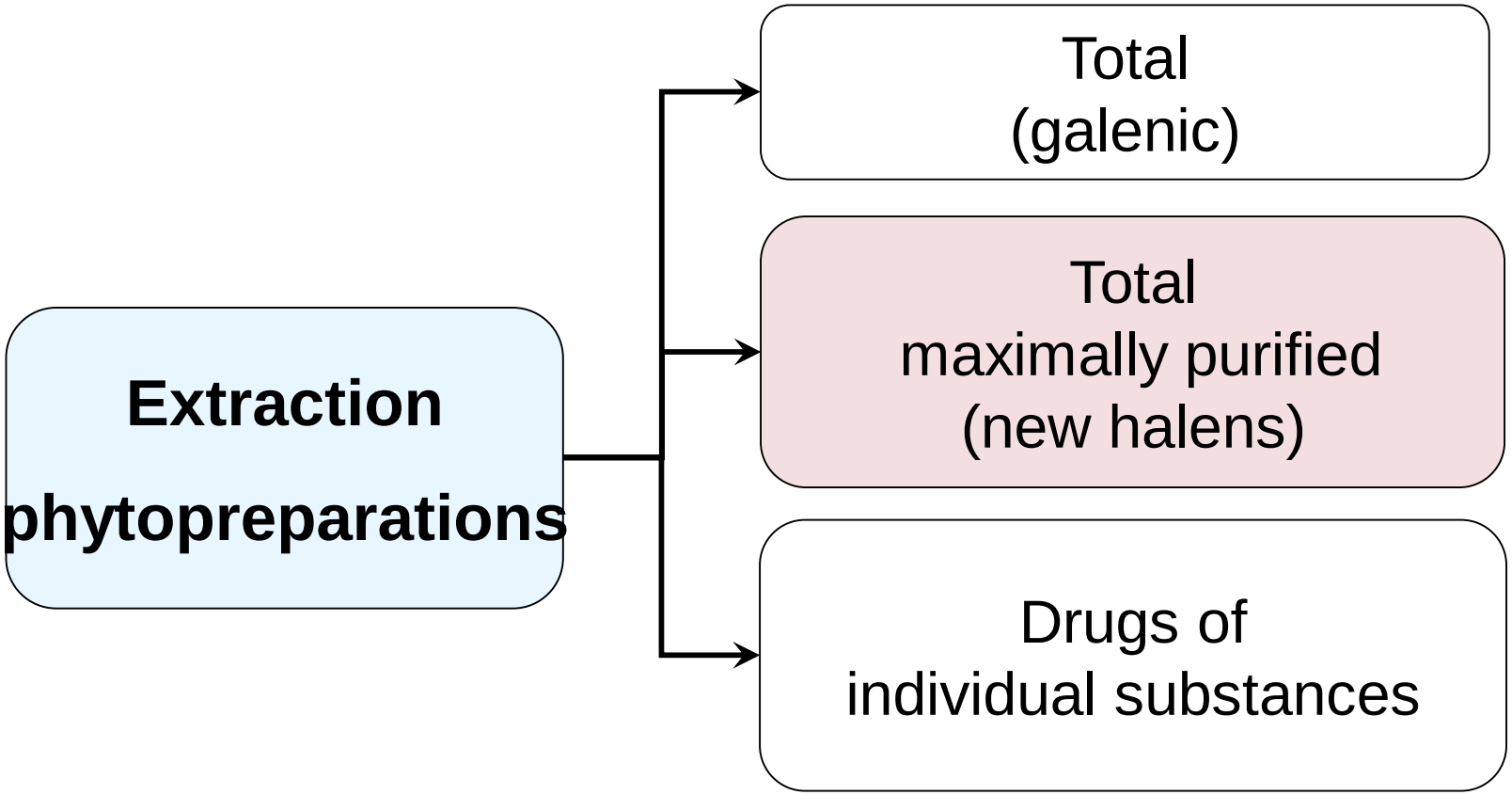
The most purified preparations from medicinal plant raw materials. Technological scheme of production. Methods of purifing. Nomenclature. Phytopreparations of individual substances.

Lecture for 4th year students of the Institute of Pharmacy of KSMU

Maximum purified phytopreparations

- Maximum purified phytopreparations (new halens) Is a group of herbal extractive drugs containing a complex of active substances in their native (natural) condition, free from ballast as much as possible.
- Highlighting maximally purified phytopreparations appeared a new direction in drug technology, the purpose of which, on the one hand, was to isolate not individual, but a complex of active substances, on the other - their maximum purification from accompanying and ballast substances.
- In pre-revolutionary Russia, there was no production of the most purified (or Neovogalenic, as they were called at the time) drugs. The country consumed only imported drugs of this group. Domestic production of highly purified drugs was established only after the Great October Socialist Revolution.

