of the substance to be added are reduced to prevent a possible overdose of the powder. If necessary, the substance is sampled using a plastic or celluloid plate. After weighing, first remove the weights from the balance (and count the weight of the weights a second time), and then the drug substance. After each weighing of the medicinal substance from the caliper, the neck and stopper of the caliper, as well as the balance scale, are thoroughly wiped with a gauze cloth [1-2].

## DOSAGE BY VOLUME AND DROPS

The volumetric method of dosing liquid substances in the preparation of medicines is widely used in pharmacy practice. It is more cost-effective, greatly simplifies and facilitates the work of a pharmacist. In addition, patients take all liquid medicines for internal use not by weight, but by volume (spoons, drops, etc., or milliliters for medicines administered by means of a lance) [1].

Measuring devices. In the preparation of liquid dosage forms, dosing is done using special measuring utensils graduated in a certain number of milliliters. The International System of Units (SI) uses the cubic meter (1 m-1) as a unit of capacity. In pharmacy practice, such a unit is the milliliter (1 ml), which is equal to a millionth of a cubic meter (1 ml = 1 x10'9 m3). Measuring utensils must bear the mark of the State Industry Standard.

Cylinders, beakers, measuring flasks, pharmacy burettes, and pipettes are used to dispense water (the mass of 1 ml of water at room temperature is almost equal to 1.0 g) and other liquids of the same density as water. Thick, viscous, sedentary liquids (fatty oils, syrups, glycerin) are usually dosed by weight [1].

Measuring flasks (with a mark on the neck) come in different capacities (Fig. 5). They are most commonly used in the preparation of concentrated solutions for burette systems and injection solutions.


**Fig. 5. Measuring flask** **Fig. 6. Measuring cylinder**

Measuring cylinders (cylindrical vessels), beakers (conical vessels) - for dispensing relatively large amounts of liquids when no special precision is required (Fig. 6).

Pharmacy burette. Burettes are designed for precise measurements of water, solutions and in the form of a burette system (a set of special burettes and pipettes) are used in pharmacies for the preparation of medicines from concentrated solutions (Fig. 7).

**Fig. 7. The ticketing system**

A burette is a glass graduated tube connected to a feeding tube with a feeding vessel. The pharmacy burette works as a liquid dispenser and is designed for accurate measurements of water and various aqueous and water-alcohol solutions of medicinal

substances.

Pharmacy burettes are made with a capacity of 10, 25, 60, 100 and 200 ml. They are also graduated in 0.1 ml divisions. The length of burettes of all volumes is 450 mm with a correspondingly different diameter (12-32 mm).

The burette system is a set consisting of a burette, a feeding vessel and a feeding tube (Fig. 8).

**Fig. 8. The ballot box installation.**

Pharmacy pipette. Pharmacy pipettes are part of the pipette system. These are measuring devices graduated in milliliters for measuring small (up to 15 ml) volumes of liquids that are easily mobile and not very viscous.

They are available in 3, 6, 10, and 15 ml capacities with a price in 0.1, 0.2, and 0.5 ml increments, respectively.

Pharmacy pipette (consists of a graduated glass pipette tube (1) with upper (2) and side nozzles (3), a rubber balloon (4), a ball valve (5) and a rubber ring (6). The valve is mounted on the side pipe of the pipette and consists of a rubber tube with a glass ball inside. Pipette reservoirs have a capacity of 100 and 250 ml.

The container must have a label with the name of the medicinal product. The end of the pipette must not touch the bottom of the vessel.

The liquid is drawn into the pipette with a rubber balloon. To do this, lift the pipette slightly above the liquid and squeeze the rubber balloon to squeeze a certain amount of air out of it. Then the pipette is immersed in the liquid and, gradually releasing the balloon, it is drawn into the liquid. To balance the pipette, press down on the bead of the

side tube. The liquid is poured out of the pipette in a continuous stream, keeping the tip of the pipette away from the vessel wall for 3 seconds. Do not allow liquid to enter the rubber balloon to avoid contamination of the balloon and, in case of repeated use, contamination of the liquid.

**SITUATIONAL TASKS**

Task 1

The pharmacist was instructed to pack 2 kg of peach oil in 50.0 vials. He picked up 40 vials, a set of weights, and labels for "External" and started working. Has he prepared everything he needs for the job?

Sample answer.

A pharmacist forgot to prepare a tare scale when preparing a workstation for packing 2 kg of peach oil.

Task 2

The pharmacist began to pack streptocide 0.5 on BP-5, which had not yet been used. What mistakes did he make?

Task 3

When packing a 30 ml solution of brilliant green, the pharmacist measured it with a 100 ml cylinder by the lower meniscus. Evaluate the correctness of his actions.

Task 4

The pharmacist has a manual balance with a maximum capacity of 1, 5, 20, and 100 g. He decided to weigh 4.0 g of a powdered substance on BP-100. Is his decision correct?

Task 5

The pharmacy independently installed tare scales that had been stored in industrial packaging for 3 years. However, the pharmaceutical inspector who inspected the pharmacy prohibited the use of these scales. Was he right to do so?

Task 6

A prescription calls for 20 drops of 0.1% epinephrine hydrochloride solution. The pharmacist took a clean, uncalibrated eyedropper and measured out the specified number of drops. What mistake did he make?

Task 7

When weighing turpentine, some of the liquid flowed down the wall of the rods and contaminated the label. What was the pharmacist's mistake?

Task 8

A check of the 50.0 talcum powder showed that the actual weight of the powder was 49.1. Can this error be attributed to the scales (the packaging was carried out on a tare scale with a maximum load of 1 kg)? Does it fall within the permissible deviation limits?

Task 9

Checking the accuracy of an unloaded hand-held scale after tying the threads on it showed that the scale arrow had deviated slightly from the balance position. How to balance the balance?

Task 10

While working with hydrochloric acid, the pharmacist spilled it on the scales and then neutralized it with sodium hydroxide solution. Evaluate the correctness of the pharmacist's actions.

**TESTS**

1 Wipe the hand scales before weighing:
a with a damp cloth;
b with cotton wool;
c with gauze;
d with a napkin moistened with an alcohol-ether mixture;
e with a cloth moistened with sterile sodium chloride solution,
2 Indicate the minimum weight of the medicinal product that can be weighed on a one-gram balance:
a 0,1;
b 0,5;
c 0,02;
d 0,05;
e 0,3.
3.It is not a viscous liquid:
a dimexide;
b terpene oil;
c methyl salicylate;
d tincture of lily of the valley;
e essential oils.
4 Volatile medicinal products include:
a ichthyol;
b vegetable oils;
c chloroform;
d syrups;
e glycerin.
5 Rinse the weights from dust and grease:
a with purified water;
b with turpentine;
c with hot water;
d with warm soapy water;
e with acetone.
6 The weight of the weights is calculated during weighing:
a twice;
b three times;
c once;
d after weighing is completed;
e at the beginning of weighing.
7 Bulk substances are weighed on hand scales by:
a capsules;
b parchment paper circles;
c filter paper circles;
d on the scales.
8 The first to be removed from the scales after weighing:
a substance;
b are heavy;
c container;
d a glass.

9 It is not recommended for taring:
a vials;
b sand;
c are heavy;
d capsules;
e banks.
10 The name of the medicinal product shall be read during weighing:
a 2 times;
b 1 time;
c From the times;
d 4 times;
e 5 times.
11 Specify the size of the hand scales:
a BP-2;
b BP-10;
c BP-5;
d BP-50;
e BP-30.
12 A milligram set of weights is made of:
a steel;
b copper;
c chrome and aluminum;
d melchior and aluminum;
e nickel.
13 50 mg has the form:
a triangle;
b square;
c circle;
d of the cylinder with the head;
e hexagon.
14 The horizontal position of the technical pharmacy scales shall be ensured:
a movable legs;
b with a rocker arm;
c Arethyrus;
d arrow;
e with lock nuts.

## GENERAL REQUIREMENTS FOR THE MANUFACTURE OF NON-STERILE MEDICINAL PRODUCTS IN PHARMACIES

In a pharmacy, the composition of prescriptions for medicines is regulated by a prescription. The word "prescription" comes from the Latin word gesirege, which means to take. A prescription is a written request (order) from a physician to a pharmacist (pharmacy) to manufacture a medicinal product and dispense it to a patient, indicating the method of administration (Figure 9).

A prescription is of great medical importance. It is a document that serves as the sole basis for the dispensing of most medicines from pharmacies and their use by patients, based on the doctor's instructions on the dose and procedure for taking them, taking into account the individual approach to the patient [2-3].

In addition to its basic medical significance, a prescription also has legal, technological, and economic significance [3].

The legal significance of a prescription is that it gives the right to purchase medicines and is determined by the rational prescription of the prescription to the patient, the date of the prescription, the patient's name and age, the name of the doctor, the use of appropriate prescription forms, taking into account the pharmacological effects of the medicines. In special cases, it can be used as material evidence, since persons who write prescriptions and prepare medicines based on them are legally liable for them.

The technological (technical) significance of a prescription is that it serves as a basis and guide for a pharmacist in the manufacture of a medicinal product (it indicates which medicinal products should be taken and into which dosage form they should be converted) [2-3].

The economic (financial and economic) significance of a prescription is that it is a document for the consumption of medicines and auxiliary materials; it serves as the basis for settlements between a healthcare facility and a pharmacy in cases of free or reduced price of medicines for outpatients. The prescription is used to determine the cost of a medicinal product. In self-supporting pharmacies, along with the monetary value of medicinal products, for medicinal products of List A and ethyl alcohol, the consumption

of their quantities according to the prescription is recorded. The prescription serves as the basis for forecasting the financial performance of the pharmacy, as well as for determining the stock-out of medicines.

The rules for issuing prescriptions are established by the Order of the Ministry of Health of Ukraine No. 360 dated 19.07.05.

The right to prescribe is granted to doctors, paramedics, midwives of healthcare institutions regardless of their form of ownership and subordination, who, if there are appropriate indications, are obliged to issue prescriptions to patients certified by their signature and personal seal.

Prescriptions for medicinal products that are dispensed on preferential terms or free of charge are allowed to be issued by doctors of state and municipal healthcare institutions, heads of paramedic and midwifery stations in coordination with the healthcare authorities of local state administrations.

Prescriptions must be written taking into account the patient's age, the procedure for paying for medicines and the nature of the medicines' effect on forms printed in the prescribed forms f-1 and f-3.

The Order of the Ministry of Health of Ukraine No. 494 dated 15.03.2023, which entered into force on 01.04.2023, amended the Rules for Prescribing Medicinal Products and Medical Devices (hereinafter - the Rules), approved by the Order of the Ministry of Health of Ukraine No. 360 dated 19.07.2005 No. 360 "On Approval of the Rules for Issuing Prescriptions for Medicinal Products and Medical Devices, the Procedure for the Release of Medicinal Products and Medical Devices from Pharmacies and Their Structural Subdivisions, the Instruction on the Procedure for Storage, Accounting and Destruction of Prescription Forms" (hereinafter - Order No. 360), which, in particular, approved a new form of prescription forms No. 3 (hereinafter - F-3) and prescription forms No. 1 (hereinafter - F-1).

The new prescription forms ***do not contain the column "Number of the card of an outpatient or inpatient patient",*** and the special form of prescription form ***F-3 does not contain the column "Place for mark"***. As a result, when prescribing narcotic drugs, a doctor does not need to put a mark "CHRONICALLY SICK" and additionally certify it

with his or her signature and seal. Instead, it is now mandatory to indicate the course/term of treatment for narcotic (psychotropic) drugs.

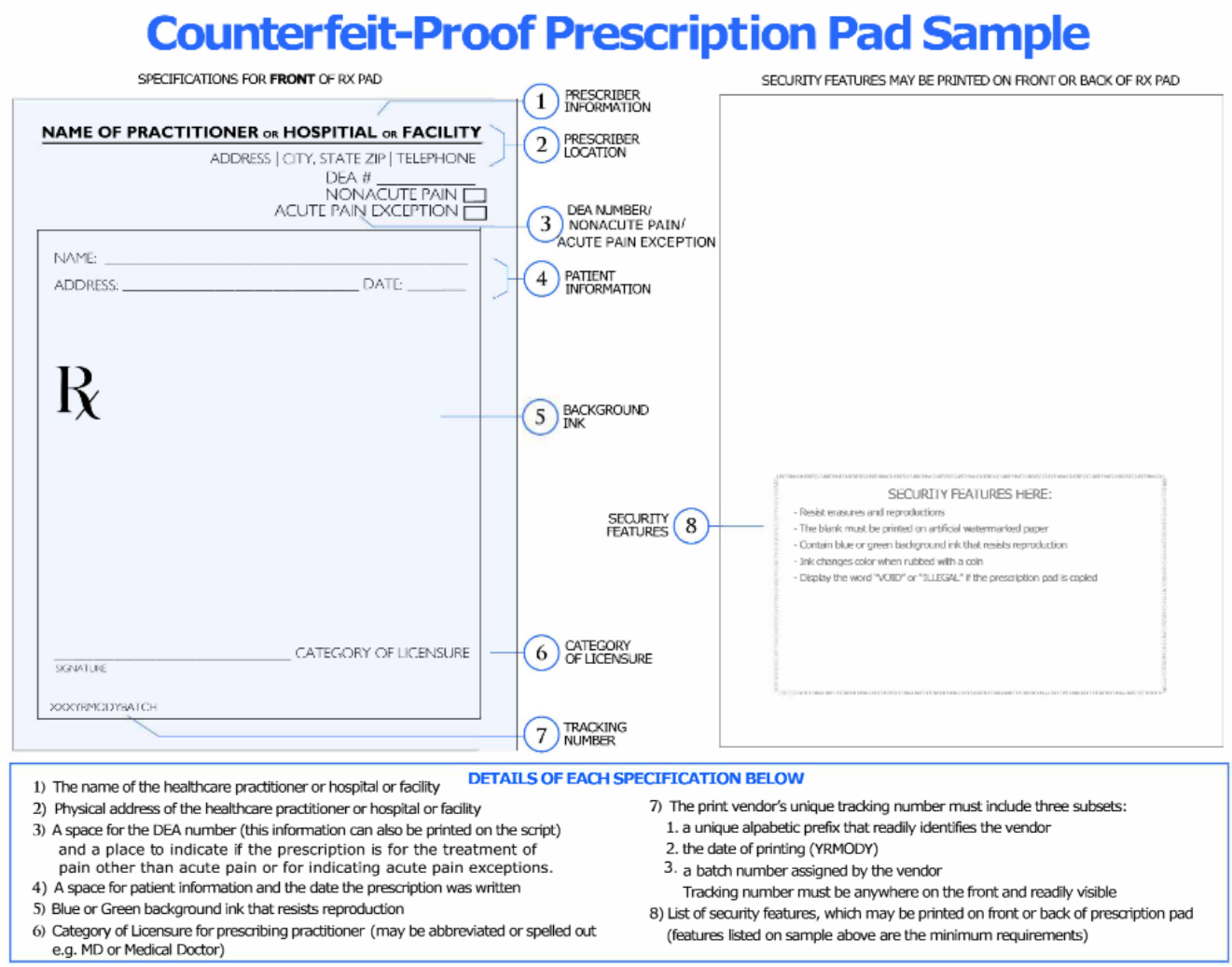


**Figure 9. Forms of prescription forms**

**Components of the prescription. The prescription** must be written out in ink or ballpoint pen, clearly and distinctly, in the sequence indicated below, with all the boxes provided for in the form being filled in. It must be remembered that corrections to the prescription are not allowed: if errors are made, the prescription must be rewritten.

1 Inscriptio - an inscription (from the Latin inscribere - to write). The inscription indicates the name, address and telephone number of the medical institution where the prescription was issued. The code of the healthcare facility is printed in full or stamped. A private practitioner's prescription must contain the name, home address, and telephone number (if any). This information is necessary for the pharmacist in case of need to clarify various issues with the doctor: clarification of the dosage, method of administration of

the medicinal product, the possibility of replacing missing ingredients with others, etc.

2 Datum - the date of issue of the prescription (specify the full date, month, year).

3 Nomen aegroti - the name and initials of the patient. The prescription must contain the patient's name and initials, as well as their age. The information about the patient's age is necessary because the pharmacist is obliged to control the correctness of the prescription of toxic and

potent medicinal substances. If the patient is the doctor who wrote the prescription, it is written "pro me" (for me).

4 Nomen mcdici - name and initials of the doctor (legible).

5 Invocatio - appeal (from the Latin invocare - to cry out, to beg). In a prescription, this part is represented by a single word Recipe (usually written in abbreviated form: Rp.: or R.:) and legally characterizes the doctor's order to the pharmacist. It indicates that this document is a prescription and is subject to the prescription laws.

6 Designatio materiarum or Orginatio is a list of medicinal substances and the ingredients used to prepare the drug. This is the most important part of the prescription. Medicinal substances are prescribed in Latin in the genitive case by chemical names (according to the nomenclature of the State Pharmacopoeia). When listing ingredients, each substance is written on a separate line with a capital letter. The names of poisonous and potent medicines must always be written in full. Abbreviations of ingredients that are similar in name and do not allow to identify the prescribed drug are prohibited. The use of the most important prescription abbreviations is permitted only in accordance with the accepted medical and pharmaceutical practice.

After the name of the medicinal product, its quantity is indicated on the right side. When prescribing medicinal substances dosed in biological units of action (antibiotics, some other substances), the number of units of action (UA) is indicated in the prescription. In cases where medicinal products are prescribed in equal amounts, "ana" is written after the name of the last one before the quantity (Fig. 10). Liquid medicines are prescribed in milliliters and drops, while all other medicines are prescribed in grams. If the amount of liquid is less than one milliliter, it is usually prescribed in drops, indicating the amount with a Roman numeral. For example, gti IV (gtt - gitttas - drop). As for the

excipients, the doctor may not specify their amount, but prescribe "q.s." (quantum satis - how much is needed).

