N. S. GOLYAK, O. G. SECHKO

PHARMACY TECHNOLOGY OF MEDICINES: DOSING, TECHNOLOGY OF POWDERS

Student's Name _____

Group _____

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МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
КАФЕДРА ФАРМАЦЕВТИЧЕСКОЙ ТЕХНОЛОГИИ

Н. С. Голяк, О. Г. Сечко

АПТЕЧНАЯ ТЕХНОЛОГИЯ ЛЕКАРСТВЕННЫХ СРЕДСТВ: ДОЗИРОВАНИЕ, ТЕХНОЛОГИЯ ПОРОШКОВ

PHARMACY TECHNOLOGY OF MEDICINES: DOSING, TECHNOLOGY OF POWDERS

Практикум

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PHARMACEUTICAL TECHNOLOGY. BASIC TERMS AND NOTIONS. GOOD PHARMACY PRACTICE

Issues for discussion:

1. Basic terms and concepts: pharmaceutical technology, active ingredients, auxiliary substances (excipients), medicinal plant raw materials, dosage form.
2. Extemporaneous medicines.
3. Good pharmacy practice (GPP): requirements and roles of a pharmacist.
4. Prescription handling.
5. Pharmacopoeias.
6. Extemporaneous preparations (GPP).
7. Information for patients.

THEORETICAL PART

Pharmaceutical technology is a set of applied techniques to obtain drugs from medicinal plant raw materials or medicinal substances.

Active ingredients or medicinal plant raw materials → technology → Product/drugs

Active ingredients (active pharmaceutical ingredients) are chemical substances or other components used in diagnosis, treatment, prevention of human and animal diseases (e.g. bismuth subnitrate, chloramphenicol, omeprazole, bisoprolol, morphine sulfate, oxymetazoline, sildenafil, etc.). Active ingredients have the pharmacological effect.

Auxiliary substances (excipients) are ingredients in the corresponding concentration required for preparation of a medical form, but without pharmacological effects (e.g. lactose, macrogols, mannitol, parafin, oleo cacao, saccharin, starch, lanolin anhydrous, white wax, gelatin, polyethylene oxide 400).

Dosage Form (DF) is a physical form of a chemical compound or a medicinal plant dose used as a drug intended for administration (eg. tablets, capsules, solution for external use/for internal use, injections, infusion, ointment, liniment, cream, gel, paste, suppositories etc.).

A medicinal product is a pharmacological agent approved by the authorized National Committee applied for treatment, prevention or diagnosis of human and animal diseases.

Medicinal plant raw materials are substances approved by authorized National Committee (e.g. cortex Quercus (Oak bark), folia Belladonnae (Leaves of Belladonna), Radices Belladonnae (roots of Belladonna) etc.).

Medicinal products manufactured in **chemist's shops** (syn. pharmacy, drugstore, apotheca) are called extemporaneous medicines (from Latin *ex tempore* — as necessary). Extemporaneous compounding is therapeutic product preparation in the conditions of the chemist's shop for an individual patient in response to an identified need. Extemporaneous medicines are medical forms prepared under strict supervision of the pharmacist who has special permission.

Compounding is the process used to create custom medications from base ingredients. The pharmacist starts with base drugs and combines or prepares them to best fit

the patient's needs. Compounding is a process of combining, mixing, or altering ingredients to create a medication tailored to the needs of an individual patient.

For example, compounding may be useful for patients with dysphagia who are unable to swallow solid medications, or when an appropriate dose or dosage form is not commercially available.

Thus, pharmaceutical compounding is an essential component in pharmacy practice allowing pharmacists to provide commercially unavailable dosage forms. Medications compounded for a patient-specific needs contribute to personalized medicine.

Pharmaceutical manufacturing is the industrial-scale development of commercially-available drugs. Unlike compounding, pharmaceutical manufacturing creates drugs in pre-set formulas or doses on an industrial scale. Often, pharmaceutical manufacturing companies generate millions of doses or formulas per year. The large scale benefits society by providing quick and easy access to pre-formulated medications, but leaves little room for customization when patients have special needs.

Below (fig. 1) you can see 2 types of pharmaceutical production.

a ***b***

Fig. 1. Two types of pharmaceutical production:
a — extemporaneous compounding; *b* — pharmaceutical manufacturing

Are Compounded Medications Safe?

When people first hear that compounded medications are not FDA-approved, they often grow concerned about the safety of these custom medications. As mentioned above, registered and licensed compounding pharmacies do have oversight from state pharmacy licensing boards. These regulations ensure that the compounding pharmacy is working with safe substances using reliable methods and empirical evidence for every medication they create. Provided that you work with a *licensed pharmacy*, your medications are safe and reliable.

Medications, when broken down to their base ingredients, are all virtually identical from a chemical perspective. Compounding pharmacies often get their base ingredients from the same pharmaceutical manufacturing companies that make commercial drugs. The only difference is that the compounding pharmacy processes or combines them in-house, rather than simply receiving a pill, injection, topical, or pre-combined formula in a box or bottle.

Pharmacopoeias

Pharmacopoeias have been in use for almost as long as medicines have been compounded. Perhaps the first widely recognized pharmacopoeia was the Dispensatorium of Valerius Cordus (first edition 1546). This contained many old formulae derived from traditional sources, including Galen, Avicenna, but also contained a number of unique references to medicines, including many preparations of essential oils. The Dispensatorium of Valerius Cordus was adopted by the Senate of Nuremberg, which gave rise to the work being known later as the «Nuremberg Pharmacopoeia».

The British Pharmacopoeia

The Medical Act (1858) led directly to the production of the first British Pharmacopoeia (BP) in 1864. The British Pharmacopoeia is a book listing medicines and compounds, their method of preparation together with weights and measures necessary for preparation and mixing. Pharmacopoeia need to alter, amend and republish in response to scientific developments.

The current edition of the British Pharmacopoeia comprises six volumes, which contain nearly 3,000 monographs for drug substances, excipients, and formulated preparation, together with supporting general notices, appendices (test methods, reagents etc.), and reference spectra, used in medical practice.

The European Pharmacopoeia (Ph. Eur.) is a major regional pharmacopoeia which provides common quality standards throughout the pharmaceutical industry in Europe to control the quality of medicines, and the substances used to manufacture them. There is a collection of monographs which describe both the individual and general quality standards for ingredients, dosage forms, and methods of analysis for medicines. These standards apply to medicines for both human and veterinary use.

State Pharmacopoeia of the Republic of Belarus is a collection of pharmacopoeial articles, methods of analysis and other regulatory documents approved by the National Healthcare Committee.

A pharmacopoeial article is the regulatory and technical document, created on the basis of the national standards, concerning the quality of medicinal products or medicinal plant raw materials.

According to the State Pharmacopoeia of the Republic of Belarus, a medicinal product must be of high quality, effective and safe.

Good pharmacy practice

Good pharmacy practice (GPP) responds to the needs of people using the pharmacists' services to provide optimal, evidence-based care. To support this practice it is essential to develop established quality standards and guidelines.

Requirements to GPP. The core of pharmacy activity is to help patients make the best use of medicines via:

- supplying of medication and other health-care products of assured quality;
- provision of appropriate information and advice;
- administration of medication;
- monitoring medication adverse effects;
- promotion of rational and economically justified prescribing and dispensing.

Roles of a pharmacist in GPP:

– prepare, obtain, store, distribute, administer, dispense and dispose medical products;

– provide effective medication therapy;

– maintain and improve professional performance;

– contribute to the effectiveness of the health care system.

Prescription handling

Customers must be made to feel attended and comfortable by friendly gesture and ambience as soon as they come into the pharmacy. Communication should be open to encourage the customer to convey his/her needs by producing a prescription or by asking for other products or advice.

Upon receiving the prescription, the pharmacist should confirm:

a. Identity of the customer.

b. Whether the prescription is presented by the customer himself or by someone on the customer's behalf.

The customer may be politely requested to wait while the pharmacist reviews the prescription.

Prescription should be complete with regard to:

a. Name of the prescriber, his/her address and registration number.

b. Name, address, age, sex of the patient.

c. Name(s) of the medicine(s), potency, dosage, total amount of the medicines to be supplied.

d. Instruction to the patient.

e. Refill information if any.

f. Prescribed prescribers' usual signature.

Any ambient, confusion, shortcoming or anomalies should be brought to notice of the prescriber.

Correctness of prescribed medicines

The prescription should be checked for:

a. Dosage: whether the dosage prescribed is within the standard minimum and maximum dose range.

b. Double medication (same drug or different drug with same pharmacotherapeutic effect) concurrently prescribed.

c. Interaction between the currently prescribed medicines, OTC medicines being taken by the patient & the medicines being taken from any past prescription (records of which may be available in the Patient's Medication Medicine Use Records). Any drug interaction which is likely to cause undesirable effects to the patients should be brought to notice of the prescriber.

d. Contraindication: age, sex, disease(s), conditions or other characteristics of a patient that may cause certain prescribed medicines to be contraindicated.

e. History of overuse, under use, or misuse of medicines by the patient.