Classification of phytopreparations extraction



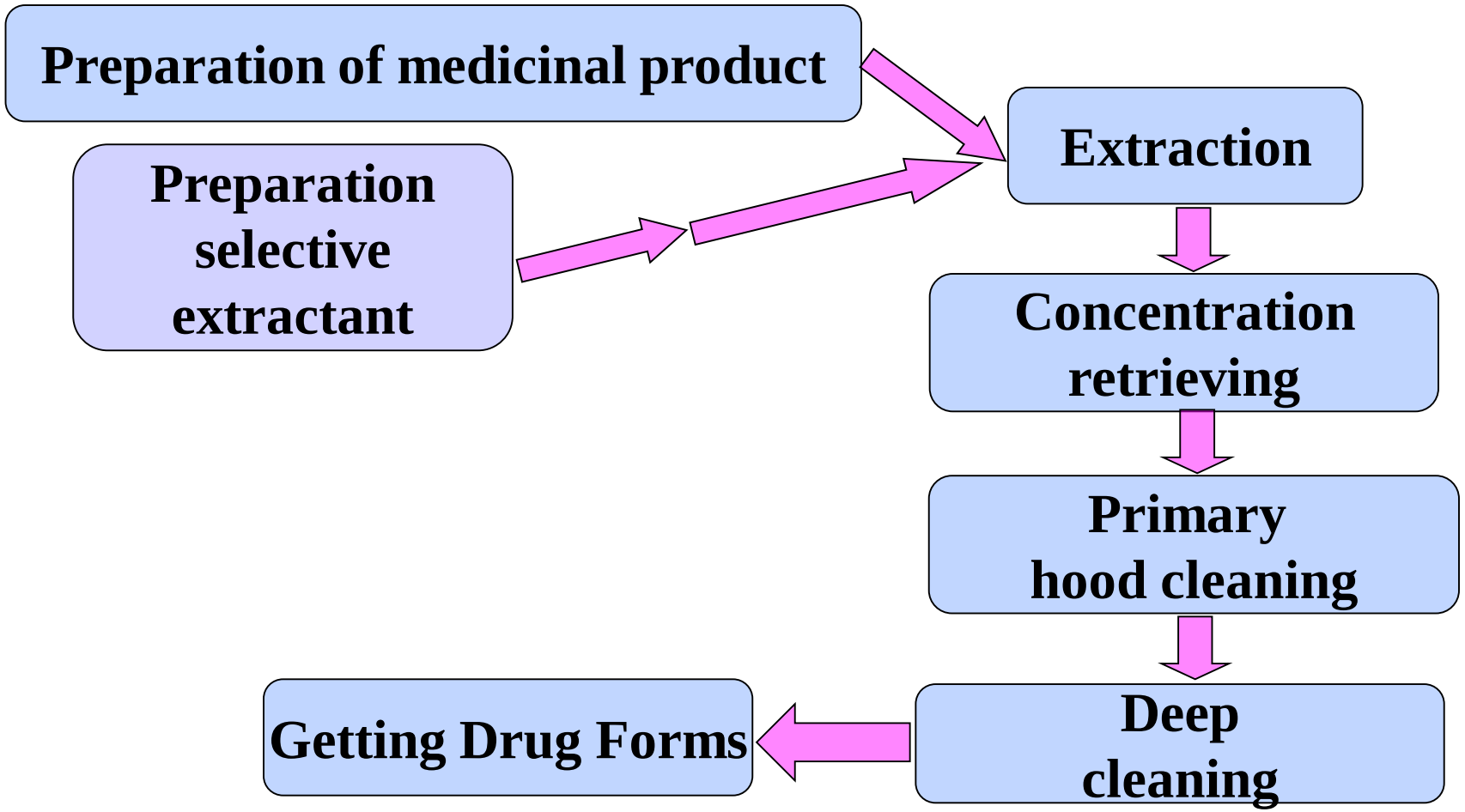
advantages

Due to deeper cleaning from related substances, Neovogalenic drugs in comparison with galenic, the following advantages appear:

- Can be used as an injection.
- Less side effects.
- Great storage stability.

Firstly the new halen drug was developed at the end XIX century in Germany. In Russia - in 1923. for the first time professor Stepun suggested the drug "Adonilen".

Technological stages of obtaining novogalenic drugs



Technological scheme of obtaining Novogalenic preparations is individual (depends on the properties of the allocated amount substances), but general technological stages can be distinguished.

