Extracted dosage forms from medicinal plant raw materials.

1. Infusions and decoctions.
2. Technological aspects of making infusions and decoctions from plant raw materials.
3. Galenic preparations (tinctures, extracts, elixirs).
4. Plant raw materials -sources of obtaining tinctures, extracts.
5. Nomenclature of tinctures, extracts (liquid, thick, dry, oil), elixirs.

Theoretical bases of extraction

The production of extractive preparations is based on extraction processes. The chemical-pharmaceutical industry has established production of such dosage forms from medicinal plant raw materials as tinctures, liquid, thick and dry extracts, extracts-concentrates, maximally purified (novogaleno) preparations, extracts from fresh plants, etc., and from raw materials of animal origin - preparations of hormones, enzymes and preparations of non-specific action (pantocrine, vitohepat, etc.).

The extraction process refers to mass-exchange processes based on such phenomena as diffusion, osmosis, dialysis. As a result, the transfer of biologically active substances from the internal structures of material particles to the extractant takes place and ends when balance concentrations are reached. In the balance state, the same number of molecules are transferred from the material to the extractant as from the extractant to the material, i.e. the concentration remains constant. The concentration is usually higher in the material than in the extractant.

To obtain various types of phytochemicals, mainly dried plant material is used. Fresh plants are used in small quantities, mainly for obtaining juices, due to the complexity of their storage and transportation, as well as the rapid processes of enzymatic hydrolysis of active substances.

In the process of drying, plant material undergoes significant changes: cell sap turns into dry residue, the interior of the cell is filled with air, the cell wall and

membranes of cell organoids after drying acquire the properties of porous partitions.

herefore, when processing the crushed plant material, the extractant used in the process of phytopreparation extraction due to wetting and capillary forces penetrates through the pores inside the cell, displacing the air. The surface tension and viscosity of the solvent are of great importance in the extraction process. Absorbed liquid should spread over the surface of the cell, which leads to a significant increase in the contact surface and accelerates the process of dissolution of extracted substances. The greater the surface tension of the extractant, the more difficult it is for the liquid to penetrate the plant material.

The solvent inside the cell comes into contact with the cellular contents. Soluble substances dissolve, high molecular weight compounds (HMCs) and colloidal substances swell. The degree of swelling of raw materials depends on the chemical nature of the solvent (extractant). The strongest swelling is caused by water, the least - by non-polar solvents (oil, petrol, etc.). Swelling of raw materials during alcohol extraction depends on their water content.

The extractant flushes out soluble and insoluble substances (starch, mucus, proteins, pectin substances, etc.) from the outer plant cells destroyed in the process of grinding. Through the macropores of the cells the diffusion process takes place, and through the micropores of the cell membrane the processes of osmosis and dialysis take place. Thus, the solvent penetrates into the cell (the process of osmosis), and through the cell membrane into the extraction - various salts and other compounds (the process of dialysis).

As a result of the extractant penetrating into the cell, a concentrated solution ("primary sap") is formed in the cell. Due to the difference in osmotic pressure, the soluble substances leave the cell and the solvent penetrates into it. The collision of the osmosis and dialysis processes leads to swelling of the plant material.

The main physical and chemical process of extraction is diffusion (transfer of substance from the zone with higher concentration to the zone with lower concentration), which takes place until the dynamic equilibrium of dissolved

substance concentrations in and outside the cell. Consequently, the extraction of substances is never complete, i.e. a part of soluble substances always remains in the plant cell. Therefore, in order to reduce the loss of active substances, extraction from the cells of plant material is often carried out by forced extraction (pressing, squeezing of processed plant material), as well as using methods of intensification of the extraction process (e.g., heating, stirring, etc.) to obtain a greater yield of biologically active substances.

The main factor determining the mass transfer rate is the internal resistance of the solid phase. Reducing the particle size of plant raw materials leads to a decrease in resistance. The smaller the particle radius, the faster the diffusion.