Any of the above as well as handwriting legibility problem should be brought to the notice of the prescriber.

Any necessary change made by the prescriber should be recorded on the prescription, with the words «Changes made over the telephone in consultation with the Dr……(name) at (time) on (date)» and should be signed and stamped by the pharmacist.

Dispensing

Filling the prescription. The medicine should be removed from the storage area, counted and invoiced. In all cases, final review of prescription and the correctness of dispensed medicines must be personally made by the pharmacist.

As a final step, the pharmacist should personally dispense the medicines, at which stage appropriate counseling should be given for the patient.

Extemporaneous preparations

Written standard operating procedures, as well as standard formulations, should be maintained for commonly made extemporaneous preparation. Proposed adjuvants, their quantities and method of preparation must be written down before any compounding activity is initiated. Each step should be followed methodically and step by step record maintained.

Batch numbers of each medicines used for compounding should be recorded. All such preparation should preferably be compounding by the pharmacist.

Only medicinal (pharmaceutical) quality or better grade ingredient should be used for compounding.

The preparation area should be cleaned immediately before and after compounding. All necessary weighing, measuring instrument must be calibrated periodically and records maintained.

After compounding, the product should be transferred to a suitable container and closed securely.

The container should be appropriately labeled stating the name of the preparation, date of preparation, name of the patient, direction, quantity, a reference (batch) number generated by the pharmacy, storage conditions and the name of the pharmacy. These details must be recorded in a register or electronically for suitable reference and retrieval as and when required.

Information for patients

The pharmacist must help the customer in making well — informed decision about proper use of medicines & other health care products. He should support the customer in making well — considered decision with regard to self-care.

Whenever the pharmacist has doubt or reasons to believe that it would be in better interest of the customer, he/she must advice the customer to see a prescriber or another health care provider as soon as possible.

The pharmacist should provide oral and written information (in one of the local languages requested by the customer) about various medicines & other health care products to increase the awareness level of the customer regarding his illness and his medicines. The goal of consultation is to achieve maximum compliance.

All dispensed medicines should ideally be provided with a label, which clearly states:

I. Name of the patient.

II. Name, strength, batch number and expiry of the medicine, in case the medicine has been repacked or cut out from a larger pack.

III. Dosage and usage instructions.

IV. Date of delivery.

V. Storage.

VI. Instructions.

VII. Name and address of the pharmacy.

VIII. The statement «For External Use Only» for medicines used topically.

IX. The statement «Shake before Use» for relevant liquid formulations.

Dosage and drug application information must also be given verbally to the customer.

It must be ensured that the information and advice given is correct, clear, explicit, up-to-date and understandable for the customer. It should be given in a language and at a level of complexity that is easily understood by the customer.

Patient Counseling

The Pharmacist must work out strategies to provide professional counseling with regard to use of medicines and related products, so as to improve the quality of the patient's life. While dispensing, the patient should be explained:

I. How to take medications

II. For how long.

III. When to take the medicines: before, during or after meals, etc.

IV. What foods/beverages to avoid during the therapy.

V. What side effects to expect and how to manage them.

VI. What to do if one or more doses get skipped.

VII. Any other precautions.

Appropriate discretion should be exercised while discussing the nature of illness, its cause, prognosis (course of the disease), and the expected outcome of the therapy.

As far as possible, oral information, given to customers, should be supplemented by additional written information (in the form of Patient Information Leaflets) about their illness and the medicines.

PRACTICAL PART

Pharmaceutical technology is _____

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Active ingredients (active pharmaceutical ingredients) are _____

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Auxiliary substances (excipients) are _____

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A dosage form is _____

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A medicinal product is _____

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Medicinal plant raw materials are _____

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Extemporaneous medicines are _____

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Compounding is _____

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The European Pharmacopoeia is _____

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State Pharmacopoeia of the Republic of Belarus is _____

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Pharmacopoeial article is _____

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According to the State Pharmacopoeia of the Republic of Belarus a medicinal product must be _____

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Good Pharmacy Practice (GPP) is _____

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Roles of pharmacists in GPP: _____

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STATE REGULATION OF PHARMACEUTICAL MANUFACTURING OF MEDICINES. THE RIGHT TO MANUFACTURING MEDICINES. THE STRUCTURE OF THE PRESCRIPTION

Issues for discussion:

1. State regulation and state control of all aspects of circulation medicinal products.
2. Prescription structure.
3. Storage rules for medicines.
4. Internal control in the chemist's shop.

THEORETICAL PART

The consumer can't assess the quality and conformity of the purchased product, therefore, there is strict regulation of medicinal products circulation in all developed countries at all stages, including:

– research and development (Good Laboratory Practice (GLP), Good Clinical Practice (GCP));

– manufacturing (Good Manufacturing Practice (GMP));

– whole sale trade and retail (Good Distribution Practice (GDP), Good Pharmacy Practice (GPP)).

State regulation of medicines manufacturing is a set of requirements to:

– their composition;
– raw materials (medical substances, excipients, auxiliary and packaging materials);
– technological process;
– quality;
– stages of manufacturing;
– methods of medicines manufacturing.

The right to pharmaceutical manufacturing of medicinal products is granted on the basis of a license to a chemist's shop I (first) category.

According to the government regulations of the Republic of Belarus there are the following 4 categories of the prescribed drugs:

– medicines, sold in a pharmacy at full cost;
– narcotic drugs;
– psychotropic substances and medicines with anabolic activity, sold in a pharmacy at full cost;
– medicines and dressings, sold on the preferential basis.

While writing a prescription the doctor is recommended to:

– fill in all the columns provided in the form;
– legibly indicate the name of the medicinal product, its form, dosage and amount;
– put a clearly identified stamp and seal imprints of a healthcare institution;
– certify with the signature and a personal seal.

In case of prescribing a poisonous, narcotic or strong-effective substance in a dose exceeding the highest single dose, the doctor must write in words the dose of this substance

and put an exclamation mark. If the appropriate registration of the overdose in the prescription is absent, the pharmacist must dispense this medicinal substance in amount equal to 1/2 of the established highest single dose.

Incorrectly written prescriptions are left in the pharmacy; they are stamped with the «invalid prescription» stamp, and are recorded in a special journal. Information about incorrectly written prescriptions is sent to hospital managers to eliminate medical prescription errors.

The recommended structure of the prescription:

1. **Inscriptio** — name of the medical institution (stamp) and code.
2. **Datum** — date of prescribing.
3. **Nomen aegroti** — surname and initials of the patient.
4. **Aetas aegroti** — patient's age.
5. **Nomen medici** — surname and initials of the doctor.
6. **Praescriptio** — designation of medicinal substances and their amount (information for a pharmacist).
7. **Signatura** — designation of the medicine application method.
8. **Sigillum medici** — doctor's signature and a personal seal.

Other prescription rules include:

– name of pharmaceutical ingredients written as International Nonproprietary Name (INN);

– the amount of solid substances indicated in grams (the word *gram* is omitted);

– liquid substances prescribed in milliliters, grams and drops;

– all prescribed ingredients must be listed in following sequence:

a) ***basis*** — the main pharmaceutical substance (narcotic, psychotropic, strong-effective);

b) ***adjuvans*** — pharmaceutical substance contributing to that from the general list;

c) ***corrigens*** — excipients correcting taste or odor;

d) ***constituens*** — remaining excipients (stabilizers, preservatives, isotonizing etc.).

Storage rules for medicines

In storage rooms medicines are placed separately in accordance with:

– pharmacotherapeutic groups, taking into account the physical and chemical properties;

– toxicological groups according to the list A (poisonous, narcotic), strong-effective and the general list;

– the method of application (for internal use, for external use);

– the established shelf-life for every medicine;

– the state of aggregation (liquid, solid etc.).

It is not recommended to place nearby medicines with the similar name, for internal use with very different higher doses.

Medicines, requiring protection from light: antibiotics, herbal preparations (tinctures, extracts, concentrates from medicinal plant raw materials), medicinal plant raw materials, vitamins; corticosteroids, essential oils, fatty oils, dragee preparations, salts of

iodic and hydrobromic acids, halogenated compounds, nitro and nitroso compounds, nitrates, amino- and amide- compounds, phenolic compounds, derivatives of phenothiazine.

Storage of medicines, requiring protection from light. Medicines requiring protection from light should be stored in a container made of light-protective materials (glass containers of orange glass, metal containers, packaging from aluminum foil or plastic materials painted black, brown or orange), in a dark room or in cabinets with tightly fitted doors (or in tightly knit boxes) tightly fitted lid. Particularly sensitive to light medicinal products (silver nitrate, proserin, etc.) are stored in glass containers and wrapped in black opaque paper.

Medicines, requiring protection from humidity: hygroscopic substances and medicines (dry extracts, herbal medicinal raw materials, hydrolysable substances, nitrogen, nitrogenous salts, hydrochloric and phosphoric acids, alkaloids, sodium organometallic compounds, glycosides, antibiotics, enzymes), medicinal substances characterized by regulatory documents as being very easily soluble in water, and medicinal substances, the moisture content of which should not exceed the limit, established by regulatory documents, and medicinal substances oxidized by atmospheric oxygen.