Technological scheme of obtaining Novogalenic drugs

BP - 1. Sanitary preparation of production

BP - 1.1. Preparation of industrial premises

BP - 1.2. Processing equipment

BP - 1.3. Sanitary preparation of technological clothing

BP - 1.4. Sanitary training of personnel

BP - 2. Preparation of raw materials and extractants

BP - 2.1. Grinding raw materials

BP - 2.2. Preparation of extractants

TP - 3. Extraction

TP - 4. Concentration

TP - 5. Purification of concentrated extraction (obtaining a technical product)

TP - 6. Concentration and (or) drying

TP - 7. Standardization

UMO - 8. Packing, packaging, marking

PO - 9. Waste processing

Extraction methods used in the technology of novogalenic drugs

- Countercurrent extraction;

- multi-stage countercurrent extraction (repercolation);
- continuous countercurrent extraction.

- Circulating extraction;
- Fractional maceration according to the counterflow principle;
- Maceration with circulation extractant;

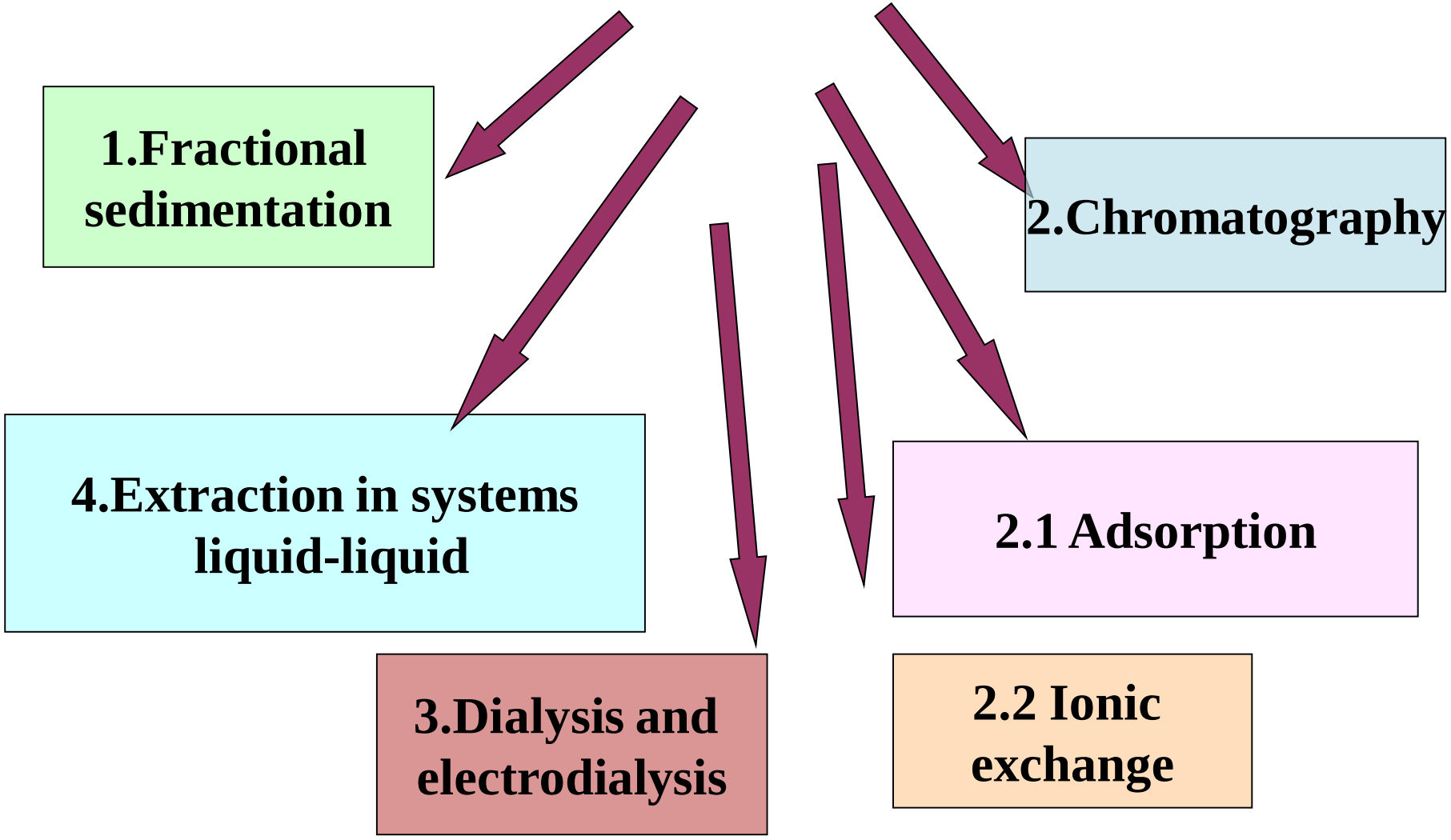
Intensification of this methods of the extraction process is widely used