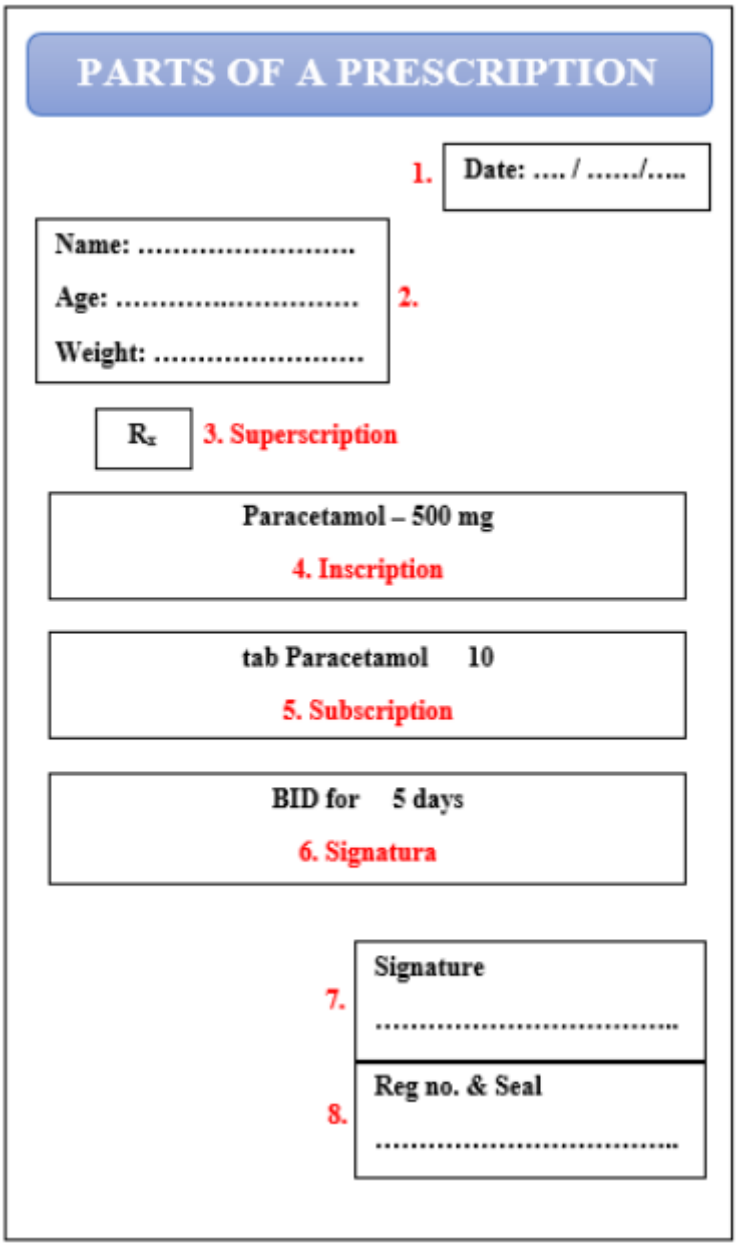


**Fig. 10. Components of the recipe**

Usually, medicines are prescribed in descending order of importance. First, the main drug is written (basis), then substances that contribute to the main drug are prescribed (adjuvuns - literally translated: the one that helps, contributes). Next, a substance that corrects the taste or odor of the drug may be prescribed (corrigens), followed by molding or consistency substances that give shape to the drug (constituent). Sometimes a doctor does not specify excipients in a prescription, but implies that they are fully defined based on the rules established by the pharmacopoeia. For example, purified water for mixtures,

petroleum jelly for ointments, sugar in powders, solid fat bases in suppositories, etc.

7 Praescriptio or subscriptio - order, signature. After listing the medicinal substances, it is indicated which dosage form should be prepared and the main technological operations to be performed (mixing, dilution, etc.), in which packaging the medicinal product should be dispensed (in capsules, ampoules, in dark glassware, etc.). When prescribing dosed medicines, the number of doses is indicated. Common abbreviations are widely used to indicate the dosage form, for example: M.f. ung. (Misce fiat unguentitm) - mix to form an ointment; M.f. pulv. D.t.d. No. 6 (Misce fiat pulvis. Da tales doses No. 6) - mix to form a powder. Give such doses in the number 6.

8 Signature - signature, designation. It begins with the words Signa, or Signatur (mark, let be marked), more often written abbreviated - S.

The content of the signature is intended for the patient, it indicates how to use the medicinal product. Therefore, the signature is written in Ukrainian or the national language. Such general instructions as "External", "Internal", "Known", "Use as directed", etc. are unacceptable, as this prevents the pharmacist from checking the dosage of poisonous, narcotic or potent medicinal products and may lead to incorrect administration of the medicinal product to the patient. The method of administration should be written in detail, indicating the dose, frequency, and, if necessary, the time of administration, i.e., before or after meals, on an empty stomach, etc.

9 Subscriptio medici - a doctor's personal signature and personal seal. By signing the prescription, the doctor assumes responsibility for the correctness of the prescription of the drug to the patient. This last part of the prescription is legally binding.

In cases stipulated by Order of the Ministry of Health of Ukraine No. 360 (clause 1.14), additionally, a round seal of a business entity engaged in activities related to medical practice.

It is prohibited to certify with the seal of a healthcare facility or other business entity engaged in medical practice activities, prescription forms that are not filled out and not signed by a medical professional.

No more than three names of medicinal products may be prescribed on prescription forms f-1. Prescription forms f-1, which remain in the pharmacy (preferential

prescriptions and those subject to subject-quantitative accounting, except for narcotic (psychotropic) drugs), and special prescription form f-3 are allowed to prescribe one name of a drug.

In addition to the above, prescriptions may contain special assessments by doctors. For example, if a patient needs to be prescribed a medication on an emergency basis, the doctor writes the following in the upper right corner of the prescription: Cito\ (quickly); Statim\ (immediately). If it is necessary to repeat the prescribed drug to the patient, the doctor writes on the prescription repetatur, or vice versa, if it is undesirable to repeat it - pop repetatur, and signs it. Prescriptions for medicinal products written on prescription forms f-1 are valid for ten days from the date of issue, and on special prescription forms f-3 - for five days from the date of issue.

A prescription that is issued in violation of the rules, in a dose that exceeds the maximum single dose without a proper prescription, or contains incompatible medicinal substances is considered invalid and no medicines are dispensed. The prescription is canceled with the stamp "Prescription is invalid" and returned to the patient.

## QUALITY STANDARDIZATION OF MEDICINES

The quality of medicinal products is directly dependent on the quality of the raw materials, the method and conditions of their manufacture. Therefore, in controlling their production, the state establishes uniform requirements and special quality standards for medicinal products, excipients and materials.

Thus, quality regulation of medicines is the process of setting and applying standards.

A standard is a normative document developed and approved by a recognized body that sets out rules, requirements, and general characteristics relating to various activities or their results in order to achieve orderliness in a particular area.

The following categories are used to define the requirements for the quality of medicinal products: State Pharmacopoeia (SP), Pharmacopoeial Article (PA), Temporary Pharmacopoeial Article (TPA).

Pharmacopoeial article (PA) is a regulatory and technical document that establishes

requirements for a medicinal product, its packaging, storage conditions and shelf life, and methods of quality control.

Initially, a temporary pharmacopoeial article (TPA) is approved for each new drug for a certain period of time (most often for Z years). If, after this time, the medicinal product regulated by this TFS has proven itself in medical practice and its production becomes stable, a permanent FS is developed for it. In the course of its preparation, the necessary clarifications, corrections and additions are made to the TFS. If necessary, the term of the FS may be extended.

FS for medicinal products that have the greatest therapeutic value and are widely used in medical practice, as well as have high quality indicators, are included in the State Pharmacopoeia.

Pharmacopoeia. Pharmacopoeia is of great importance in pharmaceutical practice. It can be literally translated as a "manual for the preparation of medicines". Initially, pharmacopoeias were really collections of medicines with a description of how to prepare them. A modern pharmacopoeia with a collection of standards for medicines provides only the basic principles of manufacturing dosage forms.

The State Pharmacopoeia is a collection of mandatory medical and pharmaceutical national standards and regulations that regulate the quality of medicines.

The Pharmacopoeia has a legislative nature, binding on all medical, including veterinary, institutions and enterprises in the country that manufacture, store, control and use medicines.

The first Russian pharmacopoeia was published in 1866, the second edition in 1871, the third in 1880. IV in 1891, V in 1902, VI in 1910.

At the present stage, the FC of the Ministry of Health of Ukraine was faced with the task of creating the State Pharmacopoeia of Ukraine (SPU). In accordance with the Resolution of the Cabinet of Ministers of 19.03.97 No. 244, Ukraine has set a course to join the European Community. In this regard, the SFP should be harmonized with the European Pharmacopoeia and at the same time reflect the level of development of the domestic pharmaceutical industry, its traditions and national peculiarities.

The SFTU is the first pharmacopoeia of Ukraine, which was published in 2001 in

the Ukrainian language. The general and private articles of the USP consist of two parts: the European part (which is a literal translation of the corresponding article of the European Pharmacopoeia) and the national part, which does not contradict the European part and supplements it with national peculiarities. The first part of the SPS includes 30 general articles: 7 articles on dosage forms, 9 on pharmacotechnological tests and 14 on methods of analysis.

## STANDARDIZATION OF CONDITIONS AND TECHNOLOGICAL PROCESS OF MANUFACTURING OF MEDICINAL PRODUCTS

To ensure the quality of medicines, the manufacturing company must have a quality assurance system in place, including good manufacturing practices and quality control.

Good manufacturing practice (GMP) is a set of requirements, rules and regulations governing the production and quality control of medicines.

The standards for accreditation of pharmacies (Order No. 2 of January 2, 1998 of the Ministry of Health of Ukraine) include a section on "Good Pharmacy Practice" (GPP).

Good pharmacy practice is a guarantor of the quality of medicines. One of the components of GPA is compliance with the conditions and technological process of manufacturing extemporaneous drugs.

Manufacturing and quality control of medicines are interdependent. Therefore, the main requirements for them are discussed in one section.

Regulation of the conditions for the manufacture of medicinal products includes:

- Compliance with a set of sanitary and hygienic measures (microclimate, lighting, contamination of the air environment, equipment, etc.), which is studied in detail in the hygiene course;
- compliance with the sanitary regime, and in the manufacture of a number of dosage forms - aseptic conditions;
- Compliance with the rules for working with poisonous, narcotic and similar substances;
- compliance with safety regulations.

The rules governing the conditions for the manufacture of medicinal products in

pharmacies are established by the relevant state authorities (Orders of the Ministry of Health of Ukraine No. 275 of 15.05.06 and No. 44 of 16.03.93).

During the production process, sources of contamination of medicines can be impurities that come from the equipment during synthesis due to imperfect purification methods (impurities of heavy metals, lead and, most dangerously, arsenic). The raw plant material also contains impurities of mineral and organic origin, which to varying degrees affects the purity of the extract. Relevant impurities in quantities above the permissible limits can have a toxic effect on the human body or affect the stability of medicines.

Sources of microbial contamination (microbiological contamination) of non-sterile medicinal products may include: medicinal and excipients, packaging and closure materials, as well as the possibility of infection of medicinal products during the manufacturing process from working personnel, equipment, etc.

In order to maintain high quality of medicinal products, their physical and chemical stability and apirogenicity, pharmacy employees must comply with the requirements of the Instruction on sanitary and anti-epidemic regime of pharmacy production and personal hygiene of pharmacy employees (Order of the Ministry of Health of Ukraine No. 275 of 15.05.06). The instruction provides for:

- requirements for the premises and equipment of pharmacies;
- sanitary requirements for cleaning the premises and maintaining the equipment of pharmacies;
- requirements for personal hygiene of pharmacy staff;
- sanitary requirements for obtaining, transporting and storing purified water and water for injection;
- sanitary requirements for the manufacture of medicines in aseptic conditions;
- sanitary requirements for the manufacture of non-sterile dosage forms;
- the procedure for processing rubber stoppers and washing pharmacy utensils.

In regulating manufacturing conditions, an equally important factor is the proper storage of medicinal products and auxiliary materials. The instructions for organizing the storage of various groups of medicinal products and medical devices in pharmacies provide for

- requirements for the equipment and operation of storage facilities;
- general requirements for the organization of storage of medicinal products;
- requirements for the storage of medicinal products depending on their physical, physical and chemical properties and the impact of environmental factors on them.

The standardization of the technological process is one of the factors ensuring the high quality of manufactured medicines. Violation of the process may result in poor quality of medicinal products. For example, when manufacturing an infusion of the herb of the cowpea with normal biological activity, a medicinal product with reduced or lost biological activity may be produced if the temperature regime is not maintained. Therefore, it is necessary to control all stages of production from the initial to the final moment of each technological operation, the sequence of transitions and the relationship between them. In doing so, the main parameters (heating or cooling rate, mixing time, pH value of the medium, etc.) are determined. The completion of a technological operation should be determined by the established main technological indicator. For example, a certain temperature, pH value, suspension dispersion, etc.

In pharmacies, the stages of the technological process are regulated by the SF, technological instructions, and information sheets that comply with the orders of the Ministry of Health of Ukraine (Order No. 197 of 07.09.93, etc.).

The first common stage of manufacturing for all dosage forms is preparatory work. This involves preparing the premises, auxiliary equipment, equipment, packaging materials, medicinal and excipients. After the preparatory work, the stages of the technological process are carried out sequentially in accordance with the specifics of the dosage form. For example, in the manufacture of liquid dosage forms, it is necessary to follow a certain procedure for dissolving and mixing medicinal products, taking into account their physical and chemical properties; in the manufacture of powders, it is necessary to comply with the rules for mixing, grinding, introducing coloring agents, etc.

The final stages of the technological process, such as packaging and preparation for release, are also standardized and common to all dosage forms. All medicinal products are packaged, depending on their aggregate state and purpose, with packaging material approved for medical purposes. There are uniform rules for the registration of medicines

prepared in pharmacies. All medicinal products are labeled with labels of a certain size and design. Depending on the method of administration, labels are divided into internal, external, injectable, and ophthalmic dosage forms. The labels have different signal colors: green for medicinal products for oral administration; orange for external use; pink for ocular dosage forms; blue for injectable dosage forms. All labels must contain the following designations: the medical emblem, pharmacy number, prescription number, surname and initials of the patient; method of administration, date of manufacture of the medicinal product, signature of the person who prepared the medicinal product, and cost, as well as the warning inscription "Keep out of reach of children". The labels of medicinal products intended for injection indicate their composition. Warning labels such as "Children's" and "Cardiac" are used to draw special attention to the intended use of the drug.

For medicinal products that are prepared individually, and depending on the dosage form and purpose, labels such as "Powders", "Mixture", "Drops", "Ointment", "Eye drops", "Eye ointment" are used.

The appearance of the packaging, its perfection, cleanliness, and tightness have a great emotional impact on the patient. It has been established that an untidy designed and released medicinal product, poorly sealed, leaking and contaminating the container from the outside, may not have the necessary therapeutic effect, despite the fact that it contains all the necessary medicinal substances. Packaging should be a carrier of scientific, advertising and aesthetic information. should fit into the technological scheme as one of the process elements, intensifying or at least not reducing labor productivity.

Quality control of medicines in pharmacies. In the state regulation of the production of medicinal products, much attention is paid to quality control of the finished product. The quality of a medicinal product is a set of properties that give a medicinal product the ability to satisfy consumers in accordance with its intended use and meet the requirements established by law.

State control of the quality of medicinal products is carried out by state control authorities using official SOPs (SOPs, current orders, instructions, etc.).

Quality control of medicines in pharmacies involves a set of measures that ensure

the manufacture of medicines of proper quality. These include:

- Compliance with sanitary norms and rules, sanitary and hygienic and anti-epidemic regimes, rules of asepsis for the manufacture of medicines, pharmaceutical procedures in accordance with applicable regulatory and methodological documents and orders;
- ensuring the terms and conditions of storage of medicinal products in the pharmacy in accordance with the physical and chemical properties and requirements of the State Pharmacopoeia, applicable orders and instructions;
- thorough review of prescriptions received by the pharmacy and requirements of healthcare facilities to verify the correctness of their prescription, compatibility of the drugs included in the medicines; compliance of prescribed doses with the patient's age;
- Compliance with the manufacturing technology of medicinal products in accordance with the requirements of the State Pharmacopoeia, applicable orders and instructions.

The quality of medicinal products prepared in pharmacies on prescription or at the request of healthcare facilities (as well as in-pharmacy preparation, packaging, concentrates and semi-finished products) is determined by the results of in-pharmacy control: written, survey, organoleptic, physical, chemical and dispensing control.

The pharmacy manager, his/her deputies, pharmacist-analyst and pharmacist-technologist are responsible for intra-pharmacy control. Order of the Ministry of Health of Ukraine (Order No. 812 and others).

1 Written control: carried out by a pharmacist and a pharmacist-technologist in the manufacture of medicinal products according to individual prescriptions and requirements of healthcare facilities by filling out a written control passport (WCP) from memory. The passport is filled in immediately after the manufacture of the medicinal product in accordance with the technology. The passport shall contain the following information: date, prescription number (requirement), medicinal products taken (in Latin) and their quantity, number of doses, signatures of persons who manufactured, packaged and tested the medicinal product. In case of manufacturing of the medicinal product by

the trainee, the signatures of the trainee and the person responsible for the industrial practice shall be affixed.

Medicines containing poisonous or narcotic substances are marked with the letter "A" at the top of the passport, and dosage forms for children are marked with the letter "D".

All calculations are made prior to the manufacture of the medicinal product and are recorded on the back of the passport. When semi-finished products and concentrates are used, their concentration and quantities are indicated. In the manufacture of powders, suppositories and tablets, the weight of individual doses and their quantity are indicated. The size of the pill or suppository mass, the amount of isotonizing and stabilizing substances added to eye drops and solutions for injection are indicated both in the passports and on the back of the prescriptions. The passport indicates the water absorption coefficients for medicinal plant material used in the calculations, the coefficients of volume increase of aqueous solutions when dissolving medicinal substances, and the calculation formulas.

Prepared medicinal products, prescriptions, and completed ACPs are submitted for inspection to the technologist or a person performing his or her functions. The control consists of checking the compliance of the records in the PKK with the prescription, the correctness of the calculations made. If the medicinal product is tested by a pharmacist-analyst with full chemical control, the passport is marked with the analysis number and the signature of the pharmacist-analyst.

When a medicinal product is manufactured and dispensed by the same person, it is also mandatory to maintain a PCR. When manufacturing solutions for injection, all records are kept in a special journal. The ACRs are kept in the pharmacy for one month.

2 Survey control is performed by a pharmacist-technologist and is applied selectively. After the pharmacist has manufactured no more than 5 medicinal products, the pharmacist-technologist shall name the first ingredient included in the medicinal product, and in complex medicinal products shall indicate its quantity, after which the pharmacist shall name all the ingredients used and their quantity.