Storage of medicines, requiring protection from humidity:

– medicines requiring protection from atmospheric water vapor, should be stored in a cool place, in a tightly sealed containers made of materials impermeable to water vapor (glass, metal, aluminum foil, thick-walled plastic container);

– medicines with expressed hygroscopic properties should be stored in a dry place in glass containers with hermetically sealed closure, embedded in paraffin on the top. When closing the container with such medicinal substances it is necessary to wipe thoroughly the bottleneck edges and plug it.

Medicines, requiring protection from volatilization and drying:

– volatile substances;

– medicines containing volatile solvent (alcohol tinctures, liquid alcohol concentrates, thick extracts);

– solutions and mixtures of volatile substances (essential oils, solutions of ammonia, formaldehyde, hydrogen chloride over 13 %, carbolic acid, ethyl alcohol of various concentrations, etc.);

– medicinal plant raw materials containing essential oils;

– medicines containing crystallization water-crystalline hydrates;

– medicinal substances that decompound to form volatile products (iodoform, hydrogen peroxide, chloramine B, sodium bicarbonate);

– medicinal substances with the moisture content lower limit (magnesium sulfate, sodium paraaminosalicylate, sodium sulfate, etc.).

Medicines, requiring protection from volatilization and drying, should be stored in a cool place in airtight sealed containers. Application of polymer containers, packaging and closures are allowed in accordance with the State Pharmacopoeia and other regulatory documents.

Crystalline hydrates, depending on the relative humidity air, can exhibit properties of both hygroscopic and losing water substances. Therefore, they should be stored in an airtight sealed glass bottles.

Medicines, requiring protection from higher temperature exposure:

- group of medicinal substances requiring protection from volatilization and drying;
- low-melting substances;
- immunobiological medicines;
- antibiotics;
- preparations obtained from different organs;
- hormonal medicines;
- vitamins and medicines, containing vitamins
- medicines containing glycosides;
- fat-based ointments and other substances.

Medicines, requiring protection from higher temperature exposure should be stored at room temperature (15–25 °C), or in cool places (8–15 °C). In some cases a lower storage temperature is required, which should be indicated on the label or in the instructions for medicine application.

Immunobiological medicines should be stored in industrial packaging separately at a temperature, indicated for each item on the label or in the instructions for application.

Immunobiological medicines of the same names are stored in batches, taking into account their expiration date.

Immunobiological medicines should be subject to visual inspection at least once a month.

Antibiotics should be stored in industrial packaging at room temperature, unless otherwise indicated.

Medicines, Requiring Protection Against Exposure to Low Temperature: medicines, the physicochemical state of which changes after freezing and during subsequent warming to room temperature, do not recover (40 % formaldehyde solution, solutions of insulin, etc.).

Storage of medicines, requiring protection against exposure to low temperatures:

- 40 % formaldehyde solution (formalin) should be stored at temperature not lower than +9 °C. When sediment appears, incubate the solution at room temperature, carefully drain it and use according to the actual content of formaldehyde;
- glacial acetic acid should be stored at a temperature not lower than +9 °C. When precipitate appears, the acid is kept at room temperature until the precipitate dissolves. In case the sediment does not dissolve, the liquid part of the acid is drained and used in accordance to the actual content of acetic acid;
- freezing of insulin is not allowed.

Medicines, requiring protection from the effects of environmental gases:

- *substances reacting with atmospheric oxygen*: various compounds of the aliphatic series with unsaturated intercarbon bonds, cyclic with side aliphatic groups with unsaturated intercarbon bonds, phenolic and polyphenolic, morphine and its derivatives with unsubstituted hydroxyl groups; sulfur-containing heterogeneous and heterocyclic compounds, enzymes and organopreparations;
- *substances reacting with carbon dioxide in the air*: salts alkali metals and weak organic acids (e.g. eight barbital sodium, hexenal, etc.), medicines containing polyhydric amines (for example, aminophylline), magnesium oxide and peroxide.

Medicines, requiring protection from the effects of gases, contained in the environment, should be stored in airtight containers.

Easily oxidized medicines should be stored in a dry place in a glass airtight container.

Barbituric acid sodium salts are required to be stored in airtight containers.

Fragrant drugs with strong odor should be stored in separate cabinets.

Storage of dyeing medicines:

– the group of dyeing medicines includes substances, their solutions, mixtures that leave a colored mark on the container, closures, equipment and other items (brilliant green, methylene blue, etc.);

– dyeing medicines should be stored in a special cabinet in a tightly sealed container. To work with dyeing substances, it is necessary to select special scales, mortar and other devices.

Flammable substances:

– alcohol and alcohol solutions;
– alcohol and ethereal tinctures;
– alcohol and essential extracts;
– ether;
– turpentine (pitch);
– lactic acid;
– chlorethyl;
– collodion;
– cleol;
– organic oils.

Combustible substances:

– bandage (cotton wool, gauze, etc.);
– sulfur;
– glycerol;
– oils;
– medicinal plant raw materials.

Storage of flammable and combustible substances:

– in warehouses flammable and flammable liquids must be kept separately from other medicines;

– the main dangerous properties of flammable and combustible liquid substances are fluidity, easy volatility and flammability from any external sources: open fire, spark, electric discharge, etc. Therefore, storage and work with flammable substances should be handled with great care and far away from fire;

– vapors of the most flammable liquids have a harmful effect on the organism and their inhalation can cause lose of consciousness. Therefore containers with such substances must be tightly sealed. It is prohibited to store flammable and combustible substances in an open container;

– flammable liquids (collodion, alcohol ethyl, turpentine, ether and others) are stored in tightly sealed strong, glass or metal containers to prevent evaporation of liquids from vessels;

– bottles, cylinders and other large containers with flammable and combustible liquids should be stored on shelves of racks in one row; it is forbidden to store them in several rows in height using different spacers. Storage of the above substances close to heating devices is not allowed. Distance of the rack to the heating element must be at least 1 meter;

– in pharmacy workplaces the amount of such substances should not exceed the amount required for the work shift. The containers must be tightly closed;

– it is not allowed to store flammable and combustible liquid substances in a fully filled container. Filling degree should be no more than 90 % of the volume. Alcohol in large quantities should be stored in metal containers filled to no more than 95 % of the volume;

– shared storage is not allowed for flammable substances with mineral acids (especially sulfuric and nitrogen), flammable substances (bandages, oils, sulfur), as well as with inorganic salts, producing explosive mixtures with organic substances (potassium chlorate, potassium permanganate, potassium chromate and etc.).

Blasting substances:

– potassium permanganate;

– silver nitrate.

Explosive substances:

– nitroglycerine.

Storage of blasting and explosive substances:

– substances of this group should be stored in an isolated fire-resistant warehouse in special rooms (compartments) with fireproof walls. Storage of silver nitrate in pharmacies and warehouses in small quantities (in warehouses up to 5 kg, in pharmacies up to 50 g) should be carried out separately in accordance with the storage rules of toxic substances;

– it is necessary to take measures against contamination with dust, which can cause explosion;

– containers with explosive substances (drums, flasks, etc.) should be tightly closed to avoid penetration;

– potassium permanganate is explosive in contact with dust, sulfur, organic oils, ethers, alcohol, glycerin, organic acids and other organic substances;

– nitroglycerin solution (explosive) should be stored in pharmacies or pharmacy warehouses in small tightly sealed bottles or metal containers in a cool dark place, taking precautions against fire. Work with nitroglycerin requires special caution, as spilled nitroglycerin may cause explosion. Skin contact even with small amounts may cause poisoning (severe headaches).

PRACTICAL PART

The structure of the prescription by sections:

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Storage rules for medicines:

Medicines, requiring protection from light:

Storage of medicines, requiring protection from light:

Medicines, requiring protection against exposure to low temperatures:

Medicines, requiring protection from higher temperature exposure:

DOSING OPERATIONS BY WEIGHT IN THE CHEMIST'S SHOP. RULES FOR WORKING WITH WEIGHTS

Issues for discussion:

1. Weight measurement.
2. Types of scales, used in the chemist's shop.
3. Systematic verification (calibration) of measuring instruments.
4. Metrological characteristics of the scales.
5. Rules for selecting the required weight scales.

THEORETICAL PART

Weight Measurement

Compounding is the process of combining or mixing the ingredients to create a medication tailored to the needs of a patient. «Weighting» involves the measurement of materials necessary for technological processes in proper proportion and quantity according to the composition.

Scales, balances have to be placed in a special, vibration-free place. They should not be easily moved and exposed to direct sunlight and heating devices.

Conditions and criteria of assuring appropriate quality involve application of scales, balances with suitable accuracy according to the standards. Periodic control and validation of weight devices (6 months in case of weighting devices and 12 months in case of weights) can be only done by the individuals having official permissions.

According to the principle of operation, the weighting devices may be operating automatically and non-automatically.