Thus, the extraction process of plant material is influenced by a number of factors:

- anatomical (or histological) structure of the plant material;
- the particle size of the plant material;
- temperature regime and duration of extraction;
- nature and viscosity of the extractant;
- physicochemical properties of biologically active compounds.

These factors should be taken into account when selecting the extraction conditions for the production of extractive dosage forms from medicinal products.

The oldest and simplest in terms of preparation technology extractive medicinal forms from medicinal plants are infusions and decoctions - these are aqueous extracts from medicinal plant raw materials, as well as dissolving in water standardised dry or liquid extracts-concentrates.

The use of aqueous extracts for various diseases dates back to ancient times. Even Claudius Galen (about 1800 years ago), who rejected the opinion of Hippocrates that medicines existed in nature in a ready-made form, argued that in addition to active substances in plants, there were also ballast substances that could have a harmful effect on the body. Already in those days, they sought by simple processing of plant material to obtain a more convenient form for use.

Paracelsus, who contemptuously referred to whole herbs as "soup seasoning", was a particularly staunch defender of the idea of replacing plant material with extracts from them.

The advantage of this dosage form is the simplicity of its preparation, and the fact that the medicinal plant material is used in its unchanged form, and aqueous extracts from raw materials have a milder effect than synthetic or isolated from raw materials in pure form, due to the complex of active or accompanying substances. Infusions and decoctions of medicinal plant materials can be used both for internal (mixtures) and external (rinses, lotions, washes, etc.) application.

The disadvantages of the dosage form include:

- instability during storage (since the extractant is water, and medicinal plant raw materials contain microorganisms and enzymes);

- instability of some plant substances to high temperature and decomposition when heated;

- the dosage form is not standardised;

- difficulty in quantitative determination of active and related substances;

- impossibility to use most aqueous extracts during intensive therapy or for seizure control (infusions and decoctions are mainly used for chronic, as well as sluggish diseases).

Despite the fact that infusions and decoctions can be prepared from any plant material, it is necessary to adhere to certain rules of their preparation. Thus, from loose raw materials (flowers, leaves, herbs) are usually prepared infusions, from dense (bark, roots, rhizomes, fruits) - decoctions. However, there are exceptions: valerian rhizomes and roots are used to make infusions, and leaves of bearberry, cowberry, senna are used to make decoctions.

Before preparation of aqueous extracts, individual morphological groups of whole medicinal plant material are preliminarily crushed. According to OFS 1.4.1.0018 "Infusions and decoctions" herbs are ground, as a rule, to particles no larger than 7 mm; leaves and flowers - to particles no larger than 5 mm (leathery leaves - cowberry, bearberry, etc.). - to particles no larger than 3 mm). Bark, roots,

rhizomes should have particle size, as a rule, not more than 3 mm. Fruits and seeds are used mainly whole, if necessary, crushed to particle size not more than 0.5 mm. Grinding of medicinal plant raw materials should be specified in the pharmacopoeial article or regulatory documentation.

The kinetics of extraction (duration of the extraction process) and the temperature regime should also be observed. For the preparation of aqueous extracts, hot (infusions, decoctions, mucilages) and cold extraction methods are used (only for the production of althea root infusion).

In case of absence of instructions for flowers, leaves, herbs, the infusion time in a water bath is 15 min, then at room temperature - 45 min (infusion mode). For bark, fruits, seeds, buds, shoots, underground organs infusion time in a water bath is 30 min, at room temperature - 10 min (decoction mode).

When making aqueous extracts of 1000 - 3000 ml, the time of infusion on a water bath is increased by 10 min and is 25 and 40 min, respectively.

Aqueous extraction	nfusion time (water bath temperature)	Cooling time (room temperature)
Infusion		
up to 1 litre	15 min	45 min
1 to 3 litres	25 min	45 min
Decoction		
up to 1 litre	30 min	10 min
1 to 3 litres	40 min	10 min

It should be taken into account that for medicinal plant raw materials containing essential oils, the time of infusion in a water bath does not depend on the morphological group of raw materials and is 15 min, at room temperature - 45 min. In this case, the vessel for infusion should be tightly capped to avoid loss of terpenoids of essential oils.