3 Organoleptic control is carried out by an analyst or pharmacist-technologist and

consists in checking the appearance of the dosage form, its color, taste, smell, homogeneity of mixing, absence of mechanical inclusions in liquid dosage forms.

The homogeneity of mixing powders, ointments, tablets, suppositories is checked before dividing the mass into doses. The check is carried out selectively by each pharmacist during the working day (but not less than 3 dosage forms per day).

Oral dosage forms are checked for taste on a selective basis and in cases of doubt about the quality of the prepared dosage form. Special attention is paid to medicinal products for children. The results of organoleptic control of dosage forms are recorded in a journal.

4 Physical control is carried out by an analyst or pharmacist-technologist and consists in checking the total weight or volume of the dosage form, the number and weight of individual doses included in this dosage form (but not less than 3 doses), and the quality of the closure is also controlled. The following are subject to physical control:

- each series of packaging and in-pharmacy preparation (from 3 to 5 sample units from each series or preparation;

- selective dosage forms prepared according to individual prescriptions per day (but not less than 3% of the total);

- dosage forms requiring sterilization after packaging before sterilization.

5 Chemical control is carried out by a pharmacist-analyst (qualitative and quantitative) and a pharmacist-technologist (selective - qualitative) and consists in determining the conformity and quantitative content of medicinal substances included in the dosage form.

The following are subjected to full chemical analysis: all solutions for injection before and after sterilization; eye drops and ointments containing narcotic and toxic substances; all dosage forms for newborns, solutions of hydrochloric acid (for internal use), atropine sulfate, mercury dichloride and argeitum nitrate; all concentrates, semi-finished products and intra-pharmacy preparations;

6 Control during dispensing is carried out by a pharmacist-technologist. All dosage forms prepared in the pharmacy are subject to control. The following is checked: packaging (must comply with the weight (volume) and type of dosage form, as well as

the properties of the ingredients), design (must comply with the requirements of applicable regulations); compliance of the doses of medicinal products specified in the prescription of lists A and B with the patient's age; compliance of the number on the prescription and the number on the label, compliance of copies of prescriptions with the prescription.

Thus, the quality control system for medicinal products involves both monitoring the manufacture of medicinal products at all stages of the process and controlling the finished product.

**SITUATIONAL TASKS**

Task 1

A pharmacy has received a prescription for a dosage form with a toxic substance, which is certified by a doctor's personal seal and signature. What should the pharmacy technologist do in this case?

The benchmark is the same as the one used in the.

When accepting a prescription for a medicinal product containing a toxic substance, the pharmacist must be particularly careful and accurate: it is necessary to clarify the patient's age, check the correct dosage, the compatibility of the prescribed ingredients and underline the name of the toxic agent with a red pencil.

Task 2

The pharmacy received a prescription on a form No. 2. The pharmacist-technologist taxed the prescription and told the patient the total cost that he must pay for the medicine. Did he do the right thing?

Task 3

A pharmacy has received a prescription that contains an excessive dose of a toxic substance. What should a pharmacy technologist do in this case?

Task 4

In the prescription received by the pharmacy, the liquid ingredients of the dosage form (syrup, tinctures) and the solvent (water) are prescribed by weight (in grams). Was the prescription written correctly? What document regulates the rules for writing prescriptions?

Task 5

The pharmacy receives a prescription in which all the medicinal substances included in the prescription are written in Ukrainian and in abbreviated form. Among the abbreviated names is "sodium, sulfur." What mistakes did the doctor make?

Task 6

A patient has come to the pharmacy to order atropine sulfate eye drops according to a prescription written by a doctor 2 weeks ago. What should you do as a pharmacy technologist?

Task 7

A pharmacy has received a prescription for ethyl alcohol without specifying the concentration. What concentration of alcohol should the pharmacist use to prepare the dosage form? Which document should be used in this case?

Task 8

The pharmacy received a prescription form No. 1, on which 2 prescriptions are written, and one of them contains a toxic drug. What decision should the pharmacy technologist make?

Task 9

A pharmacy has received a prescription for powders containing ascorbic acid with glucose, certified only by a doctor's signature. What should a pharmacy technologist do in this situation?

Task 10

A pharmacy receives a prescription in which all of its components, including the signature (method of administration), are written in Latin. What is the doctor's mistake?

## TESTS

**1** A device intended for determining the weight of medicinal products by comparison with mass standards is:

a scales;
b dosimeter;
c a measuring cup;
d pharmacy burette;
e a pharmacy pipette.

**2** A pharmacy produces medicines. Indicate what types of scales are used to prepare medicines?

a analytical;
b container and hand-held pharmacies;
c metrological;
d exemplary;
e technical.

**3** Pharmacy scales have metrological properties. Indicate what is the ability of the balance, taken out of balance, to quickly return to its original position:

a sustainability;
b consistency of readings;
c sensitivity;
d accuracy;
e correctness.

**4** Thick, viscous, sedentary liquids are generally dispensed by weight. Select the liquids listed that are dispensed by weight:

a ethyl alcohol;
b glycerin;
c the water is purified;
d fatty oils;
e The correct answers are B) and D).

**5** Depending on the permissible maximum load, there are several types of hand scales. Select the appropriate one:

a BP -100;
b BP-5;
c BP-20;
d BP-1;
e BP-10.

**6** The sensitivity of the balance is the ability to show a minimum change in load at the moment of equilibrium. The sensitivity is directly proportional:

a weight of the rocker arm;
b the mass of the cup with the cargo;
c the amount of deflection of the rocker arm;
d length of the rocker arm;

**7** The workplace of a pharmacist involved in the manufacture of powders should have the following equipment and utensils. Select the unnecessary:

a scales and weights;
b mortar and pestle;
c capsule machines and capsules;
d measuring cylinder;
e label "Powders".

**8** When preparing liquid dosage forms, dosing is done using special measuring utensils graduated in

a certain number of milliliters. For dosing water and other liquids with the same density as water, use a measuring cup:

a measuring cylinders;
b measuring flasks;
c pharmacy bureaus;
d measuring cups
e all answers are correct.

**9** The pharmacy has received a prescription that indicates the use of dessert spoons. Indicate the capacity of a dessert spoon in milliliters according to the Ukrainian pharmacopoeia:

a 8;
b 10;
c 15;
d 4;
e 5.

**10** A pharmacy received a request from a medical institution to supply 35.0 g of glycerin. What weights should be used for this purpose?

a 20.0 g, 10.0 g, 5.0 g;
b No need for weights;
c 20 g, 10 g, 3 g and 2 g;
d 25 g, 10 g;
e 25 g, 5 g and 5 g;

**11** A regulatory and technical document that establishes requirements for a medicinal product, its packaging, storage conditions and shelf life, and methods of quality control of a medicinal product is...

a Technological regulations;
b Pharmacopoeia article;
c State Pharmacopoeia;
d State Register of Medicinal Products of Ukraine;
e Temporary pharmacopoeial article.

**12** A form is used to prescribe a powder with a narcotic drug in its pure form or in a mixture with indifferent substances:

a Ф-1;
b Ф-2;
c Ф-3;
d Ф-5;
e F-1+F-1.

**13** One name of a medicinal product is prescribed in case of:

a assignment to privileged categories of the population on the form f-1;
b which are subject to itemized and quantitative accounting;
c prescription of narcotic (psychotropic) drugs on the form f-3;
d prescribing insulin drugs, the cost of which is subject to state reimbursement;
e all answers are correct.

**14** Expiration date of the prescription:

a medicinal products are prescribed on prescription forms f-1, valid for one month from the date of discharge, and on special prescription forms f-3 for five days from the date of discharge;
b medicinal products are prescribed on prescription forms f-1, valid for one year from the date of discharge, and on special prescription forms f-3 within five days from the date of discharge;
c medicinal products are prescribed on prescription forms f-1, valid for one month from the date of discharge, and on special prescription forms f-3 for 10 days from the date of discharge;
d There is no right answer;
e medicinal products prescribed on prescription forms f-1 and f-3 are valid for one month from the date of discharge;

**15** A convenient state for use of a medicinal product, which ensures the required therapeutic effect,

is...

a medicinal substance;
b a medicinal product;
c dosage form;
d medicinal substance;
e medicinal product.

**16** A pharmacy has produced a powder with a total mass of 0.3. In accordance with the requirements of PF XI, the deviation in the mass of the powder should not exceed:

a 15 %;
b 10%;
c 5%;
d 3%;
e 1%.

**17** For packaging powders, various packaging materials are used: writing, waxed and waxed paper, parchment, cellophane, cardboard, etc:

a physical and chemical properties of packaging materials;
b physical and chemical properties of powders;
c on the storage conditions of the powders;
d from the technology of powder preparation;
e use the ones available at the pharmacy.

**18** Basic requirements for powders:

a flowability;
b uniform distribution of substances throughout the entire mass of the complex powder;
c homogeneity of mixing;
d dosing accuracy and stability;
e all answers are correct.

**19** A pharmacist is choosing a packaging material for powders. Indicate whether powders with which substance should be dispensed in capsules made of glued paper:

a camphor;
b menthol;
c potassium permanganate;
d analgin;
e iodine.

## DOSING, PACKAGING, PACKAGING AND REGISTRATION FOR OVER-THE-COUNTER (OTC) SALE OF SOLID MEDICINES

Powders are one of the oldest dosage forms, used in medical practice as early as 2500-3000 BC and still important today.

The technology of powders is quite simple to perform. However, the knowledge acquired on the basic rules of powder preparation will serve as a basis for studying more complex dosage forms, such as suspensions, ointments, suppositories, pills, both pharmacy and factory-made.

The widespread use of powders in medical practice is due to their certain advantages as a dosage form.

## BASIC TECHNOLOGICAL OPERATIONS IN THE PREPARATION OF POWDERS

The technological process of preparing medicinal products in a pharmacy consists of separate stages and operations that should be carried out in proper sanitary conditions with accurate implementation of technical methods and compliance with personal hygiene rules (Order of the Ministry of Health of Ukraine No. 275 "On Approval of the Instruction on Sanitary and Anti-Epidemic Regime of Pharmacies" dated 15.05.2006).

In order to decide which technological operations to apply in the preparation of powders, it is necessary to know what requirements are imposed on powders as dosage forms, taking into account the properties of the constituent drugs.

Basic requirements for powders:

1 Flowability and optimal degree of grinding of all powder components (dispersion).

2 Uniform distribution of substances throughout the mass of the complex powder, i.e. homogeneity.

3 Dosage accuracy and stability of substances during storage.

4 4. For some, it is sterility (wound powders, for babies).

Before proceeding to consider the issues of powder technology, it is necessary to know the algorithm for performing the professional activities of a pharmaceutical

technologist:

1 Check the compatibility of the ingredients.

2 Verification of the RDA and RVD of potent and narcotic drugs and the norm of single dispensing of narcotic and intoxicating substances.

3 Calculations (written control passport, reverse side).

4 Justification and selection of the optimal technology option.

5 Passport of written control (front side).

6 Quality assessment of the finished drug product.

In order to meet all the requirements for the manufacture of powders, the following basic steps must be followed:

1 Weighing, grinding and sieving of medicinal substances.

2 Mixing ingredients (for complex powders).

3 Mass dosing, dose packaging and quality control of powders

4 Preparation of powders for release.

The need to perform certain technological steps in the preparation of powders is determined:

- the amount of prescribed medicinal substances and their physical and chemical properties;

- density, bulk or bulk weight, degree of fineness, atomization, color, odor, hygroscopicity of prescription substances, medical purpose of the powder.

## SCHEME OF TECHNOLOGY AND QUALITY CONTROL OF SIMPLE AND COMPLEX POWDERS

These factors also result in different requirements for the degree of grinding, preparation, packaging, and dispensing of powders.

Let's consider each technological stage separately. Pharmacies receive medicinal substances in crushed form, but the size of the particles usually varies greatly (from 70 to 1000 microns), so in a pharmacy, medicinal substances are crushed further. When grinding crystalline substances, a certain mechanical force must be applied (splitting, crushing, abrasion). Amorphous substances are crushed more easily.

During mechanical grinding, the processes of separation of particles under the influence of an applied force and the consolidation of small particles under the influence of mutual attraction occur simultaneously.

When the processes of separation and consolidation reach the same speed, i.e. are in equilibrium, further grinding of the substances does not make sense, so the optimal grinding time is set. This time is not the same for different substances and, when grinding in a mortar, is approximately 2 to 3 minutes. With further grinding, the powder becomes looser, sometimes moistened by absorbing moisture and gases from the air, particles may stick together into larger aggregates, or the powder may adsorb (stick) to the walls of the mortar, i.e., the free energy surface decreases.

If a greater degree of grinding is required than that achieved at the time of stabilization, it is necessary to saturate the free surface energy of the fine particles, which is done by using special techniques: grinding powders in the presence of indifferent substances, such as milk sugar, or grinding with the addition of volatile liquids. The liquid facilitates the grinding of so-called hard-to-grind substances by providing a de-wedging effect.

Substances such as zinc oxide, quinine salts, magnesium carbonate, and others stick tightly to the walls of the mortar and are compressed during grinding, so it is recommended to grind them carefully, without much force. Water-insoluble substances such as sulfur and terpene hydrate are highly electrified during grinding, which causes them to spray out, especially when trying to collect them from the mortar walls with a celluloid plate. Therefore, in order to avoid losses, these substances should be ground simultaneously with prescribed water-soluble crystalline substances or with liquids that are part of the medicine. The degree of grinding is usually determined visually. According to PF XI edition, powders should be homogeneous when viewed with the naked eye and have a particle size of no more than 0.160 mm, unless otherwise specified (No. 38). Powders for which the degree of grinding is not specified should have a particle size of no more than 0.15 mm for internal use.

In pharmacies, grinding of solids (often in combination with mixing) is carried out in mortars or various devices that allow for the mechanization of the powder preparation

process.

Mortars come in a variety of shapes and sizes and are made of different materials (Table 1). The most commonly used are porcelain mortars, which are available in different sizes, along with pestles numbered from 1 to 7. The maximum load of the mortar during grinding should not exceed 1/20 of its volume. If it is smaller, it will rub in more, if it is larger, it will spray more.

**Table 1**

**Parameters of pharmacy mortars**

| Stupki | Diameter, mm | Work surface | | Working volume, $cm^3$ | Grinding time, sec. | Max. load, g | Optimal load, g |
|---|---|---|---|---|---|---|---|
| | | $cm^2$ | coefficient | | | | |
| 1 | 50 | 45 | 1 | 20 | 60 | 1,0 | 0,5 |
| 2 | 75 | 90 | 2 | 80 | 90 | 4,0 | 1,5 |
| 3 | 86 | 90 | 2 | 80 | 90 | 4,0 | 1,5 |
| 4 | 110 | 135 | 3 | 160 | 120 | 8,0 | 3,0 |
| 5 | 140 | 225 | 5 | 320 | 150 | 16,0 | 6,0 |
| 6 | 184 | 450 | 10 | 960 | 210 | 48,0 | 18,0 |
| 7 | 243 | 765 | 17 | 2240 | 300 | 112 | 42,0 |

Sieving is used to obtain a powder with the same particle size and is carried out using different sieves (sieve set for sieve analysis). In pharmaceutical practice, nylon, silk, metal meshes, and pierced metal sieves are used. Sieve No. 61 (mesh size 0.1 mm) produces the finest powder - Pulvis longe subtilissimus. This degree of fineness is required when preparing powders for inhalation, powders or eye powders, tooth powders, or insect repellents. Powders for internal use - particle size 0.16 mm, sieve No. 38 - Pulvis subtilis (fine). Sniffing powders - sieve No. 32 (0.2 mm) - medium-fine powder - Pulvis modice subtilis.

As a rule, sieving is not used in pharmacy practice; it is used only in factory production.

**Mixing is an essential step in the** preparation of complex powders. When mixing the components, it is necessary to strive to obtain a homogeneous mixture of powders, i.e., that all the ingredients are evenly distributed in the mixture.

In pharmacies, the mixing of medicinal substances is carried out in mortars with periodic removal of the powder from the walls of the mortar and pestle with a celluloid plate. The homogeneity is checked by pressing the powder mixture collected in the center

of the mortar with a pestle - there should be no uncrushed particles or sparkles.

To obtain a homogeneous powder mixture, there are several mixing rules.

There are two cases in the variety of prescriptions for complex powders:

- The 1st case is when compound powder medicines are prescribed in equal or approximately equal amounts;

- The 2nd case is when compound powder medicines are prescribed in drastically different amounts.

Depending on the properties of the medicinal products, there are several rules for mixing medicinal products common to both cases. Moreover, in both cases, the order of mixing is determined by the physicochemical properties of the substances (crystal structure, bulk or volumetric weight, mortar pore grinding, odor, color, density, etc.) In the first case, when medicinal substances are prescribed in equal amounts and their physical and chemical properties are the same, the order of mixing does not matter; they are usually mixed in the order of prescription.

If the prescribed amounts of substances are the same, but their physical and chemical properties differ, the **following mixing rules apply:**

1 The substance that is more indifferent is always crushed first.

2 In the absence of an indifferent substance in the prescription, the substance with the lowest percentage of rubbing into the pores of the mortar is ground first. The amount of powder loss is often explained by the electrification of the mortar and powder walls (different charges). Therefore, it is important to predict the amount of loss in order to properly address the issue of grinding ingredients in a non-grinding mortar, because the losses when grinding a substance in a non-grinding mortar are relatively high (Table 2).