The loading capacity means the highest weight measured without causing any damage to the scales.

The pharmaceutical hand-scales are conventional pharmacy type of weighting devices with accuracy at most 0.01 g.

Analytical scales balance allows to measure substances with 1 mg or 0.1 mg accuracy, usually measurement limit is 100–200 g.

Upper measurement limit of pharmaceutical fast scale is 50,00 g and the smallest measurable amount is 0.05. The accuracy of measurement is 0.01 g.

Equal-arm balance can measure maximum 1000,0 g of materials, although its accuracy is 0.1 g.

Suitable pots have to be used when measuring components in solid, semi-solid, or liquid state of matter. It is important to take into consideration that the less is the mass of pot used the more precise is the weighting. Ground measuring containers should be used to weight absorbent or easily evaporable material. *Digital scales* do sequential self-calibration, thus the weighting can ensure suitable accuracy in a wide temperature interval. The loading capacity is usually 500 g (1000 g), nevertheless the accuracy is generally 0.001 g.

Such devices speed up and simplify the work process; they are also capable to tare and perform automatic, semi-automatic calibration.

To achieve more accurate measurement digital laboratory and analytical scales are used with a glass draft shield to avoid errors possibly arisen from air flows in order. A digital dosing spoon is used to weight accurately powders, crystals, and granules.

Lever scales and electronic scales are applied for dosing of pharmaceutical substances, excipients and ready-to-use medicines in a chemist's shop.

There are 2 types of lever scales:

– hand scale = Scales for bulk materials (SBM) (fig. 2);

– calibrated (prescription) scales on a column (CSC) — Prescription Scales — Scales of Mora (fig. 3).

Fig. 2. Scales for bulk materials (SBM)

Fig. 3. Calibrated scales on a column (CSC)

Models of *scales for bulk materials* to be used in a chemist's shop are the following: SBM-1, SBM-5, SBM-20, SBM-100. The number in the model name means the max mass that can be weighed on this type of scale (e.g. the max mass that can be weighed using SBM-1 is 1 g, the max mass that can be weighed using SBM-5 is 5 g).

Fig. 4. Electronic scales

Accurate weighing for dosing by mass is based on:

– conformity with the main metrological characteristics of the scales (susceptibility, fidelity and constant weighing results) to a certain standard;

– observance of the measuring instruments operating rules.

All measuring instruments, used in the chemist's shop, are checked. Periodic verification (calibration) of measuring instruments is one of the main guarantees of their

accuracy. Compliance with standard measuring conditions is also important. Use of non-verified measuring instruments is unacceptable. All measuring instruments are subject to stamping with indication of the:

- date of verification;
- ciphers of the laboratory;
- ciphers of the state verifier.

Scales and weights are subject to compulsory verification at least once a year.

Metrological characteristics of the scales

Susceptibility — the smallest mass that can be registered when placed on a scale.

Susceptible are the scales, capable of giving the standard deviation of the arrow (not less than 5 mm for calibrated (prescription) scales and not less than ½ arrow length for hand scales) if we put load on one pan of the weights which corresponds to the permissible (absolute) error.

Metrological characteristics of Scales for Bulk Materials (SBM) and calibrated scales on a column (CSC)

Model of scale	The greatest weighing limit, g	The smallest weighing limit, g	Permissible error, mg (absolute weighing error)		
			Unloaded scales	1/10 from full load	Maximum load
SBM-1	1	0,02	±2	±3	±5
SBM-5	5	0,1	±2	±4	±10
SBM-20	20	1,00	±3	±6	±20
SBM-100	100	5,00	±5	±10	±50
CSC-1000	1000	50,0	±20	±60	±100

Fixity — is the ability of scales to return to a state of balance after no more than 4–6 swingings of the arrow.

Fidelity — is the ability of scales to show the correct ratio between mass of weighted load and mass of weights.

The scales show the correct result if all the symmetrical details of the scales are the same.

Constant weighing results — is the ability of scales to show the same results at multiple definitions of mass under the same conditions.

Rules to select the required weight scales

It is unacceptable to use scales for weighing objects (samples), the mass of which is outside the limits of the min and max loads of the scales, indicated on the beam of the scales for bulk materials or in the technical passport of the electronic scales.

To select correctly the required scales it is necessary to calculate the relative weighing error (the smaller is the error, the better the scales fit):

$$A\ (\%) = a \cdot 100\% / P,$$

A% — the relative weighing error;
a — absolute weighing error;
P — mass of load.

In case of weighing on the same lever scales, the inertia of the lever scales increases with the increase of load. Therefore, their sensitivity decreases and the absolute error increases.

The best dosing accuracy on the scales is obtained by weighing portions close to the max load, thus reducing the relative weighing error.

PRACTICAL PART

_____

are applied for dosing of pharmaceutical substances, excipients and ready-to-use medicines in chemist's shop.

There are 2 types of lever scales:

_____

_____

Models of scales for bulk materials to be used in the chemist's shop are the following: _____

_____

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Accurate weighing for dosing by mass is based on: _____

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All measuring instruments are subject to stamping with indication of: _____

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Metrological characteristics of the scales: _____

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Rules for selecting the required weight scales: _____

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Formula for calculating the relative weighing error:

_____

Calculate the relative weighing error of glucose (5.0 g) on the SBM-20

_____

Calculate the relative weighing error of glucose (18.0 g) on the SBM-20

_____

Calculate the relative weighing error of sodium chloride (4.8 g) on the SBM-5

_____

Calculate the relative weighing error of sodium chloride (3.5 g) on the SBM-5

_____

Calculate the relative weighing error of starch (10.0 g) on the SBM-100

_____

Calculate the relative weighing error of starch (25.0 g) on the SBM-100

_____

Calculate the relative weighing error of pilocarpine hydrochloride (0.03 g) on the SBM-1

_____

Calculate the relative weighing error of pilocarpine hydrochloride (0.07 g) on the SBM-1

_____

Calculate the relative weighing error of pilocarpine hydrochloride (0.6 g) on the SBM-1

_____

DOSING OPERATIONS BY VOLUME IN A CHEMIST'S SHOP. DOSING TECHNIQUE BY VOLUME

Issues for discussion:

1. Factors affecting the accuracy of dosing by volume and by droplets.
2. Substances that always dosed by volume.
3. Instruments for dosing by volume and by droplets for filling.
4. Instruments for dosing by volume and by droplets for pouring out.
5. Equipment of the manufacturing compartment in a chemist shop.
6. Metric System.
7. Scientific Notation.
8. Percent Error.

THEORETICAL PART

Volume Measurement

Volume is the amount of space occupied by a three-dimensional object as measured in cubic units (e.g. liters). The volume of containers for liquid materials is generally termed capacity.

In compounding, weight measuring is preferred in the majority of the cases to the volume measuring method. It is applied in particular technological operations (e.g. dilution, completion, titration or calculation with mixed percentage, dosing and drug administration).

In pharmacy practice, for dosing of liquid preparations various spoons are used:

- 1 teaspoon — 5 ml;
- 1 dessert spoon — 10 ml;
- 1 tablespoon — 15 ml.

Dosing by volume and by droplets is less accurate than dosing by weight, because *the following factors affect the accuracy*:

- temperature of the dosing liquid and ambient temperature during calibration and during liquid dosing;
- properties of the liquid (viscosity, surface tension, density, etc.);
- diameter and purity of the measuring device;
- time and rate of fluid flow;
- the position of the eye of a pharmacist working with a measuring device.

In the process of drug manufacturing in the chemist's shop *the following substances are dosed by volume:*

- purified water;
- aqueous solutions of medicines, including syrups;
- solutions of ethyl alcohol of different concentrations;
- water for injections;
- standard (pharmacopeia) fluids, with the exception of perhydrol (hydrogen peroxide);
- galenic and newgalenic medicines (tinctures, liquid extracts, elixirs, adonisids, etc.).

There are 2 types of instruments used for dosing by volume and by droplets: for filling and for pouring out.

For filling: volumetric flask (fig. 5), graduated test tubes (fig. 6), graduated cylinder (fig. 7) are used.

For pouring out: Pharmacy burette (fig. 8), Pipette (fig. 9) are used.

Fig. 5. Volumetric flask

Fig. 6. Graduated test tubes

Fig. 7. Graduated cylinder

Fig. 8. Pharmacy burette

Fig. 9. Pipette

Manufacturing compartment in a chemist shop is equipped with:

– burette with two-way valves used for dispensing purified water and water for injections;

– burette installation with burettes used to dispense concentrated solutions, galenic and newgalenic medicines;

– pharmacy pipettes used for measuring small volumes of concentrated solutions, galenic and newgalenic medicines, some standard solutions.

Small masses and volumes (up to 1.0 g and 1 ml) should be dosed by drops. A standard droplet meter doses 20 drops of water purified in 1 ml at 20 ℃ and normal pressure. Droplet forming surface of a standard droplet meter: outside diameter — 3 mm, inner diameter — 0,6 mm.