Decoctions of bearberry leaves, cowberry and all kinds of medicinal plant materials containing tannins (oak bark etc.) are strained immediately after

extraction, without allowing cooling at room temperature to avoid precipitation of tannins on the medicinal plant material.

A decoction of senna leaves is strained after cooling completely at room temperature. The resinous substances present in cassia leaves that cause intestinal pain are precipitated.

When making aqueous extracts from medicinal plant material containing potent and poisonous substances (e.g., herb thermopsis), in the absence of additional instructions should be taken 1 mass part of the medicinal plant material to obtain 400 volume parts of aqueous extract (1:400).

Aqueous extracts from the herb goricetum, lily of the valley herb, lily of the valerian shoots, valerian rhizomes with roots, roots of Isthodium are prepared in a ratio of 1:30.

Infusion of althea roots is prepared in a ratio of 1:20. To obtain an infusion of althea roots pour water at room temperature and insist for 30 minutes at room temperature with frequent stirring. After straining the raw material is not squeezed.

When making aqueous extracts from medicinal plant material containing alkaloids, add citric, tartaric or hydrochloric acid (in terms of hydrogen chloride). Acid is taken by weight as much as the amount of alkaloids contained in the taken amount of medicinal plant material.

From herbal medicines in filter packets prepare aqueous extracts for one use in the ratio specified in the instructions for use. To prepare an aqueous extract, the filter packet is poured with boiling water in a porcelain or ceramic bowl with a tightly sealed lid and infused for the time specified in the instructions for use, but not less than 15 minutes.

Another quite ancient form of medicinal plant material is tincture. Tinctures were introduced into medical practice by Paracelsus (1495-1541) and have not lost their relevance.

Tinctures are liquid dosage forms, which are usually coloured alcoholic or aqueous-alcoholic extracts obtained from medicinal plant raw materials (dried or

freshly harvested), as well as from raw materials of animal origin without heating and removal of extractant.

The absolute number of tinctures included in the State Register of Medicinal Products is 440. Tinctures are subdivided into simple, based on one type of medicinal plant material, and complex (complex), representing extracts from several types of medicinal raw materials.

Tinctures are prepared in a ratio of 1:5 or 1:10.

From one part of raw materials by weight, 5 or 10 volume parts of tincture are obtained.

Exceptions on the proportion of raw materials to tincture:

- **1:10** tincture of calendula, hawthorn, chilli, peony, arnica;
- **1:2** tincture of sophora japonica;
- **1:20** tincture of peppermint

To carry out the extraction process, an extractant consisting of a mixture of water and alcohol is prepared. The concentration of alcohol depends on the nature of the active substances contained in the raw material. For example, if the raw material contains tannins or salts of alkaloids, 40% ethyl alcohol is usually used as an extractant (salts of alkaloids dissolve better in diluted alcohol). In the presence of glycosides in plant raw materials, 70% ethyl alcohol is used. Together with glycosides, raw materials contain enzymes capable of catalysing the hydrolysis of glycosides. Enzymes are insoluble in alcohol, 70% alcohol allows their isolation. If essential oils are present in the raw material, concentrated (90-95%) ethyl alcohol is used, which has a greater capacity to dissolve essential oils.

Most tinctures are produced using 70% ethanol, less frequently 40% (tincture of barberry, St. John's wort) and very rarely other concentrations: 90% (tincture of mint, chilli pepper), 95% (tincture of lemongrass) and others.

In the manufacture of tinctures accepted mass-volume proportion, when one weight part of plant raw materials get 5 volumetric parts of the finished product, potent raw materials - 10 parts. In some cases, tinctures are prepared in other ratios

(tincture of arnica - 1: 5, calendula, hawthorn, peony - 1: 10, mint - 1: 20, sophora - 1: 2).