3 First, coarse crystalline substances are crushed, then fine crystalline substances, and finally amorphous substances.

4 Add heavy substances to the mortar first, then lighter substances. Easily dispersed substances are added last.

| Substance | Losses, mg | Substance | Losses, mg |
|---|---|---|---|
| Ammonium chloride | 12 | | |
| Analgin | 22 | Mercury monochloride | 44 |
| Anesthesia | 24 | Glucose | 7 |

| | | | |
|---|---|---|---|
| Fire retardant | 10 | Diacarb | 24 |
| Barbital | 13 | Dibazole | 18 |
| Sodium barbital | 12 | Benzoic acid | 34 |
| Bromizal | 19 | Nicotinic acid | 15 |
| Bromocamphor | 15 | Salicylic acid | 55 |
| Butadion | 36 | Codeine | 7 |
| Basic bismuth nitrate | 42 | Codeine phosphate | 7 |
| Hexamethylene tetramine | 26 | Caffeine | 15 |
| Hexamidine | 15 | Caffeine benzoate sodium | 16 |
| White clay | 14 | Xerophorm | 57 |
| Magnesium oxide | 16 | Levomycetin | 29 |
| Menthol | 17 | Magnesium carbonate basic | 19 |
| Methylene blue | 16 | Sugar | 21 |
| Sodium benzoate | 20 | Sulphur purified and | 24 |
| Sodium bicarbonate | 11 | Urosulfan | 31 |
| Sodium salicylate | 23 | Phenacetin | 19 |
| Norsulfazole | 22 | Phenylsalicylate | 24 |
| Omnophone | 11 | Phenobarbital | 18 |
| Osarsol | 15 | Etazol | 18 |
| Papaverine gyrochloride | 10 | Propolis preparation | 26 |
| Polenaza | 11 | Fitting | 18 |
| Pachycarpine hydroiodide | 12 | Phthalazole | 19 |
| Resorcinol | 10 | Quinidine | 21 |
| Mercury oxide yellow | 26 | Quinine chloride and sulfate | 12 |
| Mercury amide chloride | 22 | Zinc oxide | 36 |

**Table 2.**

**Losses of solid medicinal products when grinding them in mortar**

**Powders with coloring agents.**

- coloring agents: acrychine, methylene blue, brilliant green, riboflavin, ethacridine lactate, furacilin, potassium permanganate, etc. (Table 3).

**Table 3.**

**List of coloring medicines**

| № | Name | List. | Additional conditions for saving |
|---|---|---|---|
| 1. | Arykhin | B | dry, dark place |
| 2. | Brilliant green | | dry place |
| 3. | Indigocarmine for injection | | dry place |
| 4. | Potassium permanganate | | dry place |
| 5. | Methylene blue | | dry, dark place |
| 6. | Riboflavin | | dry, dark place |
| 7. | Furacilin | B | dry, dark place |
| 8. | Ethacridine lactate | B | dry place |

- colored substances: dermatol, quinazole, protargol, etc.

The group of coloring medicinal substances includes substances, as well as their solutions, mixtures that leave a colored mark on containers, closures, equipment, and other items that cannot be washed off by normal sanitation. They are stored in a separate cabinet, where there are also separate scales for weighing them.

The group of colored medicinal products includes substances that do not leave a colored trace on containers and closures, they are stored as usual and powders with such medicinal products are prepared according to general rules.

As for the preparation of powders with coloring agents, it should be borne in mind that careless handling can cause coloring agents to stain the mortar, pestle, and surrounding objects. Therefore, to prepare powders with coloring agents, it is necessary to:

1 Have a separate workstation or cook on a table covered with a sheet of paper, which is
folded and burned after work.

2 Coloring substances are usually prescribed in small quantities, so the preparation of powdered mixtures is carried out according to the rules when one of the ingredients is prescribed in small quantities. In order to contaminate the mortar and pestle less and to obtain a homogeneous mass faster, first grind the non-colored substance, then pour it onto the capsule, leaving half the amount of powder in the mortar and adding a weighed amount of coloring substance to it, over which a layer of the 2nd half of the non-colored ingredient is poured and only then mixed thoroughly. Powders with coloring substances are dispensed in parchment capsules, or, if a doctor's prescription is specified, in gelatin capsules.

**Powders with hard-to-grind medicinal substances.**

Drugs that are difficult to grind include camphor, menthol, thymol, phenyl salicylate, iodine, boric acid, streptocide, etc. (Table 4). Their grinding is improved in the presence of an auxiliary liquid, which has a de-wedging effect.

The volatile liquid used is 95% ethyl alcohol or medical ether (taking into account the solubility of the drug).

**Table 4.**

**Medicinal substances crushed with auxiliary liquids**

| Substance, 1 g | Amount of alcohol, drops | Amount of medical ether, drops | Note |
|---|---|---|---|
| Iodine | 10 | 15 | difficult to crush |
| Camphor | -"- | -"- | -"- |
| Menthol | -"- | -"- | -"- |
| Pentoxil | -"- | -"- | -"- |
| Thymol | -"- | -"- | -"- |
| Phenylsalicylate | -"- | -"- | -"- |
| Boric acid | 5 | 8 | (in case of scaly structure) |
| Sodium tetraborate (borax) | -"- | -"- | -"- |
| Salicylic acid | -"- | -"- | safety (dusty, irritates the mucous membranes of the nose and eyes) |
| Streptocide | -"- | -"- | difficult to crush |
| Arsenic anhydride | -"- | -"- | safety precautions (especially poisonous) |
| Mercury dichloride | -"- | -"- | -"- |

When grinding in dry form, camphor, menthol, thymol, and iodine clump together and stick to the walls of the mortar and pestle. For these substances, liquid is added at the rate of 10-15 drops per 1.0 g of substance. The same amount of liquid is used for phenyl salicylate, which has solid crystals. For such medicinal substances as boric acid, streptocide, sodium tetraborate, the amount of liquid is halved: 5 drops of alcohol or 8 drops of ether per 1.0 g of the substance to be crushed. Without waiting for the alcohol to completely evaporate, add the other ingredients of the compound powder.

Volatile liquids are also used for rubbing volatile substances and those that irritate the mucous membrane (salicylic acid), especially toxic substances (arsenic anhydride, mercury dichloride, etc.).

***Packaging and clearance for shipment.***

If the type of packaging is not specifically indicated in the prescription, powders are usually dispensed in paper capsules, which are paper rectangles of a certain size (7.5x10 cm).

Various types of paper are used to make capsules: glued (writing), waxed, waxed, parchment, parchment-like, and cellophane. Capsules made of glued paper

(plain capsules) are used for packaging non-hygroscopic and non-volatile powders. Waxed and waxed paper capsules (glued paper impregnated with molten wax or paraffin) are used to pack hygroscopic substances (e.g., eufillin), as well as substances that change under the influence of oxygen, carbon dioxide, and easily weathered (magnesium oxide, etc.).

Waxed and paraffin capsules are not suitable for packaging powders that are soluble in wax or paraffin (essential oils, camphor, menthol, phenyl salicylate, etc.).

Camphor and menthol form a eutectic alloy with wax, so they are released in parchment capsules (unglued paper treated with sulfuric acid, then the acid is washed off and the parchment is dried). Cellophane capsules are suitable for packaging powders containing fatty oils (carob), camphor, menthol, essential oils, and hygroscopic substances. Parchment and cellophane are slightly permeable to vapors and gases, while being grease-proof.

Powders packaged in capsules are dispensed to patients in paper bags or cardboard boxes. Powders undivided from volatile substances are dispensed in wide-mouth vials with stoppers.

Powders are labeled with the main labels of the approved sample: "External" or "Internal", "Powder", as well as warning labels: "Store in a cool dark place", "Handle with caution". Powders containing narcotic or intoxicating substances are sealed with sealing wax or plasticine.

**TESTS**

1 A pharmacist is preparing powders with a substance that is difficult to grind. State which substance is being ground with a volatile liquid:
a glucose;
b magnesium oxide;
c zinc sulfate;
d copper sulfate;
e camphor.

2 A pharmacist has prepared a powder containing platifylline hydro tartrate 0.05 g for all doses.
Did he use trituration?
a used in a ratio of 1:100;
b used in a ratio of 1:10;
c did not use it;
d I made double the amount of powder;
e a powder containing 0.05 g of a poisonous substance does not cook.

3 A pharmacy has received a prescription for camphor powder without a doctor's indication

of the type of packaging. Indicate the capsules used for dispensing the drug:
a waxed;
b cellophane;
c parchment;
d waxed;
e simple.

4 The pharmacist needs to prepare the powder according to the following prescription:
Rp: Camphorae 0.1
Glucosi 0.25 M. .f. pulv.
D. t. d. N. 10
S. 1 powder 3 times a day
Specify the best technology option:
a place camphor between the layers of glucose, mix;
b weigh out the camphor in a mortar, add glucose, and mix;
c rub the mortar with glucose, pour it on the capsule, grind camphor, mix;
d Grind glucose and alcohol in a mortar, add camphor, and mix;
e rub the mortar with glucose, pour it on the capsule, grind camphor in the presence of alcohol, mix

5 A pharmacist needs to weigh a general list drug substance - glucose. What is the minimum amount of glucose that can be weighed on a one-gram hand-held balance?
a 0,05 г;
b 0,01 г;
c 0,03 г;
d 0,04 г;
e 0,02 г.

6 The pharmacist has prepared a drug according to the following prescription:
Rp: Magnesii oxydi
Natrii hydrocarbonatis ana 0.2
M. f. pulv.
D. t. d. N. 12
S. 1 powder 3 times a day
Specify the best technology option:
a crushed magnesium oxide, added sodium bicarbonate, and mixed;
b crushed some of the magnesium oxide, added sodium bicarbonate, then the rest of the magnesium oxide, and mixed;
c crushed sodium bicarbonate with alcohol, added magnesium oxide, and mixed;
d crushed sodium bicarbonate, added magnesium oxide, and mixed;
e grind magnesium oxide with alcohol, add sodium bicarbonate, and mix.

7 A pharmacist is preparing a powder of platyphylline hydro tartrate. State the minimum load of
the poisonous substance that he can weigh on a one-gram hand balance:
a 0,05 г;
b 0,02 г;
c 0,03 г;
d 0,1 г;
e 0,15 г.

8 The pharmacist prepared the drug according to the following prescription:
Rr.: Raravegipi hudgoslogy 0.01
Sacchari 0.25
M. f. pulv.
D. t. d. N. 10.
S. Take 1 powder 3 times daily. Calculate the mass of one powder:
a ;0,25 p

b 0,23 г;
c 0,22 г;
d 0,28 г;
e 0,26 г.

9 A pharmacist needs to prepare a powder containing menthol. How should the pharmacist achieve the desired degree of menthol grinding?
a rub with glycerin;
b rub with alcohol;
c grind with purified water;
d rub with talcum powder;
e grind with chloroform.

10 A pharmacist is preparing a powder with riboflavin (B2). How should the pharmacist add riboflavin to the powder mixture?
a use the principle of mixing "from bigger to smaller";
b use pre-sifted riboflavin;
c use the principle of mixing "from less to more";
d use the "three-layer" method;
e riboflavin should be applied on top of the prepared powder mixture.

11 A pharmacist has prepared a powder with a coloring agent. What is the best option for powder technology?
a mixed with an alcohol-water-glycerin mixture;
b he added last;
c he added in the first place;
d crushed with alcohol and mixed with other ingredients;
e placed between layers of unpainted substance.

12 A pharmacist prepares 10 powders containing 0.2 g of dibasol per powder. State the balance that should be used to weigh this amount of substance:
a twenty-gram handhelds;
b manual one-gram;
c five-gram handhelds;
d manual one hundred grams;
e technical kilograms.

13 A pharmacist crushed a substance with alcohol to prepare a powder. Identify the substance that is difficult to crush:
a streptocide;
b copper sulfate;
c sugar;
d codeine;
e glucose.

14 A pharmacist prepared a powder with a substance in a separate mortar, at a separate workstation, using the "three-layer" method. Specify the substance for which this technology is characteristic:
a protargol;
b gray;
c glucose;
d methylene blue;
e copper sulfate.

15 This substance has a yellow color but, unlike coloring agents, does not leave a colored trace on filter paper, mortar and pestle; powder with it is prepared according to the general rules. Specify this substance:
a furacilin;
b ethacridine lactate;
c riboflavin;

d acrychine;
e gray.

16 The pharmacist prepared the powder according to the prescription:
Rr..: Acidi ascorbinici 0.1
Glucosi 0.2
M. f. pulv.
D. *t.d.* N. 10
S. 1 powder 3 times a day
Enter the mass of one powder:
a 0,1 г;
b 0,3 г;
c 0,2 г;
d 3,0 г;
e 1,0 г.

17 A pharmacist has prepared a powder that contains streptocide. State the correct method of administration of streptocide:
a use the "three-layer" method;
b is added in the form of trituration;
c rubbed primarily with alcohol;
d is added at the end and mixed until smooth;
e is added first of all when rubbing with glycerin.

18 A pharmacist is preparing papaverine hydrochloride powder. Use a hand balance to weigh 0.05 g of the substance:
a BP-1;
b BP-5;
c BP-20;
d BP-10;
e BP-2.

19 When preparing powders in pharmacies, the physical and chemical properties of individual ingredients are taken into account. Indicate which drug substance is mixed with the powder mass without additional grinding:
a streptocide;
b camphor;
c menthol;
d salicylic acid;
e starch.

20 A pharmacist prepares powders with camphor. What group of substances does camphor belong to?
a difficult to crush;
b narcotic;
c potent;
d paint shops;
e easy to spray.

21 A pharmacist needs to prepare menthol powder. How should the pharmacist grind the menthol to achieve the desired degree of grinding?
a grind with purified water;
b rub with glycerin or chloroform;
c rub with alcohol or ether;
d grind with other components of the prescription;
e grind with sugar.

## DOSING, PACKAGING, PACKAGING AND REGISTRATION FOR OVER-THE COUNTER (OTC) SALE OF LIQUID MEDICINES

Liquid dosage forms used in pharmacy can be prepared by weight, by mass, and by volume.

Most liquid medicines are prepared using the mass transfer method. In this method, the substance to be dissolved is weighed out and the solvent is used to make the required solution.

The volumetric method is used to produce alcohol of various concentrations, to dilute standard liquids, or to prepare mixtures using a batch system.

Solutions are prepared by weight in viscous solvents (glycerin, vegetable oils, etc.); in this case, the substance to be dissolved and the solvent are taken by weight, i.e., weighed out.

The concentration of solutions in recipes can be expressed in various ways.

1 1. As a percentage:

Rp: Natrium bromide solution 3% 200ml

Da. Signa. Take 1 tablespoon 3 times a day

2 List the substance to be dissolved and the solvent separately:

a) Rp: Natrii bromidi 6.0

Aquae purificatae 200ml

Misce. Da. Signa. Take 1 tablespoon 3 times a day.

б) Rp: Natrii bromidi 6.0

Aquae purificatae ad 200ml

Misce. Da. Signa. Take 1 tablespoon 3 times a day.

3 The ratio of the amount of substance to the total volume of the solution:

Rp: Natrium bromide solution ex 6.0 200ml

Da. Signa. Take 1 tablespoon 3 times a day.

The solution according to the specified prescription, regardless of the method of prescription, is prepared in the same mass concentration, i.e., in all cases, the volume should be 200 ml.

4 If very small quantities are prescribed, mainly solutions of poisonous and

potent substances, the prescription shall indicate the amount of the medicinal substance to the total volume of the entire solution to be dispensed.

Rp: Aethacridine lactate solution (1:1000) 200ml

Da. Signa. For wound washing.

In this case, it is indicated that a 1:1000 dilution of ethacridine lactate should be prepared in advance and 200 ml of this solution should be released. To prepare the solution, take 0.2 g of ethacridine and 200 ml of water.

In liquid medicinal products, as well as in powders, it is necessary to check the doses of poisonous and potent medicinal substances.

When prescribing these substances in powders, the single and daily dose is easy to check because it is written in the prescription, so it only needs to be checked against the pharmacopoeia.

When prescribing mixtures and drops, the doctor allows the patient to dose these medicines and indicates the method of administration (dosage method). For example, "1 tablespoon" or "15 drops 3 times a day".

It is commonly accepted that a tablespoon is 15 ml, a dessert spoon is 10 ml, and a teaspoon is 5 ml.

The pharmacist is obliged to carefully check the dosage of toxic and potent substances and compare the data obtained with the pharmacopoeia.

For example:

Rp: Code and 0.05

Hydrocarbonates 3.0

Aquae purificatae 200ml

Syrup and syrupy products 10 ml

Ammonia and anisate liquid 5 ml

Misse. Da. Signa. Take one tablespoon 3 times a day.

First of all, you need to pay attention to the correctness of the prescription, because codeine is a potent substance with narcotic effects, but it is prescribed in a mixture, so the prescription form is a regular one, but it has a stamp, a seal of the medical institution "For prescriptions" and the personal seal of the attending physician

and his signature.

Codeine should be written out first and underlined with a red pencil to draw the attention of the assistant during the preparation of the mixture and the supervisor when checking this drug. The dosage of codeine should then be checked. Given that codeine is a narcotic, it has a limited singledose rate of 0.2 grams. When checking the dosage, the total volume of the mixture is taken into account. Only liquid ingredients (solvent, tinctures, etc.) are included in the total volume. So, let's start checking the doses:

1. Determine the total volume of the mixture - in our case, the volume is 215 ml.

1 Then determine the number of doses; for this purpose, divide the total volume by the volume of one dose. The patient doses the mixture in tablespoons, i.e. 15 ml. Thus, 215:15=14 techniques.

2 Determine the amount of codeine per dose (single dose). To do this, divide the amount of the drug prescribed in the prescription by the number of doses. In our case, 0.05:14=0.0036 g.

3 The daily dose is determined by multiplying the single dose by the number of doses per day specified in the prescription, i.e. 0.0036x3= 0.0108 g.

The doses obtained are compared with the DF. In the DF, X edition: VRD=0.05, VDD=0.15. Thus, the doses are not overestimated, and the drug is to be released. It is possible to check the doses in mixtures using a simpler method, which is more commonly used in practice:

215 ml - 0.05

15 ml - X

X=0.05 15:215=0.0036 g.

When checking the doses (both single and daily) prescribed in prescriptions, the patient's age should also be taken into account, paying particular attention to the dosage for children and people over 60 years of age. In this case, you should use the tables of higher single and daily doses provided in the DF X for adults and children, as well as in our Reference Manual.

## *PREPARATION OF MIXTURES USING CONCENTRATED SOLUTIONS AND DRY SUBSTANCES PRESCRIBED IN DIFFERENT AMOUNTS*

The instructions to the Order of the Ministry of Health of Ukraine No. 197 in the section "Rules for the preparation of liquid dosage forms by the mass method" state that when preparing liquid medicinal products in order to prevent or slow down the interaction of medicinal substances that are possible in concentrated solutions, the dry substances of List A and List B, then the general list, are dissolved in the calculated amount of purified water, filtered into a dispensing bottle, then concentrated solutions of List B, then the general list are added in the order prescribed in the prescription.