The measurement accuracy depends on correct determination of the liquid level. The human eye must be at the level of the meniscus, otherwise an error is possible due to parallax (apparent displacement of liquid level). The level of colorless liquid is set along the lower meniscus, colored liquid — along the upper meniscus (fig. 10).

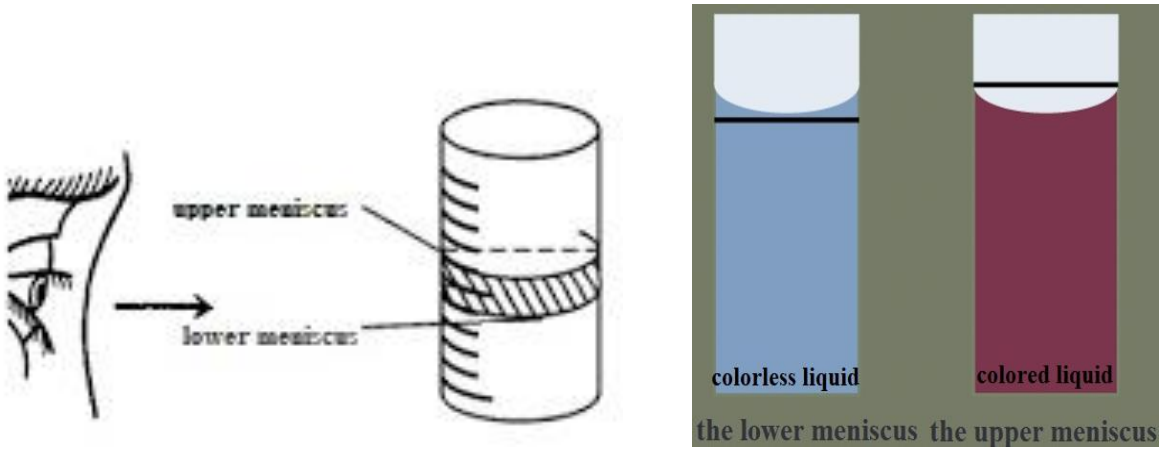

Fig. 10. The scheme to determine the level of liquid in the measuring device using the meniscus

The Metric System

The metric system is the predominant system of measurement used in pharmacy.

The primary base *units* used in pharmacy are *gram, liter, and meter*.

Each of the base units can be multiplied or divided by powers of 10 to form larger or smaller units.

Prefixes are placed before the base units to denote the larger and smaller units.

The first table below lists the most important metric units used in pharmacy.

The Metric System Basics for pharmacist

Prefix	Symbol	Multiple of base	Weight	Volume	Length
Micro	mc	1/1000000	Mcg		
Mili	m	1/1000	Mg	mL	Mm
Centi	c	1/100			Cm
		Base Unit	g (gram)	L (liter)	m (meter)
Kilo	k	1000	Kg		Km

Metric Prefixes Between 10^{18} and 10^{-18}

Prefix	Symbol	Multiplication Factor	Exponent
Exa	E	1 000 000 000 000 000 000	10^{18}
Peta	P	1 000 000 000 000 000	10^{15}
Tera	T	1 000 000 000 000	10^{12}
Giga	G	1 000 000 000	10^{9}
Mega	M	1 000 000	10^{6}
Kilo	k	1 000	10^{3}
Hector	h	100	10^{2}
Deca	da	10	10^{1}
	Base Unit	1	10^{0}
Deci	d	0.1	10^{-1}
Centi	c	0.01	10^{-2}
Milli	m	0.001	10^{-3}
micro	mc	0.000001	10^{-6}
nano	n	0.000000001	10^{-9}
pico	p	0.000000000001	10^{-12}
femto	f	0.000000000000001	10^{-15}
atto	a	0.000000000000000001	10^{-18}

Scientific Notation

Scientific Notation is an easier way to write very large and very small numbers.
Example: 107 800 000 000 000 000 becomes $1.078 \cdot 10^{17}$ scientific notation.
Example: 0.000002449 becomes $2.449 \cdot 10^{-9}$ in scientific notation.

Terminology:

Exponent — the small number written just above and to the right of a base number. It is the 17 in $1.078 \cdot 10^{17}$ and denotes the number of times 10 is used in a multiplication.

10^2 denotes $10 \cdot 10$.

10^3 denotes $10 \cdot 10 \cdot 10$.

A negative exponent denotes 1 divided by the 10´s, which results in a number less than 1. For example, 10^{-2} is $1/10^2$, or 1/100, which is 0.01.

Coefficient — the number which is multiplied by 10 raised to the exponent. It is the 1.078 in $1.078 \cdot 10^{17}$. It is always at least 1 and less than 10.

Percent Error

A 5 g error in a weight measurement may denote either an accurate or an inaccurate measurement. A 5 g error in weighing a bag of potatoes denotes a very accurate measurement, with a small percent error, while a 5 g error weighing out 12 g of active ingredient for a prescription denotes an inaccurate measurement, with a large percent error. It is important to understand and know how to calculate percent error.

Terminology:

Desired quantity — quantity, which is expected to be measured. Think of it as the target.

Actual quantity — quantity, which was actually measured.

Error quantity — absolute value of difference between desired and actual quantity. (always a positive number).

Percent error — error quantity expressed as a percentage of desired quantity.

Calculating Percent Error. *Example:* you tried to weight a quantity of 100 g, but later found that you actually a quantity of 96 g.

Desired quantity is 100 g.

Actual quantity is 96 g.

Error quantity is 4 g.

Percent error: (4 g/100 g)·100 % = 4 %.

Important: Always use desired quantity when calculating percent error.

Example: the desired weight is 130 g, but you weighed out 128 g.

Desired quantity (Target)	Actual quantity	Error quantity	Percent error
130 g	128 g	2 g	(2g/130g) ·100 % = 1,5 %

PRACTICAL PART

The following factors affect the accuracy on dosing by volume and by droplets:

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In the process of drug manufacturing in the chemist's shop the following substances are dosed by volume:

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_____

_____

There are 2 types of instruments for dosing by volume and by droplets:

_____

_____

In pharmacy practice for dosing of liquid preparations various spoons are used:

1 teaspoon — _____

1 dessert spoon — _____

1 tablespoon — _____

Small masses and volumes (up to 1.0 g and 1 ml) should be dosed by _____

A standard droplet meter doses ____ drops of water purified in 1 ml at 20 ℃ and normal pressure.

Droplet forming surface of a standard droplet meter: the outside diameter — _____ mm, the inner diameter — _____ mm.

Describe how to determine the correct and accurate liquid level in the measuring device:

_____

_____

_____

_____

Define Percent Error

1. The desired volume is 125 ml, but actually measured out is 127 ml.

Desired quantity (Target)	Actual quantity	Error quantity	Percent error

2. The desired weight is 250 mg, but the actual weight is 276 mg.

Desired quantity (Target)	Actual quantity	Error quantity	Percent error

3. The desired volume is 1,2 L, but the actual volume is 1,1 L.

Desired quantity (Target)	Actual quantity	Error quantity	Percent error

4. The desired weight is 1,5 kg, but the actual weight is 1,6 kg.

Desired quantity (Target)	Actual quantity	Error quantity	Percent error

5. The desired weight is 1,4 kg, but the actual weight is 1,5 g.

Desired quantity (Target)	Actual quantity	Error quantity	Percent error

COLLOQUIUM/TEST ON PHARMACEUTICAL SUBSTANCES, EXCIPIENTS. STATE REGULATION OF MEDICINES CHEMIST'S TECHNOLOGY. DOSAGE BY WEIGHT, VOLUME AND DROPLETS

Issues for discussion:

1. Basic terms and notions: pharmaceutical technology, active ingredients, auxiliary substances medicinal product, medicinal plant raw materials, dosage form.
2. Extemporaneous medicines.
3. Good pharmacy practice: requirements and roles of a pharmacist.
4. Prescription handling.
5. Pharmacopoeias.
6. Extemporaneous preparations (GPP).
7. Information for patient.
8. Information for patient.
9. State regulation and state control of all aspects of circulation medicinal products.
10. The prescription structure.
11. Storage rules for medicines.
12. Internal control in chemist's shop.
13. Weight measurement.
14. Types of scales used in the chemist's shop.
15. Systematic verification (calibration) of measuring instruments.
16. Metrological characteristics of the scales.
17. Rules for selecting the required weight scales.
18. Factors affecting the accuracy of dosing by volume and by droplets.
19. Substances that always dosed by volume.
20. Instruments for dosing by volume and by droplets for filling.
21. Instruments for dosing by volume and by droplets for pouring out.
22. Equipment of the manufacturing compartment in a chemist shop.
23. The Metric System.
24. Scientific Notation.
25. Percent Error.

TECHNOLOGY OF POWDERS.
MANUFACTURING OF SIMPLE AND COMPLEX POWDERS

Issues for discussion:

1. Powders: definition, advantages and disadvantages.
2. Classification of powders.
3. Methods of powder prescribing: distributive and separating.
4. The main stages of powders manufacturing. Methods to reduce agglomeration.
5. Mortar parameters.
6. The main technological procedures of preparing powders.
7. Requirements for powders.