The choice of method and mode of infusion of aqueous-alcoholic dosage form depends on the chemical composition and anatomical nature of the plant material. The following methods can be used to produce tinctures:

1. Extraction methods (maceration and its variants, percolation).

2. Dissolution of dense and dry extracts.

The main quantity of tinctures is obtained by extraction of the extracts, which are ground to the required parameters and sieved before extraction. And only a small part of tinctures is produced by dissolving dry extracts. For example, this is the way to obtain a tincture of chilibuca, which has poisonous seeds that are difficult to grind into powder because of their hardness. Thoracic elixir is prepared from a thick or dry extract of licorice.

The resulting extraction is sedimented at 8-10^{o} C, then filtered and subjected to stage control.

Quality indicators of tinctures:

- Description;
- Authenticity;
- Quantification;
- Density;
- Ethanol content;
- Methanol and 2-propanol content;
- Dry residue;
- Heavy metals;
- Volume of the contents of the package;
- Microbiological purity

Extracts are concentrated extracts from raw materials, less often from raw materials of animal origin.

In terms of consistency, a distinction is made:

 extracts dry (Extracta sicca);

 extracts dense (Extracta spissa);

 liquid extracts (Extracta fluida).

Extracts are dry - powdery masses with bulkiness and a moisture content of max. 5 %.

Extracts thick - viscous masses with moisture content not exceeding 25 %.

Liquid extracts are thick, mobile, sometimes oily liquids.

A separate group includes extracts-concentrates - extracts of different consistency, standardised in relation to the medicinal plant material in certain ratios, e.g. 1:1 or 1:2. These extracts are mainly used to produce infusions and decoctions, replacing the medicinal plant material in the specified ratios.

According to the extractant used, a distinction is made:

 aqueous extracts, obtained using purified water as an extractant (extract of three-leaved vahta thick);

 alcoholic extracts obtained using ethyl alcohol of various concentrations as an extractant (liquid hawthorn extract, liquid aqueous pepper extract, liquid thyme extract, etc.);

 oil extracts obtained using vegetable oil as an extractant (St John's wort oil extract);

 extracts obtained using various organic solvents (carbon tetrachloride, dichloroethane, etc.) (wormwood thick extract (extractant chloroform water));

extracts obtained by sequential extraction of medicinal plant material with extractants, including those of different polarity (dry extract of marshmallow root (ethyl alcohol 25%, water)).

Extracts are obtained in the process of extraction of medicinal plant material with the appropriate extractant until its complete depletion of plant material. When obtaining thick extracts, an additional stage is thickening, and for dry extracts - thickening and drying.

Liquid extracts are widespread in the pharmaceutical industry, as they have the following advantages: 1) the same ratio between the active substances

contained in the medicinal raw material and in the finished product; 2) convenience in measuring in pharmacies; 3) the possibility of obtaining without the use of evaporation allows to obtain liquid extracts containing volatile substances (essential oils).

The disadvantages of liquid extracts include: 1) their saturation with associated substances extracted from plant raw materials; 2) the appearance of precipitation at slight temperature drops or partial evaporation of alcohol; 3) the need for hermetic closure and storage at a temperature of 15-20 ° C; 4) to obtain liquid extracts are used large volumes of extractant, which are then evaporated.

Most dense extracts serve as intermediates for the preparation of various dosage forms (tablets, suppositories, ointments, syrups, etc.) and combination preparations.

The disadvantages of dense extracts include the inconvenience of their use, which requires certain methods of tasting. In addition, in dry air they dry up and become hard; in humid air they become damp and mouldy. They therefore require hermetically sealed packaging.

The most rational type of extracts are dry extracts. They are easy to handle and have the lowest possible mass. The disadvantages of dry extracts include their high hygroscopicity, as a result of which they turn into lumpy masses that lose bulkiness.

- Quality indicators of extracts
- - Description;
- - Authenticity;
- - Quantification;
- - Loss in weight on drying/ for dry and thick extracts
- - Density;
- - Bulk volume and particle size distribution / for dry extracts
- - Ethanol content;

- Residual organic solvents / if organic solvents are used in the production of extracts
- Dry residue;
- Acid number, peroxide number, iodine number, saponification number/ for oil extracts
- Heavy metals;
- Refractive index/ for oil extracts
- Volume of the contents of the package;
- Microbiological purity