Liquid medicinal products: tinctures, liquid extracts, aqueous and alcoholic solutions, flavored waters, syrups (flavoring and medicinal), novogalenic preparations are dosed by volume and added to the aqueous solution last in the following order:

- aqueous odorless and non-volatile liquids;
- alcoholic liquids, in order of increasing alcohol concentration;
- odorous and volatile liquids.

The preparation of mixtures in bulk using a batch system requires special calculations. You need:

- correctly determine the total volume of the mixture;
- Calculate the amount of concentrated solutions and water;
- measure water, concentrated solutions, and other liquids.

A very important issue in the preparation of liquid medicinal products by the mass volume method is the determination of the total volume, regardless of how the drug is prescribed, because after preparation, the volume of the drug should not exceed the tolerance limits established for this volume.

Remember that the total volume is determined by summing the volumes of the liquid ingredients.

The total volume includes solvent, aqueous and alcoholic solutions of medicinal substances, tinctures, liquid extracts, and all other prescribed liquids in milliliters.

Example:

Rp: Natural gas hydrocarbonates 2.0

Tincturae Valerianae 6ml

Syringe syrup 10ml

Aquae purificatae 200ml

Miss. Da. Signa. Take 1 tablespoon 3 times a day.

This medicinal product is an opalescent mixture, which contains a substance that is well soluble in water, sodium bicarbonate, for which there is a concentrate solution, simple syrup and valerian tincture (fragrant). We check the compatibility of the ingredients and calculate their quantities on the back of the written control passport.

The total volume in this case will be determined by summing 200 ml of water, 6 ml of valerian tincture and 10 ml of sugar syrup, which will be 216 ml.

When preparing this mixture, we can use a concentrated solution of sodium bicarbonate 5% (1:20 ratio). So, instead of the prescribed 2.0 dry matter, we should take 40 ml of this solution (2,0 □ 20).

Then you need to take 216-(6+10+40)=160 ml of water.

However, since the concentrated solution is used instead of part of the water, it is more correct in this case to calculate the water without taking into account the volumes of tincture and syrup that are prescribed in excess of the volume of the aqueous solution:

200ml-40ml=160ml

The technology of this mixture is quite simple: first, 160 ml of purified water is measured by burette, then 40 ml of sodium bicarbonate solution (1:20), then 10 ml of simple (sugar) syrup is added to a bottle of the appropriate volume, and lastly, an alcoholic tincture of valerian, because it belongs to odorous substances.

The recipe calls for sugar syrup by volume, but you can also measure it by weight, but you need to take into account the density of the syrup, i.e. (1,3d 10)=13.0. So, if you add sugar syrup by weight, you need to weigh it out at 13.0. As for the valerian tincture, it is measured with a pipette and added last.

The prescription number, the labels "Mixture", "Shake well before use" are

affixed, since the drug contains sugar syrup, a warning label "Store in a cool place" is required.

The technology of the drug is reflected in the written control passport:

PPC

Date No. of prescription

Aquae purificatae 160ml

Natrium hydrocarbonates solution (1:20) 40ml

Syringe solutions 10ml (13.0)

Tincturae Valerianae 6ml V total = 216 ml

I've got it ready:

I checked:

If the prescription specifies "water to a certain volume," the volume of galenic and new- galenic preparations, sugar syrup, and other liquid components listed in the prescription is included in the total volume of the solution.

There are two cases here: when the amount of powdered substance is up to 3% or 3% or more of the total volume of the mixture.

Consider the preparation of mixtures with a dry powdered substance content of up to 3% when there is no concentrate of this substance. What does the instruction say about this?

When determining the total volume of the mixture, the amount of dry drugs in this case is not taken into account, since the volume of the mixture increases slightly when these drugs are dissolved and does not exceed the deviation norms for the volume of mixtures.

Example:

Rp: Analgini 2,0

Kalii bromidi

Natrii bromidi ana 3,0

Tincturae Convallariae 5 ml

Aquae purificatae ad 150 ml Misce. Da.

Signa. Take 1 tablespoon 3 times a day

Signature of the doctor Personal seal of the doctor

This medicinal product is an opalescent mixture containing the potent substance analgin, which contains less than 3%, photosensitive substances, water-soluble sodium bromide and potassium bromide, and an alcoholic tincture of lily of the valley.

The compatibility of ingredients, single and daily doses of the potent analgesic substance are checked.

150:15 = 10 receptions

RD of analgin: 2.0:10 = 0.2 VD 1.0

DD of analgin: 0.2 - 3 = 0.6 VDD 3.0

The doses are not overstated.

Calculate the ingredients on the back of the written control passport. Measure 105 ml of purified water into a beaker, dissolve 2.0 of analgin weighed at BP-5. After complete dissolution, strain through a lump of long-fiber cotton wool into a vial for dispensing. Measure 20 ml of 20% potassium bromide solution, 20 ml of 20% sodium bromide solution from the burette system, then add 5 ml of lily of the valley tincture.

They are sealed, the prescription number is affixed, and the front side of the written control passport is written. They are labeled: "Internal", "Store in a cool and dark place", "Shake well before use", "Keep out of reach of children".

***Passport of written control***

(front side)

Date No. of prescription
Aquae purificatae 105 ml
Analgini 2.0
Solutionis Kalii bromidi 20% 20 ml
Solutionis Natrii bromidi 20% 20 ml
Tincturae Convallariae 5 ml
V = 150 ml
Prepared by (signature)
I have checked (signature)

Quality control is carried out in accordance with the structural and logical scheme.

**Passport of written control**

(reverse side) % dry matter
(analgin) 150 - 2
100 - X X = 1.35 <3%
Potassium bromide solution (1:5)
4.0 - 5 = 20 ml
Sodium bromide solution (1:5)
4.0 - 5 = 20 ml
Purified water:
150 - (20 + 20 + 5) = 105 ml

Consider the case when dry medicinal substances, with no concentrates, are included in a mixture in an amount of 3% or more.

In the absence of concentrated solutions of dry substances prescribed at a concentration of 3% or more, the mixture can be prepared in a measuring vessel (very rarely) or the volume of water required to dissolve the dry substances is determined by calculating the volume increase factor (similar to the preparation of concentrated solutions).

Example:

Rp: Kalii iodidi

Natrii bromidi aa 5.0

Glucose 15.0

Aquae purificatae 180ml

Miss. Da. Signa. Take 1 tablespoon 3 times a day.

This medicinal product is a mixture containing the general list substance glucose in a concentration of more than 3%, photosensitive substances, sodium bromide and potassium bromide, which are well soluble in water, and concentrate solutions.

The dry drug in this case is glucose. The volume of the mixture in the recipe is 180 ml.

First, determine the percentage of glucose in the total volume of the mixture.

180 ml - 15.0 X = 8.3%, more than 3%.

100 ml - X

A deviation of 2% is allowed for a volume of up to 200 ml.

For a volume of 180 ml, this will be

100 ml - 2 ml 180*2/100

180 ml - X X = 3.6 ml.

100

Thus, when the drug is dissolved, the deviation in the volume of the mixture should not exceed 3.6 ml.

What is the volume occupied by 15.0 glucose when it dissolves? The calculation is based on the volume expansion factor, which is 0.69 for aqueous glucose. Hence.

15.0 0,69 = 10.35 (ml), i.e. much more than the permissible deviation of 3.6 ml.

In this case, the calculation of the amount of water in the recipe is as follows: take 25 ml of concentrated solutions of sodium bromide 20% (1:5) and potassium bromide 20% (1:5); water: 180 ml-(25 ml + 25 ml + 10.35 ml) = 119.6 ml, i.e., you can round up to 120 ml.

The preparation procedure is as follows: 120 ml of water (preferably warm) is measured into a beaker and 15.0 glucose is dissolved. After complete dissolution, strain through a lump of long- fiber cotton wool into a dark glass vial. From the burette system, measure out 25 ml of 20% potassium iodide solution and 20% sodium bromide solution. Labels "Mixture", "Store in a cool place", prescription number.

PPC

Date No. of prescription
Aquae purificatae 120ml
Glucose 15.0
Potassium iodide solution (1:5) 25ml
Natriibromide Solution (1:5) 25ml
Vtotal = 180 ml

I've got it:
I checked:

If the recipe contains 2 powdered substances without concentrates, then the percentage of the total volume of their sum must be calculated. If the total content of the powdered substances is more than 3%, the volume occupied by both the one and the other powdered substance must be taken into account, according to the MPC for each of them.

# DOSAGE, PACKAGING, PACKAGING AND REGISTRATION FOR OVER-THE-COUNTER (OTC) SALE OF SOFT DRUGS

Soft medicinal products for topical use, which are conditionally united by the general term "Ointment" (Unguenta), are the official dosage form (State Pharmacopoeia of Ukraine, pp. 507511).

According to the State Pharmacopoeia of Ukraine, **soft medicinal products for topical use are** intended for application to the skin, wounds and certain mucous membranes for local therapeutic, softening, protective effects or for the penetration of medicinal substances through the skin or mucous membranes. They are characterized by specific rheological properties, a certain structural viscosity, pseudoplastic or plastic and thixotropic properties.

Soft medicinal products (SMPs) usually contain active and excipients. Excipients form a simple or complex base that can be prepared separately or obtained during the manufacturing process of a soft medicine.

The active substances should be evenly distributed in the base, which, depending on its composition and properties, can affect their release, bioavailability and therapeutic effect.

The main task of the technologist in the manufacture of ointments is to ensure that the medicinal substances are dispersed and evenly distributed in the base as much as possible, the consistency of the ointment ensures ease of application and even distribution on the skin or mucous membrane, and the stability of the ointment guarantees the unchanged composition during use and storage.

**The technological process of** manufacturing extemporaneous soft medicinal products for topical use includes the following technological stages:

- melting (bases), dissolving, extracting, grinding (dispersing), emulsifying, mixing (homogenizing);
- quality control;
- packaging and labeling (design).

The manufacturing **process of** extemporaneous soft medicinal products for

topical use, depending on the type of dispersed system, may include all or some of the above stages.

**Calculations of quantities of medicinal substances and bases**

If the prescription does not indicate the concentration of the drug substance, a 10% ointment should be prepared.

Ointments whose prescriptions are standardized (i.e., official) are prepared in accordance with the composition and concentration of medicinal substances specified in the NTC.

**The administration of medicinal substances in ointments is carried out taking into account their physicochemical properties and prescribed amounts.**

**Drugs soluble in fats** (camphor, menthol, thymol, chloral hydrate, crystalline phenol, anesthetic up to 2%, phenyl salicylate, etc.) are administered in single-phase ointment solutions by dissolving them in a fatty base or its component.

If the total amount of these substances is up to 5%, they are rubbed with a liquid that has similar properties to the base: petroleum jelly - petroleum jelly, fatty base - stone fruit oil. Take as much liquid as the substance.

If the total amount of these substances is more than 5%, they are ground with an equal amount to the weight of the dry matter of the fused base.

These substances are introduced into hydrophilic bases as a suspension.

***Production of homogeneous ointments.***

Ointments - alloys are a combination of several intermeltable and inter-soluble components.

The components are fused in a water bath in a porcelain or enamel cup (Figure 11).

The general technology of alloy ointments is as follows:

- □ melts the most refractory substances first
- □ to the resulting melt, other ingredients are added in order of decreasing melting point;
- □ liquid components are added last
- □ The resulting liquid melt is filtered through cheesecloth into a

heated mortar (50-55 °C) if necessary

- □ stir until cooled
- □ essential oils are added last at a temperature not exceeding 40 C.

In this case, the ointment becomes loose, soft, and easy to smear because stirring prevents the formation of microcrystalline frameworks, as well as the crystallization of some solid ingredients that give the ointment a coarse-grained structure.

Stirring is especially advisable if the ointment formulation includes paraffin, otherwise it can stand out in the form of large crystals. In addition, stirring gives the ointment a loose porous structure due to the incorporation of air.


***Fig. 11. Fusion of components in a water bath***

The comparative melting points of the substances in the composition of alloy ointments are given below in the following order:

1 Cerezin
2 Ozokerite
3 Wax yellow
4 White wax
5 Petrolatum
6 Solid paraffin wax
7 Spermaceti
8 Beef fat
9 Lanolin anhydrous
10 Vaseline
11 Hydrogenated fats

12 Naphthalene

13 Vegetable and artificial oils

14 Essential oils

Solution ointments are ointments containing medicinal substances that are soluble in an ointment base (regardless of its nature).

Medicinal substances are dissolved in a molten base in a porcelain (china) cup by gentle heating in a water bath. If the ointment contains a liquid in which the substance is soluble, it is dissolved in this liquid and then mixed with the other components.

**Drugs soluble in fats** (camphor, menthol, thymol, chloral hydrate, crystalline phenol, anesthetic up to 2%, phenyl salicylate, etc.) are administered in single-phase ointment solutions by dissolving them in a fatty base or its component.

If the total amount of these substances is up to 5%, they are rubbed with a liquid that has similar properties to the base: petroleum jelly - petroleum jelly, fatty base - stone fruit oil. Take as much liquid as the substance.

If the total amount of these substances is more than 5%, they are ground with an equal amount to the weight of the dry matter of the fused base.

These substances are introduced into hydrophilic bases as a suspension.

Rp: Mentholi 0.1

Vaselini 10.0

Mise, fiat unguentum

Da. Signa: Nasal ointment.

In a mortar, grind 0.1 g of menthol with a few (2) drops (0.1 g) of petroleum jelly until completely dissolved and mix thoroughly with petroleum jelly (Fig. 12-13).

**Figure 12. Adding petroleum jelly to menthol**


**Fig. 13. Removing part of the petroleum jelly for melting in a water bath**

### *SUSPENSION AND EMULSION OINTMENTS*

Heterogeneous ointments are systems that have phase separation with different boundary layers.

These include suspension (or trituration), emulsion, and combined ointments.

The administration of medicinal substances in ointments is carried out taking into account their physicochemical properties and prescribed amounts.

Medicinal substances insoluble either in water or in a base (zinc oxide, basic bismuth nitrate, white clay, dermatol, norsulfazole, sulfur, streptocide, talc, etc.) are usually added to suspension ointments in the form of powders ground to the maximum degree of dispersion according to Deryagin's rule for the type of suspension.

Water-soluble substances that require a significant amount of water to dissolve (sodium tetraborate, boric acid, sulfonamide preparations, etc.) are also introduced

into suspension ointments.

Zinc sulfate and resorcinol are used as suspensions in dermatological ointments.

If the total amount of these substances is up to 5%, they are ground with a liquid that has similar properties to the base: hydrophilic base - purified water, petroleum jelly - petroleum jelly, fatty base - stone fruit oil. The liquids are taken according to the Deryagin rule of ІЦ by weight of dry matter.

If the total amount of these substances is more than 5%, they are ground according to Deryagin's rule with ІЦ of the dry weight of the melted base.

**Water-soluble drugs** (alkaloid salts, potassium iodide, novocaine, silver nitrate, etc.) are mainly administered in emulsion ointments by dissolving them in a minimal amount of water or in the base if the base is hydrophilic.

If the base is hydrophobic and the total amount of these substances is up to 5%, they are dissolved in water, aqueous solutions, liquid extracts, if they are prescribed in the recipe, and emulsified with lanolin. If a hydrophilic liquid is not specified in the prescription, it is deducted from aqueous lanolin (30%) and emulsified with aqueous lanolin (70%)

**Drugs soluble in fats** (camphor, menthol, thymol, chloral hydrate, crystalline phenol, anesthetic up to 2%, phenyl salicylate, etc.) are administered in single-phase ointment solutions by dissolving them in a fatty base or its component.

If the total amount of these substances is up to 5%, they are rubbed with a liquid that has similar properties to the base: petroleum jelly - petroleum jelly, fatty base - stone fruit oil. Take as much liquid as the substance.

If the total amount of these substances is more than 5%, they are ground with an equal amount to the weight of the dry matter of the fused base.

These substances are introduced into hydrophilic bases as a suspension.

### *Production of heterogeneous ointments*

Suspension ointments are ointments containing solid powdered medicinal substances crushed to the smallest size, insoluble in the base and water and distributed in it by the type of suspension (exceptions are zinc sulfate and resorcinol).

Suspension ointments are prepared by thoroughly rubbing solid powdered

substances with an ointment base (Fig. 14).

***Fig. 14. Dispersion of solids***

If insoluble drugs are included in the ointment in an amount of up to 5% of the total weight of the ointment, they are thoroughly rubbed into the foot, first in dry form, and then in the presence of a liquid suitable for the base. As an auxiliary liquid, depending on the nature of the base, use petroleum jelly (with hydrocarbon bases), peach or almond oil (with fatty bases) and water or glycerin (with hydrophilic bases). These liquids are taken in half the amount of the weight of the medicinal substances (Deryagin's rule) (Fig. 15).


***Figure 15. Dispersion with petroleum jelly***

If the amount of insoluble substances in the ointment is from 5 to 20 %, they are thoroughly ground in a mortar, first in dry form, and then with half the amount of the dry matter of the molten base (Fig. 16-17). The use of auxiliary liquids in this case is inappropriate, as it will cause the ointment to thin and reduce the concentration of

medicinal substances.

***Figure 16. Adding petroleum jelly***

***Fig. 17. Mixing substances with the base***

The last stage is transferring the finished ointment to the ointment jar (Fig. 18).

***Fig. 18. Transferring the finished ointment to the ointment jar***

Typical representatives of suspension ointments are official ointments: white mercury ointment, xerophore ointment, zinc ointment, and others. The mainstream prescriptions for topical ointments are extremely diverse.

Rp: Unguenti Streptocidi 3 % 10.0

Da. Signa: To lubricate wounds.

It is a suspension ointment with a solids content of less than 5 % (3 %). Streptocid (0.3 g), as a substance that is difficult to grind, is crushed in the presence of a few drops of alcohol or ether, and then thoroughly rubbed with a few drops (0.15 g) of petroleum jelly and petroleum jelly is added to the resulting mushy mass in 2-3 steps with constant stirring until a homogeneous mass is obtained.

ACC (l.b.)

Date No. of prescription

Streptocidi 0.3

OleiVaselini gtts IX

Vaselini 9.7 m = 10,0 I've got it ready: I checked:

***Ointment-emulsions are heterogeneous systems consisting of two phases and having a phase-media interface.***

They consist of aqueous solutions or water-soluble drugs that form emulsions, mainly of the B/O type, with an ointment base. Unlike triturated ointments, emulsion ointments penetrate the skin faster, and the drug substances in the aqueous phase also act faster.

In the manufacture of emulsion ointments, the amount of liquid that can be absorbed by the base is taken into account.