THEORETICAL PART

Powders are solid medicinal dosage forms for external and internal application consisting of one or more medical substances and having a loose property.

Advantages of powders:

– simplicity of the technological process;

– sufficiently high pharmacological activity due to the high dispersion of active substances (great bioavailability comparing with tablets);

– possibility of providing local and general effect on the organism;

– convenience of application;

– universality of the composition (the composition of powders may include small amounts of liquid and viscous substances, as well as substances of organic and inorganic origin);

– high accuracy of dosing;

– less irritant effect of certain substances (salicylates, halides, etc.) as compared with tablets;

– better stability (as compared with liquid dosage forms);

– convenience of storage and transportation.

Disadvantages of powders:

– slower onset of pharmacological effect compared to liquid dosage forms;

– change in the properties of certain substances under the influence of the environment (oxidation under humidification, loss of water or conversely absorption of water and carbon dioxide from the air);

– some substances have bitter taste, unpleasant smell and ability to dye. Such powders should be sold in gelatin capsules;

– irritant effects on the mucous membranes of certain substances (bromides), they do not manifest such effects when used as solutions.

Classification of powders:

1. ***According to composition:***

– simple — consisting of one ingredient;

– complex — consisting of some substances.

2. ***According to the method of application:***

- for internal oral use (0.1–1 g *per dose)*;
- for external use (dusting powder, snuff for blowing, powder for solution).

3. ***According to quantity of doses powders may be:***

- powders with separate doses — each dose is packaged in the separate capsule;
- undivided powders (dosing is performed by the patient).

Methods of powder prescribing

Distributive — the prescription indicates the amount of a substance per one dose and amount of doses necessary to prepare (most frequently used).

Consider the prescription, where the physician uses the *distributive method*.

Rp.: Thymoli 0,01
Acidi salicylici
Acidi borici aa 0,02
Amyli 0,3
Misce, fiat pulvis
Da tales doses N 5
S. Dusting powder. Apply on the affected place.

Separating — the prescription indicates a medicinal substance for all powders and the quantity of doses the total mass is expected to be divided.

Rp.: Riboflavini 0,05
Acidi nicotinici 0,15
Acidi ascorbinici 1,0
Glucosae 2,0
Divide in partes aequales N 10
S. One powder dose 3 times a day.

The main stages of powder manufacturing:

- pre-grinding (dispersing of substances);
- sifting (rarely used within a chemist's shop);
- sequential grinding and blending;
- batching;
- sealing up;
- marking.

Note: finely ground substances blend better!

Excessive grinding can lead to:

- agglomeration of powder particles;
- adsorption of powder particles on the mortar walls;
- powder adsorption of foreign impurities and moisture from the air.

Methods to reduce agglomeration:

- grinding with solid indifferent substance (sucrose, lactose);
- grinding with auxiliary liquid (ethanol, ether).

Preparatory activities:

- to choose appropriate scales;
- to choose a mortar.

There are 7 sizes of mortars.

Mortar parameters

№ mortar	Diameter, mm	Working area		Working volume, sm^3	Powdering time, sek	Load, g	
		sm^2	coefficient			max	optimal
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	112.0	42.0

In all variety of formulas of complex powders two cases may be distinguished:

1. The medicine of a complex powder prescribed in equal or approximately equal amounts.

2. The medicine of a complex powder prescribed in extremely different amounts.

The Main Technological Powder Preparation Procedures

In the first case, when medicinal substances are prescribed in equal amounts and their physical and chemical properties are the same, the order of blending is not significant; they are mixed in order of prescribing, as a rule.

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

1. A substance without activity should be powdered first.

2. If there is no substance without activity in the formula, then a substance having the least percent of rubbing in pores of a mortar is triturated first. The value of powder losses is often explained by electrization of mortar's walls and powder (different charges). Therefore, it is important to foresee the value of losses correctly to solve the problem of ingredients' trituration in a clean mortar because the losses while triturating a substance in a clean mortar are high enough.

3. First the coarse-crystalline substances should be powdered, then fine-crystalline and, at last, amorphous ones.

4. The heavy substances should be added in the mortar first and then the lighter ones. The easily spraying substances are added last.

In case medicinal substances of a complex powder are prescribed in different amounts, the main rules of blending are the following:

1. Start powdering in the mortar with medicinal substances without the therapeutical activity, and if there is not such a substance in the formula, the preparation should begin with a component prescribed in greater quantity and which is less lost in the mortar's pores (taking into account the crystalline structure and spraying ability of a substance).

2. Add medicinal substances with a component prescribed in the smallest amount (in the mortar where the substance without activity previously added).

3. Then add gradually the remaining components, taking into account their amounts. The procedure of blending from the smallest component to the biggest one must be the same.

The homogeneity of the powder mixture is reached when components are prescribed in the ratio 1 : 1 (for poisonous and strong-effective substances) to 1 : 5 (for substances from the general list).

When the ratio is increased more than 1 : 5 the homogeneity of a mixture is greatly disturbed.

Powder Requirements:

– ***dispersibility —*** loose property and the optimum size of particles of all components of a complex powder;

– ***homogeneity —*** proportional distribution of substances in the total mass of complex powder;

– ***correct dosing;***

– ***stability of substances during storage;***

– ***sterility*** (for dusting powders applied on wounds and powders for newborns).

PRACTICAL PART

Powders are _____

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Advantages of powders: _____

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Disadvantages of powders: _____

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_____

_____

Classification of powders according to:

– composition

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_____

– the method of application

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_____

– the quantity of powder doses:

_____

_____

Methods of powder prescribing:

_____

_____

Main stages of powder manufacturing:

_____

_____

Excessive grinding can lead to _____

_____

_____

Methods to reduce agglomeration:

_____

_____

Requirements for powders:

_____

_____

_____

_____

SPECIFIC TECHNOLOGY OF SOME POWDERS COMPOUNDING. POWDERS WITH POISONOUS AND STRONG-EFFECTIVE SUBSTANCES

Issues for discussion:

1. Technology of powders compounding.
2. Powders with poorly powdered medicinal substances.
3. Powders with poisonous and strong-effective substances.
4. Powders with dyeing medicinal substances.

THEORETICAL PART

When choosing the optimal technology for compounding complex powders, it is necessary take into account the following:

- degree of crystallinity;
- crystal size;
- solubility in ethanol (for poorly powdered medicinal substances);
- ability to spray;
- ability to electrify;
- degree of hygroscopicity;
- presence of crystallized water in the structure;
- adsorption activity;
- coloring ability;
- volatility.

Technology of powder compounding include:

1. **Preparatory activities** (choose scales, a mortar with a pestle, a special celluloid plate of a certain shape, packaging material.
2. **Grinding (dispersing).**
3. **Mixing.**
4. **Dosing.**
5. **Packaging.**
6. **Labeling.**

According to the State Pharmocopeia of the Republic of Belarus:

– powders for internal use: all ingredients must be powdered to the size of individual particles not exceeding 0.18 mm;

– powders for external use: all ingredients must be powdered to the size of individual particles not exceeding 0.125 mm.

Sequence of adding ingredients should be the following:

- first poisonous and narcotic substances (substances from List A);
- then strong-effective substances;
- at the end other substances are added in the order of the mass increase (M1 < M2 < M3 …), while paying attention to the nature of the crystals — first add coarse crystalline substances, then fine crystalline substances and amorphous substances.

Powders with poorly powdered medicinal substances

Poorly powdered medicinal substances must be ground with excipient liquid!

They can be divided into two groups:

1) especially difficult to grind (10 drops of alcohol or 15 drops of ether to grind 1 g of such substances):

- menthol;
- thymol;
- camphor;
- iodine;

2) less difficult to grind (5 drops of alcohol or 8 drops of ether to grind 1 g of such substances):

- boric acid;
- salicylic acid;
- sodium tetraborate;
- streptocide.

Note: while compounding of powders with poorly powdered medicinal substances after grinding the substance with the excipient liquid, **the next component should be added immediately**, prior to the solvent evaporation and the solvation shell collapsing.

E.g.: Rp.: Camphorae 0.1
Sacchari 0.3
Misce, fiat pulvis
Da tales doses No. 10.
Signa. 1 powder dose 3 times per day.

The given medicine is a complex dosed powder for internal use, with aromatic, volative and poorly powdered medicinal substance (camphor).

Procedure: at first grind 3.0 g of sugar in the mortar and pour it completely on the capsule. 1.0 g camphor is grinded with 10 drops of alcohol in the mortar, then add immediately the remaining amount of the powdered sugar to prevent alcohol evaporation. Weigh out 0.4 g and pack in the parchment capsules. (waxed capsules are not recommended, because camphor with paraffin and wax form eutectic mixtures.)

Powders with Poisonous and Strong-Effective Substances

In case poisonous and strong-effective substances are prescribed in the amount of less than 0.05 g for the whole mass, the pharmacist must use **triturations 1 : 10** or **1 : 100** then follow the recommendations of the State Pharmacopoeia of the Republic of Belarus.