Medicinal substances that are easily soluble in water and are prescribed in small amounts (up to 5%}. dissolve in a minimal amount of water (Fig. 19). If they are prescribed in large quantities, they are not dissolved in water (except for colargol, protargol, tannin), but are introduced into the ointment as a suspension. Dry and thick extracts are added to ointments after preliminary grinding them with an alcohol-water-glycerin (1:6:3) mixture.

When aqueous solutions of drug substances are mixed with a base, an emulsion system is formed, which obeys the general laws governing the behavior of emulsions. To form a stable emulsion system, it is necessary to use an emulsifier, which is most often lanolin. Spermaceti and waxes are used much less frequently because they have weak emulsifying properties. The technique of manufacturing emulsion ointments is to thoroughly mix lanolin or another emulsifier with an aqueous solution of medicinal substances in a mortar until it is completely absorbed, and then add the base (Fig. 20-21).

*Fig. 19. Dissolution of substances*

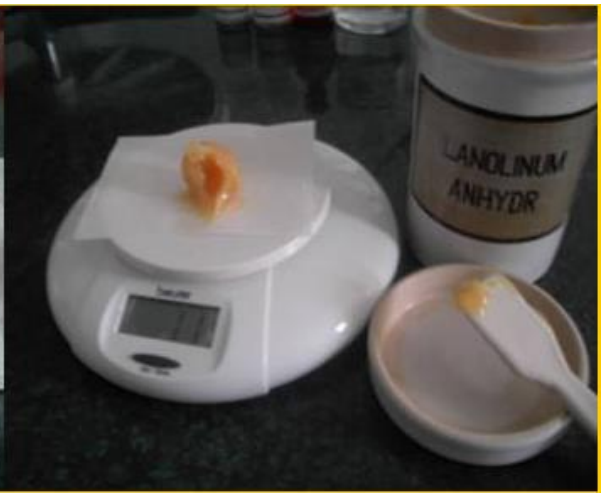


*Fig. 20. Weighing of lanolin in purified anhydrous water*

*Fig. 21. Emulsification*

## QUALITY ASSESSMENT OF OINTMENTS

The quality of prepared ointments is assessed in the same way as other dosage forms, i.e., documentation (prescription, passport), packaging, design, absence of delamination and mechanical inclusions, and weight deviations are checked. The authenticity is determined visually by appearance and organoleptic characteristics (smell, color, etc.), which depend on the properties of the constituent medicinal substances and ointment bases used.

## PACKAGING AND STORAGE OF OINTMENTS

In pharmacies, ointments are packaged in glass, porcelain, or plastic jars with a capacity of 10.0 to 100.0 g with screw-on or pull-off plastic lids. In all cases, parchment or waxed paper or cardboard pads with double-sided polyethylene coating are placed under the lid and the ointment is packaged accordingly. Ointments and pastes containing substances that change under the influence of light are dispensed in light-tight jars.

The finished ointments and pastes are transferred from the mortar to the jars using a spatula and a celluloid plate, which is used to collect the ointment first from the pestle and then from the walls of the mortar. Jars should be selected according to the volume of ointment. When filling the jar with ointment, there should be no free spaces (cavities), for which it is necessary to add the ointment in separate portions and compact it by tapping the bottom of the jar against the palm of your hand.

It should be noted that, along with their undoubted advantages (chemical inertness, impermeability to drugs, water vapor, gases, sealing capability, and affordability), glass jars also have disadvantages: low mechanical strength, inconvenience of transportation, and laboriousness of washing. Plastic polystyrene jars with lids are also used, but they are unsuitable for storing ointments containing tar, methyl salicylate, turpentine, camphor, phenol, and essential oils.

### *GENERAL RULES FOR THE PREPARATION OF SUPPOSITORIES*

Suppositories (Latin Suppositoria) are dosage forms that are solid at room temperature and melt at body temperature. Suppositories are used for insertion into body cavities.

The literature also provides such definitions:

Suppositories are a solid dosage form consisting of a base and medicinal substances that melt (disintegrate, dissolve) at body temperature. Suppositories are used for insertion into body cavities.

Suppositories are a complex dosage form consisting of medicinal substances that carry therapeutic properties and excipients - bases that provide suppositories with the proper weight, required consistency of medicinal substances, and certain physical and

chemical properties.

***Classification of suppositories.***

1 Suppositories are distinguished by the method of application and purpose:

A Rectal suppositories - suppositoria rectalia;

B) Vaginal - suppositoria vaginalia;

B The sticks are called bacili.

2 By shape, weight and size.

The appearance of suppositories and their characteristics are shown in Table 5.

***Table 5***

**The most used types of suppositories by shape, mass, size and application**

| | | | | |
|---|---|---|---|---|
| Pessaries, sticks | cylindrical, flat, pointed | specified in the recipe, or 2-5 mm thick, up to 10 cm long | | gynecology, urology |
| Type of candles | Form. | Weight, g | Size. | Common applications |
| Rectal | cone, cylinder and other shapes | from 1.1 to 4.0 g (**3.0)** for children from 0.5 to 1.5 g | maximum permissible diameter of 1.5 cm and length from 2.5 to 4.0 cm | pharmacotherapy of emergency conditions, proctology, urology, etc. |
| Vaginal | balls, ovoid | 1.5 to 6.0 g (**4.0**) | | gynecology |

Rectal suppositories can be in the form of a cone, a cylinder with a pointed end, or another shape with a maximum diameter of 1.5 cm.

The weight of one suppository should be between 1 and 4 g. If the weight is not specified, the suppository is manufactured with a weight of 3 g. The weight of a suppository for children should be between 0.5 and 1.5 g.

Vaginal suppositories can be spherical (globuli), ovoid (ovula), or in the form of a flat body with a rounded end (pessary). Their weight should be between 1.5 and 6 g. If the weight is not specified, vaginal suppositories are manufactured with a weight of at least 4 g.

The sticks have the shape of a cylinder with a pointed end and a diameter of at

least 1 cm. The weight of the stick should be from 0.5 to 1 g.

3 Based on the physical and chemical properties of the dosage form, it should be considered as a dispersed system consisting of a dispersion medium (base) and a dispersed phase (various drugs in solid and liquid form). Therefore, suppositories can also be classified as:

- "Heterogeneous" systems are systems formed when the drug substance is distributed in the base by suspension or emulsion type;
- "Homogeneous" systems are those formed when the drug substance dissolves in the base.

4 4. Suppositories can be designed for local and resorptive action. When dispensing suppositories, it should be borne in mind that absorption from the rectum and vagina is rapid and that drugs intended to have a resorptive effect enter the bloodstream, bypassing the liver barrier. Therefore, it is mandatory to check single and daily doses of toxic and potent substances. In this case, higher doses of substances for internal use are used.

### *Requirements for suppositories*

1 All suppositories, especially rectal suppositories and sticks, should be of sufficient hardness to overcome sphincter and tissue resistance, otherwise they will deform or break during insertion, which limits their use.

2 Suppositories made on bases that do not dissolve in mucosal secretions should melt at a temperature not exceeding 37°. However, the standardization of the upper melting point does not fully resolve the issue of the quality of suppositories and bases. It is important that melting occurs in a short temperature range (1-2°), and not stretched with the passage of the softening stage. In the latter case, the suppositories will be easily deformed in the patient's hands, and their use will become impossible.

3 The liquid formed as a result of melting or dissolving the suppositories should spontaneously spread over the mucous membranes, forming a more or less uniform layer, which will ensure closer contact of the drug substances with the

tissues and accelerate their absorption (or local action). To facilitate the mixing of the liquid with mucosal secretions, lanolin is added to the suppositories (it is also used as a binder in the manufacture of suppositories by the rolling method). The introduction of lanolin also accelerates the absorption of drugs.

4 Suppositories should release their drug substances easily, unless they are expected to have a prolonged therapeutic effect. The ease of release of medicinal substances depends on the properties of the base, as well as on the method of administration of the substances into the base. Water-soluble bases (except for polyethylene oxides) release drugs easily due to their ability to dissolve in mucosal secretions. Drug release from fatty bases is slower. Drug substances introduced into suppositories in the form of aqueous solutions are absorbed more easily than those introduced in dry form.

5 Suppositories should not have an irritating effect, as they come into contact with mucous membranes rich in nerve endings.

6 Suppositories should have a regular and uniform shape and homogeneous mass. The homogeneity of the mass is determined visually on the cut by the absence of inclusions, glitter or pieces of the base.

7 Deviations in the weight of suppositories are allowed within ±5%.

8 Suppositories, especially factory-made ones, should be well stored. They should be resistant to light, air, moisture and microbial flora. The Pharmacopoeia allows the use of preservatives or antioxidants in these cases.

There are two groups of components in the composition of suppositories: medicinal substances and excipients - bases (Basis seu Constituens), which provide suppositories with the proper volume, the required concentration of medicinal substances, and the necessary physical properties: plasticity, melting, etc.

The main technological challenge in the preparation of suppositories is to distribute the most dispersed medicinal products evenly not only in the suppository mass, but also in each candle, ball or stick, giving them the required geometric shape.

If the weight of the candle is not specified in the recipe, then they are prepared with a weight of 3.0 g. In pediatric practice, the weight of the candle must be specified

in the recipe - it should be from 0.5 to 1.5 g.

If the weight of vaginal suppositories is not specified, they are prepared in 4.0 g. The size of the sticks should be specified in the prescription.

For the preparation of suppositories in a pharmacy, the pumping method is used, and if smallscale mechanization is available, the pouring and pressing methods are used.

1 Drug substances soluble in the base are dissolved in an amount of up to 5% in a liquid of the same type as the base, if more than 5%, they are dissolved in a part of the molten base.

When using the pouring method, these substances are dissolved in the entire molten base, regardless of their concentration.

2 When using the pumping method, water-soluble drugs prescribed in amounts up to 5% are dissolved or ground with a few drops of water, glycerin or alcohol, and then mixed with the base. If the soluble substance is more than 5% and requires a significant amount of solvent, it is thoroughly ground in a mortar, first dry, then with a small amount of water, and then the base is added in parts.

When using the pouring method, water-soluble substances are added to lipophilic bases as a suspension, and to hydrophilic bases by dissolving them in a small amount of water or glycerin and then mixing them with a semi-chilled base.

3 Medicinal substances that are insoluble in either the base or water, prescribed in small amounts (less than 5%), are rubbed with a few drops of vegetable oil and then mixed with the base.

If these substances are prescribed in large quantities (more than 5%), then when using the pumping method, they are thoroughly crushed and mixed with finely grated cocoa butter chips, and then the rest is added. If necessary, to obtain a more plastic mass, it is advisable to add anhydrous lanolin at the rate of 1.0 per 30.0 suppository mass.

When using the pouring method, these substances are thoroughly ground and mixed with a portion of the molten base, and then the resulting mixture is added to the entire molten base.

4 Medicinal substances in the form of thick liquids are mixed directly with the crushed fatty base without the addition of a plasticizer. Liquid ingredients that do not contain volatile substances can be thickened by evaporation.

5 Thick extracts are administered after preliminary mixing with an equal amount of alcohol-water-glycerin mixture (1:6:3) or immediately as a solution of thick extract (1:2).

6 Thermolabile substances are added to the semi-cooled mass immediately before pouring the suppository mass into molds.

**Technology for the preparation of suppositories by manual pumping**

Suppositories are both homogeneous and heterogeneous dispersed systems, so the main technological challenge is to distribute the maximum dispersed drug evenly not only in the suppository mass, but also in each candle, ball or stick, giving them the required geometric shape.

If the weight of the candle is not specified in the prescription, then according to the guidelines of the NTD, they are prepared with a weight of 3.0 g. In pediatric practice, the weight of the candle must be indicated in the prescription, it should be from 0.5 to 1.5 g.

If the weight of vaginal suppositories is not specified, they should be prepared with a weight of at least 4.0 g. The size of the sticks should be specified in the prescription.

Methods of manufacturing suppositories. Suppositories can be manufactured by three methods: rolling out (manual molding), pouring into molds, and pressing.

The use of one or another method depends on the properties of the base, its ability to produce plastic masses, the speed of solidification after melting, and its fluidity under pressure. **Only cocoa butter or its substitutes are used to produce suppositories by pumping; cocoa butter, butyrrol, PEO (many of them soften during pressing); water-soluble and all fatty bases (except cocoa butter, which turns into a low-melting modification when heated).**

During the manufacturing process, suppositories can easily become

contaminated with microorganisms, so special attention should be paid to strict compliance with sanitary rules (clean hands and devices, protection of the suppository mass from microorganisms, dust, etc.) It is not recommended to touch the mass directly with your hands; if necessary, it is taken with a piece of cellophane or waxed paper.

The administration of medicinal substances in suppositories depends on the nature of the base, the amount and physical and chemical properties of the medicinal substances to be administered, and, above all, on their solubility in the base.

***Introduction of drugs into hydrophobic bases:***

1 **Medicinal substances soluble in the base** (camphor, chloral hydrate, phenol, phenyl salicylate, thymol, anesthetics, etc.), depending on the amount of them, dissolve in part or all of the molten base. If these substances are introduced in large quantities, eutectic alloys with a lower melting point are formed. In these cases, it is necessary to add substances in the amount of 4-5% by weight of the fatty base, which increase the melting point of the mass to 36-37 °C. Such sealants are paraffin, wax, spermaceti, etc. If the suppository contains phenol, it is taken in crystalline form and dissolved in a portion of the molten fatty base.

It should be noted that the method of dissolving medicinal substances in a molten base is more suitable for pouring the molten mass into molds. It is inconvenient when manufacturing suppositories by manual molding (pumping).

2 **Water-soluble drugs** (alkaloid salts, resorcinol, quinazol, novocaine, ethacridine lactate, protargol, colargol, tannin, etc.) prescribed in an amount of up to 5% are first dissolved in a few drops of water or glycerin, or, in extreme cases, alcohol, rubbed with the specified liquids, and then emulsified and mixed with the base. Dissolution facilitates the uniform distribution of small doses of drug substances in the base, improves absorption conditions and provides rapid local action.

Anhydrous lanolin (B/O emulsion) is used as an emulsifier, which is added in minimal amounts to avoid the formation of a mass of ointment-like consistency If the above-mentioned drugs are mixed directly with the fatty base in undissolved form (which is possible in principle due to its high viscosity), their small particles are

covered with a fatty membrane, and the absorption process is very slow. When drugs are injected into a fatty base in the form of an aqueous solution without an emulsifier, a mass is formed that is difficult to form and easily crumbles during handling.

If there is a lot of soluble substance (more than 5%) and it requires a significant amount of solvent, it is thoroughly ground in a mortar, first in dry form, then with a small amount of water (i.e., introduced without dissolving the substance), and then the base is added in parts.

3 **Medicinal substances insoluble neither in the base nor in water** (xeroform, dermatol, streptocide, basic bismuth nitrate, theophylline, zinc oxide, osarsol, etc.) are added to the mass in the form of a fine powder. In the manufacture of suppositories by the pouring method, the substances are first ground to the maximum degree of dispersion (their exact dosage in suppositories and therapeutic activity significantly depend on this), then ground with a part of the molten base (according to the Deryagin rule) and the resulting mixture is added with constant stirring to the molten, semi-molten base. The mass is then poured into appropriate molds. The thermolabile substances should be added to the semi-solidified base before pouring it into the mold.

In the manufacture of suppositories by the pumping method, depending on the amount, these medicinal substances are administered twice. If they are prescribed in small quantities, i.e. up to 0.1 g per candle, they are first rubbed with a few drops of fatty oil (peach, almond, etc.) and then mixed with a crushed base. If these medicinal substances are prescribed in large quantities, i.e., more than 0.1 g per candle, they are thoroughly crushed and mixed with part of the melted or finely grated base, and then the rest is added. Direct mixing of crushed medicinal substances with the entire base does not ensure uniform distribution of bulk substances in a thick base.

4 **Medicinal substances in the form of liquids** (ichthyol, balsams, naphthalene oil) with adhesive properties are administered by directly mixing with a crushed fatty base, without adding a plasticizer. Liquid ingredients that do not contain volatile substances can be thickened by evaporation at the lowest possible temperature.

5 **Thick extracts** (e.g., extract of holly, etc.) are introduced into the suppository

mass after preliminary mixing with an equal amount of alcohol-water-glycerin mixture (1:6:3) or as a readymade solution (1:2).

***Introduction of drugs into hydrophilic bases:***

1 Water- or glycerin-soluble drugs are first dissolved in a portion of the water or glycerin intended for the base and then added to the molten, ready-to-pour base.

2 Medicinal substances that are insoluble in neither water nor glycerin are first ground with a portion of glycerin into a fine suspension and then added to the finished, molten base before pouring into molds.

3 Medicinal substances that are well soluble in polyethylene oxide base, collagen gel are injected directly into the molten part or all of the base (gel), followed by mixing and pouring the finished homogeneous mass into molds. Insoluble substances are first mixed with the liquid component of the base, and then mixed into the entire mass and poured into molds.

***Production of suppositories by pumping out.***

**The manual pumping method has the** advantage of not requiring any special equipment. This method achieves an even distribution of all ingredients in the suppository mass. On the other hand, it is economically inefficient, because in the absence of mechanization, a lot of labor is involved, and the resulting products have a worse appearance than when making suppositories using mechanization.

The production of suppositories by the pumping method involves several stages:

- preparation of the base,
- administration of medicinal substances
- preparation of suppository mass,
- dosage,
- forming suppositories, - packaging and design.

The pumping method can be used to prepare suppositories only from plastic bases that are pre-crushed using special devices. The crushed **base is much easier to dose and more convenient to use for the manufacture of suppositories.**

**Figure 22: Weighing the base** ***Figure 23. Mixing medicinal substances***

In accordance with the above rules, the prescribed medicinal substances are injected into the crushed, weighed base (Fig. 22), mixing them in a porcelain mortar (Fig. 23).

The resulting mixture is crushed with a pestle, gradually increasing the pressure on the pestle until a plastic mass is formed that lags behind the walls of the mortar (Figure 24).

**Fig. 24. Crushing the mixture in a mortar**

If the suppository mass contains a lot of powdered substances, the mass is difficult to form and crumbles. **In this case, a small amount of anhydrous lanolin should be added to impart plasticity (on average, 1-1.5 g of lanolin per 30.0 g of weight).**

The resulting mass is removed from the mortar using wax paper, compressed into a lump, and weighed (Fig. 25), and the result is indicated on the recipe or signature and in the PCR.

***Fig. 25. Preparation of a suppository lump***

After that, the mass is transferred to a plastic plate or glass of a pill machine covered with white paper, and a flat plate, also covered with a smooth white sheet of paper, is used to roll out a smooth tetrahedral bar (or cylindrical rod) of equal thickness along its entire length (Fig. 26).

***Fig. 26: Rolling out the suppository bar***

The length of the bar should be equal to the number of divisions of the cutter of the pill machine (or double the number of divisions) corresponding to the prescribed or multiple number of candles or balls. The bar is placed on the lower cutter of the pill machine and, pressing it down with the upper cutter, divisions are made along which the prescribed number of candles or balls is cut with a thin knife or celluloid

and the accuracy of the mass dosage is checked by weighing (Fig. 27).

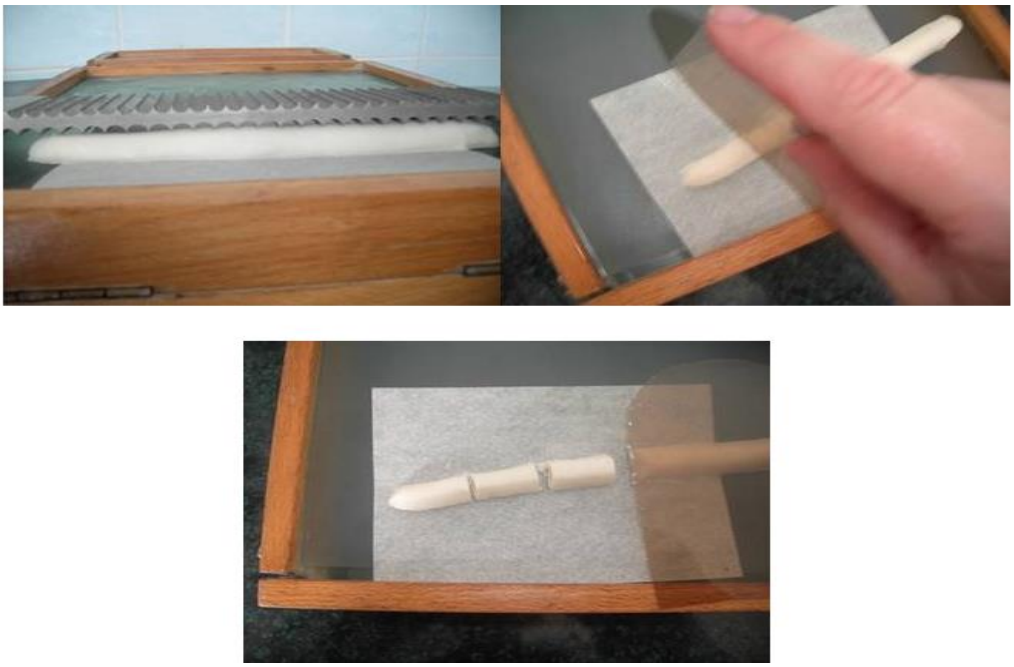

***Figure 27. Cutting the suppository bar into equal pieces***

Then, using a plate, each individual portion of the mass is shaped into a ball, from which candles of a conical or other shape are rolled out using a plate placed at a 30° angle (Figure 28).

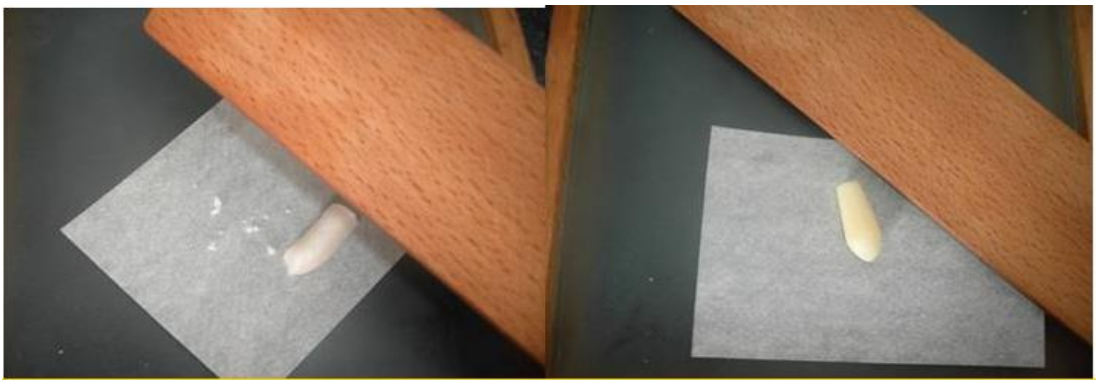

***Figure 28: Shaping a suppository***

The finished candles, each one individually, are wrapped in cellophane, aluminum foil, or thin wax paper, which has the shape of a triangle (kerchief) measuring 7.5-12 cm.

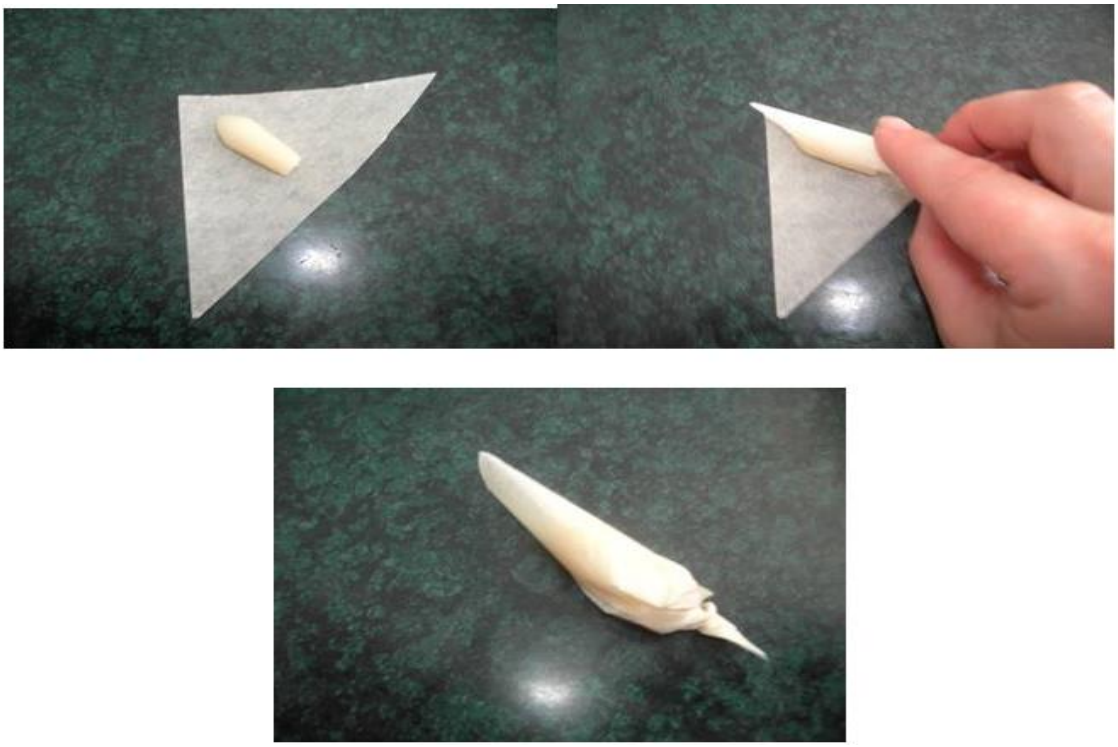

***Figure 29. Wrapping candles.***

Wrapped candles are placed in cardboard or plastic boxes.

***Quality assessment of suppositories***

The quality of prepared suppositories is evaluated in the same way as other dosage forms, i.e., the documentation (prescription, passport), packaging, design, color, odor, and absence of mechanical inclusions are checked.

Specific to the quality of suppositories are: size, shape, which must comply with the prescription.

Homogeneity of mixing - the suppository mass should be homogeneous on the cut, without inclusions, the presence of an air rod or a funnel-shaped depression is allowed.

The weight of candles must be within the range specified by the SFS. Deviations in the weight of individual candles shall not exceed -5%.

Finished suppository dosage forms must have a certain hardness to ensure their use, otherwise they are unsuitable because they can deform in the hands of the patient before they are used.

***Production of suppositories by pouring***

The pouring method, being versatile, allows for the preparation of suppositories

of the same shape using a variety of bases, which is not possible with other methods. The manufacturing process is much faster, more hygienic, and the appearance of candles, balls and sticks is better compared to the pumping method.

The disadvantage of this method is the disturbance of the homogeneity of the mixture during drying, especially due to liquids that do not mix with the bases and the solid phase.

**The pouring method consists of the following steps:**

- manufacturing and melting of a suitable base;
- mixing prescribed medicinal substances with a molten base
- preparation of forms
- Pouring the cooked semi-cooked mass into molds;
- cooling;
- packaging;
- design.

First, weigh out the required amount of base (Fig. 30).


***Fig. 30. Weighing the substrate***

If one substance, for example, butyrol, is prescribed as a base, it is melted in a ladle or porcelain cup in a water bath to mix with medicinal substances (Fig. 31).

***Fig. 31. Melting the base***

If the base consists of several substances, an alloy is prepared accordingly, and then the medicinal substances are added in the form of a solution or the finest powder The mass should be heated carefully, preventing the temperature from rising above 38-40 °C. Overheating increases the time required for its subsequent solidification in the mold, and the quality of the suppositories deteriorates. If it is necessary to heat the base to a higher temperature, it is advisable to heat only a part of the base (70-80%), and add the rest in solid form to the molten mass after its temperature has decreased to 37-38 °C.

Medicinal substances are added to the base according to the rules described above.

Special metal or plastic molds are used for casting (Figure 32).

***Fig. 32. Pouring molds***

Before pouring, the cells of the molds are wiped with a gauze swab dipped in petroleum jelly if the suppositories are prepared on hydrophilic bases.

The cells of the mold are wiped with a gauze swab moistened with soapy water if the suppositories are prepared on fatty bases.

The prepared suppository mass is quickly poured from the porcelain cups into the prepared molds (Fig. 33).

**Figure 33. Pouring the suppository mass into molds**

Filling the mold with the mass should be gradual, otherwise the suppositories will be heterogeneous and brittle. The filled mold is shaken slightly to remove air bubbles and placed in the freezer of a refrigerator for 10-15 minutes, after which the frozen mass protruding from the mold cells is scraped off with a knife. The frozen suppositories are released (after the mold elements have been separated) by pressing on their bases toward the top.

**Fig. 34. Prepared suppositories are wrapped and prepared for release.**

The finished candles, each one individually, are wrapped in cellophane, aluminum foil or thin waxed paper, which has the shape of a triangle (kerchief) measuring 7.5-12 cm.

Wrapped candles are placed in cardboard or plastic boxes.

# GENERAL REQUIREMENTS FOR THE MANUFACTURE OF STERILE MEDICINAL PRODUCTS IN PHARMACIES

Solutions for injections are prepared in accordance with the requirements of the State Fund, orders of the Ministry of Health, and instructions.

The manufacturing process of solutions for injection consists of the following stages:

1 Preparatory work.

2 Solution preparation (stabilization, isotonization if necessary).

3 Filtering and packaging.

4 Sterilization of the solution.

5 Control of finished products.

6 Design.

The preparatory work (training of personnel, preparation of the aseptic unit, organization of work in aseptic conditions; preparation of utensils and auxiliary materials; preparation of solvents and preparations) is given shortly.

Let's consider the stages of direct manufacturing of solutions for injection.

Preparation of the solution.

Solutions for injection may be manufactured only in pharmacies that have a permit issued by an authorized body.

It is not allowed to prepare solutions for injection in the absence of methods for their complete chemical analysis, sterilization regimen, data on the chemical compatibility of the input ingredients and technology.

The personal responsibility for the organization of work of aseptic units and preparation of solutions for injection lies with the heads of pharmacies or an authorized person. They are obliged to conduct annual briefings and test the knowledge of employees of aseptic units on the rules for the manufacture of solutions for injection, as well as when hiring or transferring them to work in an aseptic unit. Persons who do not know the technology of solutions for injection are not allowed to work in the aseptic unit.

Due to the highly sensitive nature of the application and the high risk of errors that can be made during operation, the production of injectable solutions requires strict regulation and strict adherence to technology.

It is not permitted to simultaneously manufacture several injectable solutions containing different ingredients or the same ingredients in different concentrations. During the preparation of injectable solutions, the workplace should not contain vials with medicinal substances that are not related to these solutions.

The preparation of injectable solutions is carried out by the mass-volume method, in which the drug substance is taken by weight and the solvent is added to obtain a certain volume of solution. The need to prepare solutions in mass concentration is explained by the fact that when administered by syringe, the drug is dosed by volume.

The technological stage "Solution preparation" includes technological operations:

- Preparation of raw materials (calculations, weighing substances and measuring solvent (Figures 35-36),

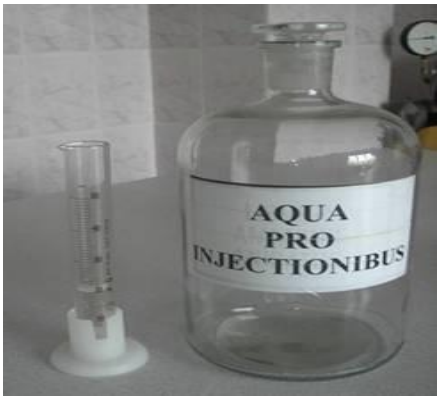


***Fig. 35. Measuring the solvent***


***Fig. 36. Weighing a substance***

- Direct solution production (dissolving substances, if necessary, adding a stabilizer, obtaining the required volume.

The drug substance taken by weight is placed in a sterile volumetric flask, dissolved in a small amount of solvent, and then brought to a specified volume. In the absence of a measuring vessel, the amount of solvent required to make the solution is determined by calculation using the density of the solution of a given concentration or the volume expansion factor.

Immediately after the solution is prepared, a survey control is carried out. Then the prepared solution for injection is subjected to a complete primary chemical control, which consists in determining the identity (qualitative analysis) and quantitative content of active ingredients and stabilizer (quantitative analysis).

The results of full chemical control of solutions for injection are recorded in a journal in the prescribed form.

If the result is satisfactory, the process of filtering and packaging is started.

Filtering and packaging of solutions for injection. One of the requirements for injectable dosage forms is the absence of mechanical inclusions. Injectable solutions should not contain particles visible to the naked eye, i.e. particles 10 microns and larger. However, it is advisable to bring the efficiency of filters to 5 microns, i.e. injectable solutions should not contain particles larger than the diameter of blood cells (5-9 microns). The presence of suspended particles is unacceptable, as embolism is

possible during injection.

***Fig. 37. The process of filtering solutions***

Injection solutions are freed from mechanical impurities by filtering (Fig. 37). Injectable solutions are filtered through 5-7 layers of sterilized polypropylene, all other solutions are filtered through a three-layer filter. Polypropylene plates can also be used as prefilters in membrane filtration.

Filtering of solutions is combined with their simultaneous filling into prepared sterile vials. Deviations from the volume indicated on the label (nominal) are allowed within ±10% for vials up to 50 ml. ±5 % - for dishes with a capacity of more than 50 ml.

Two types of containers are used for packaging injectable dosage forms: ampoules and vials made of glass, polyethylene or other material that does not change the properties of the medicinal substances.

Ampoules are a more advanced form of packaging because they allow medicines to remain sterile until they are used. This is a prefabricated form of packaging, so their production is covered in the course on prefabricated drug technology.

It is customary for hospital pharmacies to deliver sterile solutions to hospital departments in wide-mouth standard (graduated) vials of various capacities with a standard rubber stopper secured with a crimped aluminum cap.

Filtered solutions for injection after filling them into vials are visually checked for the absence of mechanical inclusions (Figure 38).

***Figure 38. Viewing vials for transparency***

If mechanical inclusions are detected, the solutions are re-filtered, re-examined, capped (Fig. 39 - 40) (check for leaks), labeled and sterilized.

**Fig. 39. The rolling machine**

**Figure 40. Capping vials**

Vials of solutions for injection are labeled by writing or stamping on the lid,

using metal tags, or other methods.

Sterilization of solutions for injection should be carried out no later than three hours after the start of production under the supervision of a specially designated specialist.

Control of finished products. After sterilization, secondary control for the absence of mechanical inclusions, qualitative and quantitative analysis is performed. For analysis, one vial of solution from each batch is selected (one batch of solution is considered to be products obtained in one container from one loading of the drug substance).

At the same time, the quality of the vial closure is checked (the aluminum cap should not scroll when turned manually) and the volume of the vial filling (±5%). Control of solutions for injectable sterility and pyrogenic substances is carried out in accordance with the requirements of the current instructions. Solutions that meet all of the above requirements are suitable and are subject to release.

Registration of solutions for injection. Solutions for injection for outpatients are labeled with the main blue label "For injection" (it should contain the pharmacy number, composition, method of administration, date of manufacture, prescription number), an additional label "Sterile" and, if necessary, warning labels about storage conditions ("Store in a cool and dark place", "Keep out of reach of children", etc.). An additional label "Prepared aseptically" is affixed to the vial with solutions prepared under aseptic conditions without sterilization.

## *TESTS*

1 A pharmacy prepares aseptic medicines. Indicate which rooms comprise the aseptic unit of a pharmacy that manufactures sterile dosage forms?

a Gateway, aseptic assistant's room, room for obtaining water for injections, packaging, sealing and sterilization of medicines;
b An aseptic assistant room, a room for obtaining water for injections, packaging, sealing and sterilization of medicines;
c An aseptic assistant room, a room for obtaining purified water, packaging, sealing and sterilizing medicines;
d Gateway, aseptic assistant's room, room for receiving purified water, packaging, storage and sterilization of medicines;
e Gateway, aseptic assistant's room, room for obtaining water for injections, sealing and sterilization of medicines.

2 What kind of ventilation should the aseptic unit be equipped with?

a Supply and exhaust ventilation with the advantage of air exhaust over inflow, which provides at least 10 times the air exchange per hour;

b Supply and exhaust ventilation with the advantage of air inflow over exhaust, which provides at least 100 times the air exchange per hour;

c Supply and exhaust ventilation with the advantage of air inflow over exhaust, which provides at least 10 times the air exchange per hour;

d Supply and exhaust ventilation with the advantage of air exhaust over inflow, which provides at least 100 times the air exchange per hour;

e There is no right answer.