Trituration is a mixture of poisonous substance (a substance from List A) or strong-effective substance with the excipient filler (most often lactose monohydrate (milk sugar)). It is recommended to be used due to the following reasons:

1) inability to weigh with sufficient accuracy a sample of a substance in the amount of less than 0.05 g on a manual weights;

2) inability of uniformly distribute a small amount of poisonous or strong-effective substance in the total mass of the powder.

Most often, milk sugar is used as an excipient substance in triturations compounding because lactose is characterized as:

- chemically and pharmacologically indifferent;
- non-toxic;
- odorless;
- sweet taste;
- density is 1.52 g/cm^3. It can prevent separating into layers;
- not hygroscopic.

Usually triturations from poisonous substances dosed in milligrams are prepared in the ratio of 1 : 100 (i.e. 1 part of a poisonous substance and 99 parts of lactic sugar). When substances are prescribed in centigrams it is necessary to use triturations in the ratio of 1 : 10 (i.e. 1 part of a substance is mixed with 9 parts of lactic sugar).

On the bottle with trituration should be an inscription (example)

Trituratio Platyphyllini hydrotartratis (1 : 10) (0.01 = 0.1 triturationis) Trituratio Platyphyllini hydrotartratis (1 : 100) (0.001= 0.1 triturationis)

Triturations at a chemist's are prepared by the pharmacist for a term of not more than 15 days. The preparation of triturations should be registered in the special laboratory journal.

E.g. : Rp.: Platyphyllini hydrotartratis 0.0025
Papaverini hydrochloridi 0.02
Sacchari 0.35
Misce, fiat pulvis
Da tales doses No. 10
Signa. 1 powder dose 3 times per day.

The medicine is a complex dosed powder for internal use, with a poisonous substance (Platyphylline hydrotartrate) in the amount of less than 0.05 g for all powders (0.0025 × 10 = 0.025), a strong-effective medicinal substance is Papaverine hydrochloride and an auxiliary substance is sugar.

Single and daily doses are to be checked up with the State Pharmacopoeia (the highest single dose for Platyphylline hydrotartrate is 0.01, the highest daily dose is 0.03); according to the formula a single dose is 0.0025, a daily dose — 0.0025 × 3 = 0.0075 of Papaverine hydrochloride is 0.2–0.6; according to the formula a single dose is 0.02, a daily dose is 0.02 × 3 = 0.06. Therefore, the doses are not excessive. The quantity of sugar is required to be decreased taking into account Platyphylline hydrotartrate triturations 3.5 – 0.25 = 3.25 g.

WCP — written control passport

WCP (reverse side)

Platyphylline hydrotartrate 0.0025 × 10 = 0.025
Triturations of Platyphylline hydrotartrate (1 : 10) 0.025 × 10 = 0.25
Papaverine hydrochloride 0.02 × 10 = 0.2
Sugar 0.35 × 10 = 3.5 3.5 – 0.25=3.25
Weight of one dose: (0.25 + 0.2 + 3.25) / 10 = 0.37

WCP (front side)

Date No. Pr.
Sacchari 3.25
Triturationis Platyphyllini hudrotartratis (1 : 10) 0.25
Papaverini hydrochloridi 0.2

Total mass = 3.7; p = 0.37; No. 10
prepared by_____
checked up by_____

Poisonous substances should be weighed by a pharmacist responsible for such substances dispensing and storage using the special weights locked in a special case designed for poisonous substances.

A pharmacist makes a note in the written control passport about dispensing of a poisonous substance, and the pharmacist signs when he receives it (request).

Procedure: place 3.25 g of sugar in a mortar, carefully grind, put a portion of sugar on the capsule, leaving approximately 0.25 g in the mortar, add 0.25 g of Platyphylline hydrotartrate trituration (1 : 10) (following the safety rules of working with poisonous substances), carefully mix, add 0.2 g of Papaverine hydrochloride, carefully mix, then add the remaining amount of powdered sugar. This homogeneous mixture is weighed in 10 doses of 0.37 g. Pack powders in parchment or waxing capsules (note that sugar is a hydroscopic substance), place in a paper envelope or cartoon box.

Request

Triturationis Platyphyllini hydrotartratis (1 : 10) 0.25 Series No.
Issued by: Signature
Date

Triturationis Platyphyllini hydrotartratis (1 : 10) 0.25 Series No.
Received by: Signature
Date

Labels for dispensing: (prescription #, signature) and labels «To be handled with caution», «Keep out of the reach of children». If sugar is not prescribed write down the weight on the reverse side of the formula.

Powders with Dyeing Medicinal Substances

Medicinal substances, which have colour, can be divided into **two groups**:

1. ***Dyeing substances:*** furaciline, brilliant green, methylene blue, iodine, riboflavine, potassium permanganate, etc. (fig. 11).

2. ***Coloured substances:*** dermatol, protargol, etc.

Fig. 11. Samples of certain dyeing medicinal substances

Dyeing medicinal substances, as well as their solutions, mixtures leaving a coloured trace on containers, equipment and other subjects belong to the 1-st group. This trace is impossible to wash out by usual sanitary and technical means. They are stored in a separate case and are weighing on separate manual balances.

Coloured medicinal substances do not leave the trace on containers and packing materials. They are stored according to the general rules.

Technology features of powders with dyeing medicinal substances:

– compounding of powders with dyeing medicinal substances should be made on a specially designated table using separate mortars and scales;

– to avoid dyeing medicinal substances to be rubbed into the pores of the mortar and pestle, it is recommended to grind other unstained substances in the mortar first;

– place the colorless medicinal substances in the mortar first, make the hole, put dyeing medicinal substances in the hole, cover the top layer with colorless medicinal substances and carefully mix;

– another way to compound is to place a dyeing medicinal substance between two layers of colorless medicinal substances.

PRACTICAL PART

When choosing the optimal technology for compounding complex powders, it is necessary to take into account the following: _____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Sequence of adding ingredients in powders compounding: _____

_____

_____

_____

_____

Poorly powdered medicinal substances must be ground with _____

Trituration is _____

_____

_____

_____

Usually triturations from poisonous substances dosed in milligrams are prepared in the ratio of _____

When substances are prescribed in centigrams it is necessary to use triturations in the ratio of _____

Dyeing substances _____

_____

_____

Coloured substances _____

_____

_____

Technological features of powders with dyeing medicinal substances

_____

_____

_____

_____

_____

_____

SPECIFIC TECHNOLOGY OF SOME POWDERS COMPOUNDING. EXTRACTS, USED IN CHEMIST'S TECHNOLOGY FOR COMPOUNDING POWDERS

Issues for discussion:

1. Extracts, used in chemist's technology for compounding powders.
2. Technology features of powders with extracts.
3. Technology of powders with antibiotics.
4. Technology of sparkling powders.
5. Technology of powders for children.
6. Packing of powders.

THEORETICAL PART

Extracts — concentrated essence from medicinal plant raw materials. The pharmaceutical industry produces different types of extracts:

1. Liquid Extracts — Extracta fluida.
2. Thick Extracts — Extracta spicca (1 : 1), i.e. 100 %.
3. Dry Extracts — Extracta sicca (1 : 1) 100 % or (1 : 2), i.e. 50 %.

In the compounding of powders with extracts, belladonna extracts are most often used. **Belladonna extracts = Extractum Belladonnae.**

Extractum Belladonnae spicca contained of alkaloids 1,5 % in terms of hyoscyamine.

Extractum Belladonnae sicca contained of alkaloids 0,75 % in terms of hyoscyamine.

It should be taken into account that the content of alkaloids in the thick extract is taken as 100 %, while, in the dry extract, their content is 50 %.

Compounding of powders with extracts

If there is no indication in the prescription about the Belladonna extracts state of aggregation — it means that the thick extract is prescribed. If there is no thick extract in the pharmacy — dry extract or a solution of a thick extract are used depending on the stock. But remember that the amount of dry extract or solution of a thick extract should be taken in double amount in relation to the mass of the prescribed thick extract, so the total mass of the obtained dosage form increases.

In the pharmacy solution **Extractum solutum — in a ratio of 1 : 2** from a thick Belladonna extract is made for ease of use. It means to 1 part (by mass) of the thick extract 1 part of the solventis added. Any solvent for making a solution of a thick extract has a complex composition, with each component having a specific function.

1 part of ethanol (mass)
3 parts of glycerin (mass)
6 parts of aquae purificatae (mass)

Ethanol — increases the solubility of the thick extract and reduces the growth of microorganisms in solution.

Glycerin — solubilizer protects the solution from particle enlargement and coagulation.

Aquae purificatae — main solvent.

The solution of extract is usually dosed by drops. A bottle with a solution of a thick extract is supplied with a calibrated droplet meter. The bottle label indicates:

Extractum Belladonnae solutum (1 : 2) 0.1 solution of thick extract – 3.5 drops of solution, 0.1 thick extract — 7 drops of solution.