3 Cleaning of premises for manufacturing of medicinal products under aseptic conditions is carried out:

a No more than 1 time per shift at the end of work in a wet way using disinfectants;

b At least 1 time per shift at the end of work in a wet way using disinfectants;

c At least 1 time per day at the end of work in a wet way using disinfectants;

d At least 1 time per shift at the end of work in a wet way with detergents;

e At least 1 time per shift at the end of each shift in a wet way using disinfectants.

4 What do people involved in the manufacture of medicines in aseptic conditions do when they enter the gateway?

a They wash and disinfect their hands, put on a sterile gown, a gauze mask in four layers, which is changed every 4 hours, a cap (with hair carefully removed), and shoe covers;

b They wear special shoes, wash and disinfect their hands, a gown, a gauze mask in four layers, which is changed every 4 hours, a cap (with hair carefully removed), and shoe covers;

c They wash and disinfect their hands, put on a sterile gown, a gauze mask in four layers, which is changed every 5 hours, a cap (with hair carefully removed), and shoe covers;

d They put on special shoes, wash their hands, put on a sterile gown, a gauze mask in four layers, which is changed every 2 hours, a cap (with hair carefully removed), and shoe covers;

e They put on special shoes, wash and disinfect their hands, put on a sterile gown, a gauze mask in four layers, which is changed every 4 hours, a cap (with hair carefully removed), and shoe covers.

5 What kind of processing does the technological clothing undergo?

a Sterilize in boxes and store in an open state, but not more than 3 days;

b Sterilized in boxes and stored in a closed state for more than 3 days;

c Sterilize in boxes and store in a closed state, but not more than 2 days;

d Sterilize in boxes and store in an open state, but not more than 2 days;

e Sterilize in boxes and store in a closed state, but not more than 3 days.

6 When working in an aseptic unit, pre-cut sheets of vegetable parchment or tracing paper and a ballpoint pen are used for recording. What are the requirements for their storage?

a The paper is stored in plastic folders or bags. Wipe the ballpoint pen once per

shift with 60% ethyl alcohol or an alcohol-ether mixture;

b The paper is stored in plastic folders or bags. Wipe the ballpoint pen three times per shift with 70% ethyl alcohol or an alcohol-ether mixture;

c The paper is stored in paper folders or bags. Wipe the ballpoint pen once per shift with 60% ethyl alcohol or an alcohol-ether mixture;

d The paper is stored in plastic folders or bags. Wipe the ballpoint pen once per shift with 70% ethyl alcohol or an alcohol-ether mixture;

e Store the paper in paper folders or bags. Wipe the ballpoint pen once per shift with 70% ethyl alcohol or an alcohol-ether mixture.

7 During the manufacture, control, packaging of medicines, employees shall comply with the following standards.

a Trimmed nails, covered with transparent varnish, and no rings on the fingers;

b Trimmed nails, not covered with varnish, and no rings on the fingers;

c Trimmed, varnished nails are allowed, and small rings on the fingers are allowed;

d Varnished nails and no rings on the fingers;

e Trimmed nails, covered with colored varnish, and no rings on the fingers.

8 The use of small mechanization equipment for manufacturing solutions for injections and eye drops is allowed under the following conditions

a If they are related to the latest technologies;

b If the size of the room allows;

c If there is a possibility of their regular verification in the metrological service;

d If they are accompanied by detailed instructions on how to use them;

e If it is possible to disinfect and sterilize them.

9 The staff of the pharmacy shall:

a Store outerwear and footwear separately from process clothing and special footwear in a designated place (closet, etc.);

b Disinfect hands before and during work;

c Before going to the toilet, take off your technological clothing, and after going to the toilet, wash and disinfect your hands thoroughly;

d Do not go outside the pharmacy in technological clothing and special footwear;

e All answers are correct.

10 What is not included in the list of things that should not be in the aseptic block?

a Outerwear of the staff;

b Auxiliary materials, tables that are not subject to wet cleaning;

c Equipment that is not in use;

d Heaters;

e There is no right answer.

# WORKPLACE OF A PHARMACIST ENGAGED IN THE MANUFACTURE OF INTRA-PHARMACY PREPARATIONS

A pharmacy is one of the institutions of the healthcare system whose main function is to timely supply medicines, patient care items, sanitary items and other medical goods to the population and healthcare facilities.

The pharmacy uses concentrates, semi-finished products and in-pharmacy blanks to quickly and efficiently manufacture dosage forms according to doctor's prescriptions and the requirements of healthcare facilities. The pharmacist-in-charge Is responsible for the intra-pharmacy preparation. He/she is responsible for the availability and nomenclature of concentrated solutions and semi-finished products used for the manufacture of extemporaneous medicinal products, as well as the list of extemporaneous medicinal products made for reserve according to frequently repeated prescriptions. By analyzing the extemporaneous formulation and manufacturing the appropriate pharmacy preparation, the defect thereby contributes to the efficiency and scientific organization of the pharmacist's work.

***Concentrated solutions*** *are* working solutions of medicinal substances in specified concentrations higher than those prescribed in prescriptions with the expectation of appropriate dilution with water to the specified concentration.

Concentrated solutions are used in pharmacies to manufacture medicines using the bulk method. The use of such solutions greatly facilitates the work of a pharmacist and helps to improve the quality of prepared medicinal products and accelerates their release to the public. The nomenclature of concentrated solutions is determined by the requirements of an individual formulation, and the list of concentrated solutions may vary depending on the need.

When preparing concentrated solutions, concentrations close to saturated solutions should be avoided, as precipitation of the dissolved substance may occur when the temperature of the solution decreases. When preparing concentrated solutions, use measuring flasks, cylinders, or scales, using the calculation table in the latter case.

Since concentrated solutions are made for future use, they can be a breeding ground for microorganisms and should be prepared under aseptic conditions with freshly distilled or boiled water to make them more stable during storage.

All auxiliary materials used, as well as the utensils, must be sterilized, and the solutions must be filtered. Due to the fact that the quality of concentrated solutions determines the correct preparation of mixtures, concentrated solutions are checked for authenticity, purity, and quantitative content of active ingredients after preparation.

In a pharmacy, concentrated solutions are prepared by a pharmacist-technologist (defectician) and checked by a pharmacist-analyst. Concentrated solutions should be stored in well-sealed vials (burette units) (Fig. 41), in a place protected from sunlight, at a temperature not exceeding $25^0$ C or at a refrigerator temperature (3-$5^0$ C).

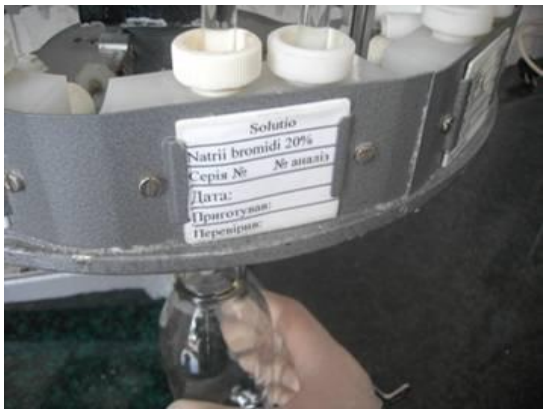


**Figure 41. Concentrated solution of Natrii bromidi 20 % in a burette setup**

A label with an indication is glued to the rod:

-name and concentration of the solution;

-series number;

-date of preparation and analysis number.

Concentrated solutions are prepared in pharmacies as needed, taking into account the volume of work of the pharmacy and the shelf life of the solution.

Discoloration, clouding of the solution, the appearance of flakes, plaque indicates that the solution is unsuitable. The shelf life of concentrated solutions is also specified in the instructions to Order No. 197.

***TESTS***

1 What is the general name for the furniture used to equip the workplace of a pharmacist engaged in the manufacture of in-pharmacy preparations?

a Medical;
b Pharmaceuticals;
c Typical;
d Special;
e Laboratory.

2 What is not included in the list of furniture for a pharmacist's workplace that is used to manufacture in-pharmacy preparations?
a Safe for narcotic and psychotropic substances;
b Wooden cabinet for poisonous and potent substances;
c Cabinet for medicines of list A;
d Cabinet for medicines of list B;
e Cabinet for odorous and coloring substances.
3 Wet cleaning is performed in the room where the workstation of a pharmacist engaged in the manufacture of in-pharmacy preparations is located:
a Every day;
b Every week;
c Every shift;
d Every hour;
e Every two days.
4 The workplace of a pharmacist engaged in the manufacture of in-pharmacy preparations necessarily has turntables. What types are there?
a Desktop and floor standing;
b Small and large tabletop;
c Desktop and wall mounted;
d Manual and mechanical;
e Regular and multifunctional.
5 The workplace of a pharmacist engaged in the manufacture of internal pharmacy preparations must be equipped with :
a With fluorescent lamps;
b An auxiliary table;
c Supply and exhaust ventilation with mechanical inducement;
d Supporting materials and tables;
e With a computer.
6 What is the equipment used by a pharmacist engaged in the manufacture of compounding pharmacy preparations to store solutions of concentrates required for the preparation of medicines?
a Calipers;
b Measuring flasks;
c The ballot box;
d Cylinders;
e There is no right answer.

7 What should be in the desk drawer of a pharmacist who manufactures in-pharmacy preparations?
a Additional chemical utensils;
b Poisonous substances;
c Prescriptions for the manufacture of medicines;
d Reference literature;
e Personal belongings.
8 The workplace of a pharmacist engaged in the manufacture of internal

pharmacy preparations is organized for sitting. What should be located to the right within an arm's reach?

a Handle;
b Pencil;
c Scissors;
d Glue;
e All answers are correct.

9 What should be the quality of all pipettes used for measuring liquid substances for the convenience of a pharmacist engaged in the manufacture of in-pharmacy preparations.

a Glass;
b Disposable;
c Labeled;
d New;
e Low-fat.

10 What book should be a pharmacist's "desk book"?

a State Pharmacopoeia of Ukraine;
b Pharmacopoeia of the USSR, X edition;
c Pharmacopoeia of the Russian Federation;
d European Pharmacopoeia;
e British Pharmacopoeia.

**REFERENCES**

*Basic*

1. Mnushko Z.M. History of Medicine and Pharmacy: textbook for students of higher schools/ Z.M. Mnushko, O.Yu. Rohulya, I.V. Timanyuk. – Kharkiv: NUPh: Golden Pages, 2011. – 192 p.
2. Organization and economics of pharmacy: Part 1. Organization of pharmaceutical provision of population: National Handbook for Students of Higher Educational Institutions – Ed. A.S. Nemchenko – Kharkiv: NUoPh: Golden Pages, 2015. – 360 p.
3. Pharmacy – based technology of drugs: the manual for applicants of higher education/ O. I. Tykhonov, T.G.Yarnykh, O.A. Rukhmakova, G.B.Yuryeva; Edited by O. I. Tykhonov and T.G.Yarnykh. – Kharkiv: NUPh: Golden Pages, 2019. – 488 p.
4. History of medicine and pharmacy: textbook. way. for students of higher pharmacy. textbook lock and pharmac. AA Kotvitska, VV Gorbanyov, OO Surikov and others. – Kharkiv: NUPh: Golden Pages, 2016. – 168 p.
5. History of medicine and pharmacy: a textbook for students of a foreign faculty / A.A. Kotvitskaya, V.V. Gorbanev, A.A. Surikov, A.V. Volkova. - Kh .: NUPh, 2014 .- 124 p.
6. Anderson S. Making Medicines: A Brief History of Pharmacy and Pharmaceuticals / S. Anderson. – London: Pharmaceutical Press, 2005. – 318 p.
7. Duffin J. History of medicine: a scandalously short introduction / J. Duffin. – Toronto: University of Toronto Press, 2016. – 480 p.
8. Magner L. N. A History of Medicine / L. N. Magner, O. J Kim. – 3rd ed. – Boca Raton: CRC Press, 2017. – 446 p.
9. Remington: An Introduction to Pharmacy – Editer by Allen L.V. Jr. – London: Pharmaceutical Press, 2013. – 665 p. 16
10. Pharmacy: what it is and how it works / William N. Kelly. Abingdon, Oxon; New York, NY: Routledge, 2018. – 398 p.

*Supporting*

1. Organization of pharmaceutical supply of the population: Textbook. for students. higher textbook lock / A.S. Nemchenko, A.A. Kotvitska, G.L. Panfilova and others; For order. A.S. Nemchenko. – H.: Avista-VLT, 2007. – 488 p.
2. Fundamentals of the organization of pharmacies in questions and answers: Textbook / Edited by: A.S. Nemchenko. – H.: NUPh, 2015. – 73 p.
3. Fundamentals of organization and economics of pharmacy in questions and answers: Uch. allowance. for foreigners stud. farm. universities in 2 hours / Under common. ed. A.S. Nemchenko. – H.: NUPh, 2009.
4. Workbook for practical classes in pharmacy on drug technology: textbook. way. for students. 1st year special. "Pharmacy" / Vishnevskaya LI, Polovko NP, Kovaleva TM etc. – H.: NUPh Publishing House, 2015. – 46p.
5. Drug technology. Training manual: Textbook. way. for students. higher textbook lock / OI Tikhonov, PA Logvin, SO Tikhonova, OV Mazulin, TG Yarnykh, OS Shpychak, OM Kotenko; Edited by OI Tikhonov. – H.: NUPh; Original, 2009. – 432 p.
6. History of medicine / O. Golyachenko. – Ternopil: LILY, 2004. – 248p.
7. History of Medicine / S.A. Verkhratsky SA, P.Yu. Zabludovsky. – K.: Higher

school, 1991. – 431p.
8. Van Mil J., Nelson I. Public pharmacy in Denmark. // Pharmac. magazine. – 2002. – №2. – P. 15-17.
9. History of Medicine and Pharmacy / ZM Mnushko. – Kh.: NUPh Publishing House: Golden Pages, 2009. – 208 p.
10. Meshkovsky AP Proper practice of drug storage // Pharmacist. – 2001. – № 1. – P. 6-8. 11. Sautenkova NL Organization of work in a Danish pharmacy // Pharmac. magazine. – 2001. – № 2. – P. 41-43.
12. Semenchenko VF History of pharmacy. – M.: Alpha, 2010. – 592 p.
13. Sorokina TS History of medicine. – M .: IC "Academy", 2008. – 560 p.
14. Syatinya ML History of pharmacy: a textbook for higher education institutions. – Lviv, 2002. – 660 p.
15. Tereshchuk TO, Kalenyuk TG Formation of pharmacy legislation in Galicia // Pharmac. magazine. – 1995. – № 4 – P. 88-92.
16. Pharmaceutical Encyclopedia / Chairman, ed. council and the author of the foreword VP Black. – K.: Morion, 2005. – 848 p.
17. Chekmn IS, Viktorov OP Medicine of Kievan Rus // Pharmacist. magazine. – 1982. – № 2. – P. 75-78.
18. Yarnykh, TG Extemporaneous formulation (technology, analysis, application): method. rivers / TG Yarnykh, Fr. I. Tikhonov, IS Grishchenko and others. – H., 2015. – 379 p.
19. Fierke K. K. Teaching Resources in the History of Pharmacy: Teaching a Historical Perspective Using a Digital Resource / K. K. Fierke, P. L. Ranelli, R. C. Smith // Pharmacy in History. – 2012. – Vol. 54, № 4. – P. 112–114. 20. Higby G. J. A. Cornerstone of Modern Institutional Pharmacy Practice: Mirror to Hospital Pharmacy / G. J. A. Higby // Pharm. Hist. – 2014. – Vol. 56, № 3-4. – P. 59–65.

*Legal framework*

1. State Pharmacopoeia of Ukraine / State Enterprise "Ukrainian Scientific Pharmacopoeial Center for Quality of Medicines" – 2nd ed. – Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for Quality of Medicines", 2015. - Vol. 1. -1128 p.
2. State Pharmacopoeia of Ukraine / State Enterprise "Ukrainian Scientific Pharmacopoeial Center for Quality of Medicines" – 2nd ed. – Kharkiv: State Enterprise "Ukrainian Scientific Pharmacopoeial Center for Quality of Medicines", 2015. – Vol. 3. – 732 p.
3. State Pharmacopoeia of Ukraine / State Enterprise "Scientific and Expert Pharmacopoeial Center" – 1st ed. – H.: RIREG, 2001. – 556 p. 17
4. Order of the Ministry of Health of Ukraine № 44 of 16.02.93 "On the organization of storage in pharmacies of various groups of drugs and medical devices".
5. Order of the Ministry of Health of Ukraine № 197 of 07.09.93 “On approval of the Instruction on preparation in pharmacies of dosage forms with liquid dispersion medium”.
6. Order of the Ministry of Health of Ukraine № 275 of 15.05.2006 "Instruction on the sanitary and anti-epidemic regime of pharmacies".
7. Order of the Ministry of Health of Ukraine № 360 of 19.07.2006 “On approval of

the Rules for prescribing prescriptions and requirements-orders for medicines and medical devices, the order of release of medicines and medical devices from pharmacies and their structural units, instructions on storage, accounting and destruction of prescription forms and order requirements ”.
8. Order of the Ministry of Health of Ukraine "List of pharmacy positions in health care facilities" dated 28.10.2002 №385
9. Order of the Ministry of Health of Ukraine № 812 dated 17.10.2012 "On approval of the Rules of production (manufacture) of medicines in a pharmacy".
10. Guide to Good Practice for the Storage of Pharmaceutical Products // Pharmacist. – 2004. – № 18.
11. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of nonsterile drugs in pharmacies" ST-N MOZU42 - 4.5: 2015 // Ed. prof. OI Tikhonov and prof. T.G. Bright. – Kyiv, 2015. – 109p. (Approved by the order of the Ministry of Health of Ukraine № 398 of 01.07.2015).
12. Standard of the Ministry of Health of Ukraine "Requirements for the manufacture of sterile and aseptic drugs in pharmacies" ST-N MOH 42 - 4.6: 2015 // Ed. prof. OI Tikhonov and prof. T.G. Bright. – Kyiv, 2015. – 76 p. (Approved by the order of the Ministry of Health of Ukraine № 398 of 01.07.2015).

*Information resources*

1. www.moz.gov.ua - the official website of the Ministry of Health of Ukraine
2. fp.com.ua - site of «Pharmacist Practice» magazine
3. www.provisor.com.ua - the official site of «Provisor» magazine