The expiration date of a thick belladonna extract solution is no more than 15 days.

E.g.: Rp.: Extracti Belladonnae 0.015
Natrii hydrocarbonatis
Phenylii salicylatis ana 0.3
Misce, fiat pulvis
Da tales doses No.12
Signa. One powder dose 3 times per day.

The given medicine is a complex dosed powder for internal use with a strong-effective substance Belladonna extract and poorly powdered substance — phenyl salicylate.

WCP *(reverse side)*

Thick Belladonna extract (1 : 1) 0.015 × 12 = 0.18
Dry Belladonna extract (1 : 2) 0.18 × 2 = 0.36
Or the solution of a dense Belladonna extract (1 : 2)
0.1 thick extract — 7 drops of a solution
0.18 thick extract - X,
X = 12.6 drops ≈ 13 drops
Sodium hydrocarbonate 0.3 × 12 = 3.6
Phenylsalicylate 0.3 × 12 = 3.6
Alcohol 95 % — 36 drops
Weight of one dose:
(0.015 × 2) + 0.3 + 0.3 = 0.63
0.015 + 0.3 + 0/3 = 0.61 with solution of a dense Belladonna extract

WCP *(front side)*

Date No. Pr.
a) Using solution of a dense Belladonna extract:
Date No. Pr.
Natrii hydrocarbonatis 3.6
Phenylii salicylatis 3.6

Extracti Belladonnae solute (1 : 2) gtts. XIII (0.1 = 7 drops)

_____

0.63 No. 12

Has prepared:
Has checked:

b) Using of a dry Belladonna extract:

Date No. Pr.

Natrii hydrocarbonatis 3.6
Phenylii salicylatis 3.6
Extracti Belladonnae sicci (1 : 2) 0.36

_____

0.63 No. 12

Has prepared:
Has checked:

Procedure: place 3.6 g of sodium hydrocarbonate in the mortar, triturate and put it on the capsule. Place 3.6 g phenylsalicylate and triturate with 36 drops of 95 % alcohol, then add 13 drops of a dense extract solution according to recalculation by prescription, triturate sodium hydrocarbonate add it to the mortar from the capsule, mix to homogeneity and preservation of looseness. Weigh out per 0.63 in 12 doses. Then pack in the parchment capsules.

The solution of a dense extract is convenient for use if there are powdered substances possessing high adsorbic ability, poorly soluble in water (magnesium oxide, magnesium cardonate, phenylsalicylate ect.).

E.g.: Rp.: Extracti Belladonnae 0.01
Anaesthesini 0.3
Magnesii oxydi 0.15
Misce, fiat pulvis
Da tales doses No. 20
Signa: 1 powder 3 times in a day.

In case of **dry extract** application the WCP (front side) must contain the following information:

Anaesthesini 6.0
Extracti Belladonnae sicci (1 : 2) 0.4
Magnesii oxydi 3.0
Total mass = 9.4; p = 0.47; No. 20

In case of **thick** extract application the WCP (front side) must contain the following information:

Anaestesini 6.0
Extracti Belladonnae spissi (1 : 1) 0.2
Aquae purificatae (seu Spiritus aethylicus 20 %) gtts V
Magnesii oxydi 3.0
Total mass = 9.2; p = 0.46; No. 20

Compounding of powders with antibiotics

Compounding of powders with antibiotics:

1. Compounding should be carried out in aseptic conditions.

2. Do not grind substances of antibiotics too fine (penicillins, erythromycin, griseofulvin, etc.), since it can lead to destruction and change in the structure of antibiotics molecules under the influence of mechanical force and can lead to the loss of the pharmacotherapeutic effect.

3. Loss of antibiotic activity may occur under the influence of heavy metal salts and other factors.

The activity of many antibiotics is expressed in units of action (UA). The ratio between the unit of action and the mass is established using the article of the pharmacopoeia for this antibiotic.

Reference data from the Pharmacopoeia of the Republic of Belarus (not to memorize!).

Correspondence of 1 000 000 units of action to the mass of antibiotics

Name of antibiotic	Grams
Amoxicillin	1.0
Kanamycin sulfate	1.0
Nystatin	0.25
Streptomycin sulfate	1.0
Tetracycline hydrochloride	1.0
Cefazolin	1.0
Erythromycin	1.11

Compounding of sparkling powders

The sparkling powders contain:

- sodium bicarbonate;
- citric acid;
- tartaric acid;
- acetylsalicylic acid.

The substances included in the effervescent powders should not contain water or adsorbed moisture, to avoid CO_2 losses.

When the patient takes sparkling powder — water is added into the dosage form — and a chemical reaction between an acidic and alkaline substance begin, CO_2 is released.

Released CO_2 in the dosage form enhances the secretory activity of the gastrointestinal tract, thereby improving the absorption of medicinal substances. (mineral water has a similar effect).

Sparkling powders are prepared in heated mortars from pre-dried substances without excessive grinding, because the increase of free surface of the substance will facilitate the adsorption of moisture from the air.

Sparkling powders are especially promising in pediatric practice and for treatment of geriatric patients with a weakened secretory function of the gastrointestinal tract.

Compounding of powders for children

Compounding of powders for children:

– manufactured dosage forms for newborns should be sterile;

– dosage forms for children under 1year old should meet the microbiological standard for microbiological purity: not more than 50 bacteria and fungi in total in 1 g or 1 ml of the dosage form in the absence of *Enterobacteriacaeae, P. aeruginosa, S. aureus*.

Normally the use of tablets for powders compounding for children is not allowed because the tablets contain fillers, stabilizers, colorants and other excipients. Pharmacicst should use separate substances, according to the prescription.

The mucous membrane of the oral cavity and esophagus of newborn children is delicate, rich in blood vessels, easily injured, dry, since the mucous glands are practically not developed, which, naturally, does not allow newborns to take the medicine in powder form.

Therefore, the powder is not the optimal dosage form (especially for newborns) since it should be dissolved or suspended when taken. Flavoring agents are often added at home (juices, syrups etc.), which can change the pharmacological effect.

Replacing powders with solutions has a number of advantages:

- it excludes the use of excipients that promote microbial contamination;
- provides a higher rate of absorption;
- ensures sterility.

Examples of powders prescriptions for children

Powders for newborns	
Composition	**Shelf life**
Dimedrol (diphenhydramine) 0,001 or 0,002 Sugar (glucose) 0,2	90 days
Phenobarbital 0,002 or 0,005 Sugar (glucose) 0,2	90 days
Euphylline 0,003 Sugar 0,2 (substitution of sugar for glucose is prohibited)	20 days

Batching of powders

Separation of the powder mass into doses is one of the important stages in the technological formulation.

The pharmacological effect depends on the dose of a medicine.

The batching of powders can be carried out by two cases:

– by weight;

– by volume.

Batching by weight is the main method used in the chemist s production. It is more accurate than batching by volume.

Batching by weight is carried out by weighing separate doses on the manual chemist s balances or the electronic one.

Batching by volume in the chemist s conditions is carried out by a volumetric doser types TK-3, DPR-2.

Packing of powders

In case the type of the packing material is not indicated in the prescription, powders are accepted for dispensing in plain paper capsules rectangles of a certain size (7.5 × 10 sm).

Capsules are applied with the following purpose:

1. Masking of unpleasant odour or taste.
2. Protection of mucous membranes of the stomach from irritation or coloring (chloral hydrate, acryquine).
3. Localization of the action.

In the chemist's practice solid gelatin capsules consisting of two parts are used. Seven numbers of capsules (No. 1–7) containing about 0.1–1.5 g of the powdered substances are distinguished.

Formalization procedure

The following inscriptions on labels for powders are used: «External» or «Internal», «Powder»; or preventive inscriptions: «Keep in a dark cool place», «Keep out of the reach of children», «To be handled with caution». Powders with poisonous or narcotic substances are registered, signed and sealed.

PRACTICAL PART

Extracts — concentrated essence from medicinal plant raw materials. The pharmaceutical industry produces different types of extracts including:

_____

_____

Extractum Belladonnae spicca containes

_____

Extractum Belladonnae sicca containes

_____

Compounding of powders with antibiotics

_____

_____

_____

Compounding of powders for children

_____

_____

_____

COLLOQUIUM/TEST ON TECHNOLOGY OF POWDERS

Issues for discussion:

1. Powders: definition, advantages and disadvantages.
2. Classification of powders.
3. Methods of powder prescribing: distributive and separating.
4. The main stages of powders manufacturing. Methods to reduce agglomeration.
5. Mortar parameters.
6. The main technological procedures of preparing powders.
7. Requirements for powders
8. Powders with poorly powdered medicinal substances.
9. Powders with poisonous and strong-effective substances.
10. Powders with dyeing medicinal substance.
11. Extracts used in chemist's technology to compound powders.
12. Technology features of powders with extracts.
13. Technology of powders with antibiotics.
14. Technology of sparkling powders.
15. Technology of powders for children.
16. Packing of powders.

SOURCES OF INFORMATION

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Практикум

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