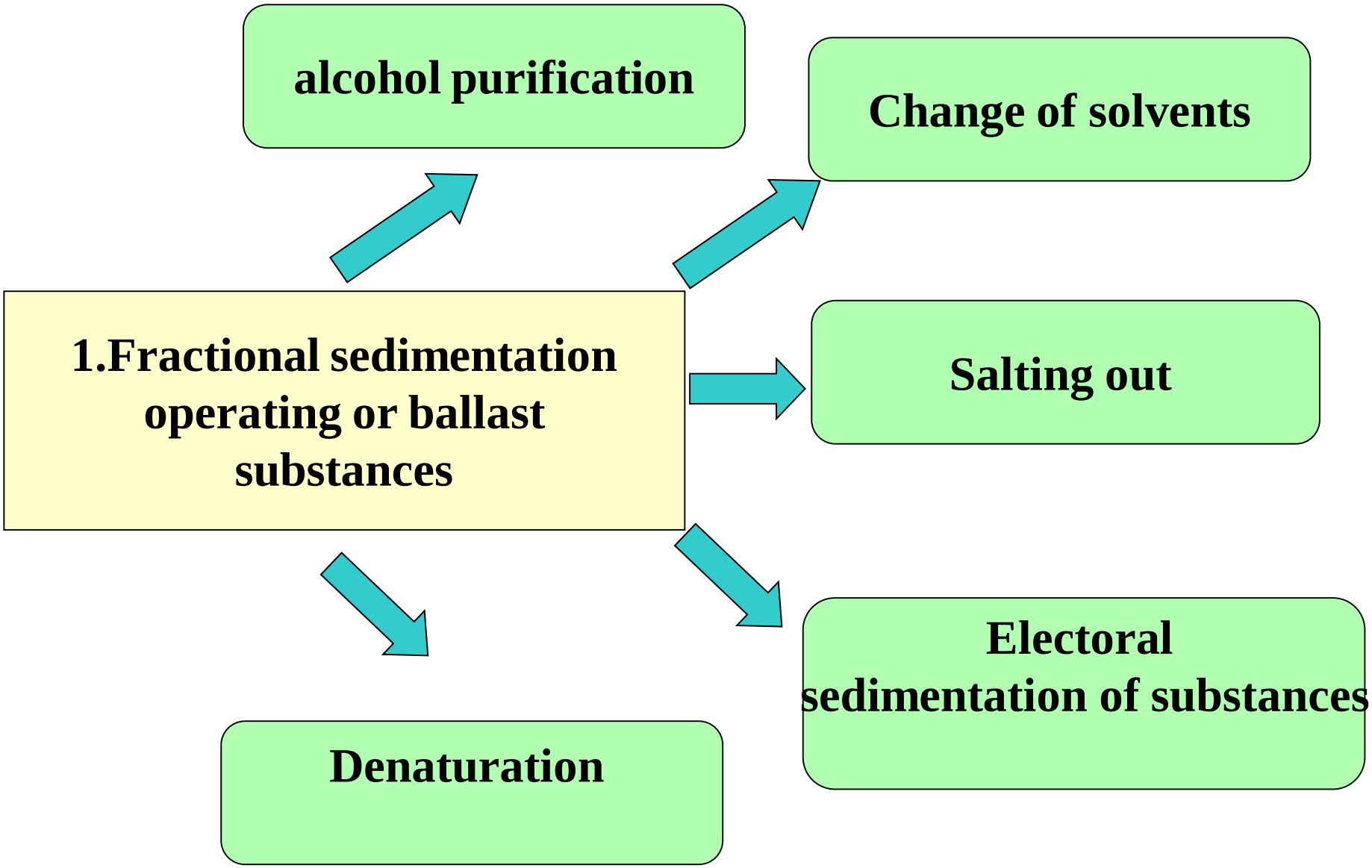
Purification of concentrated extraction and obtaining a technical product.

For purification of the obtained extracts from accompanying substances and the isolation of the required amount of substances have found a wide variety of techniques and methods. The following methods are most widely used:

- Fractional deposition of biologically active substances or related substances.
- Dialysis and electrodialysis.
- Liquid extraction.
- Chromatography.
- Ion exchange
- adsorption

Extraction cleaning methods in the technology of obtaining newgalenic drugs




alcohol purification
Change of solvents
1.Fractional sedimentation operating or ballast substances
Salting out
Electoral sedimentation of substances
Denaturation

Liquid extraction can be:

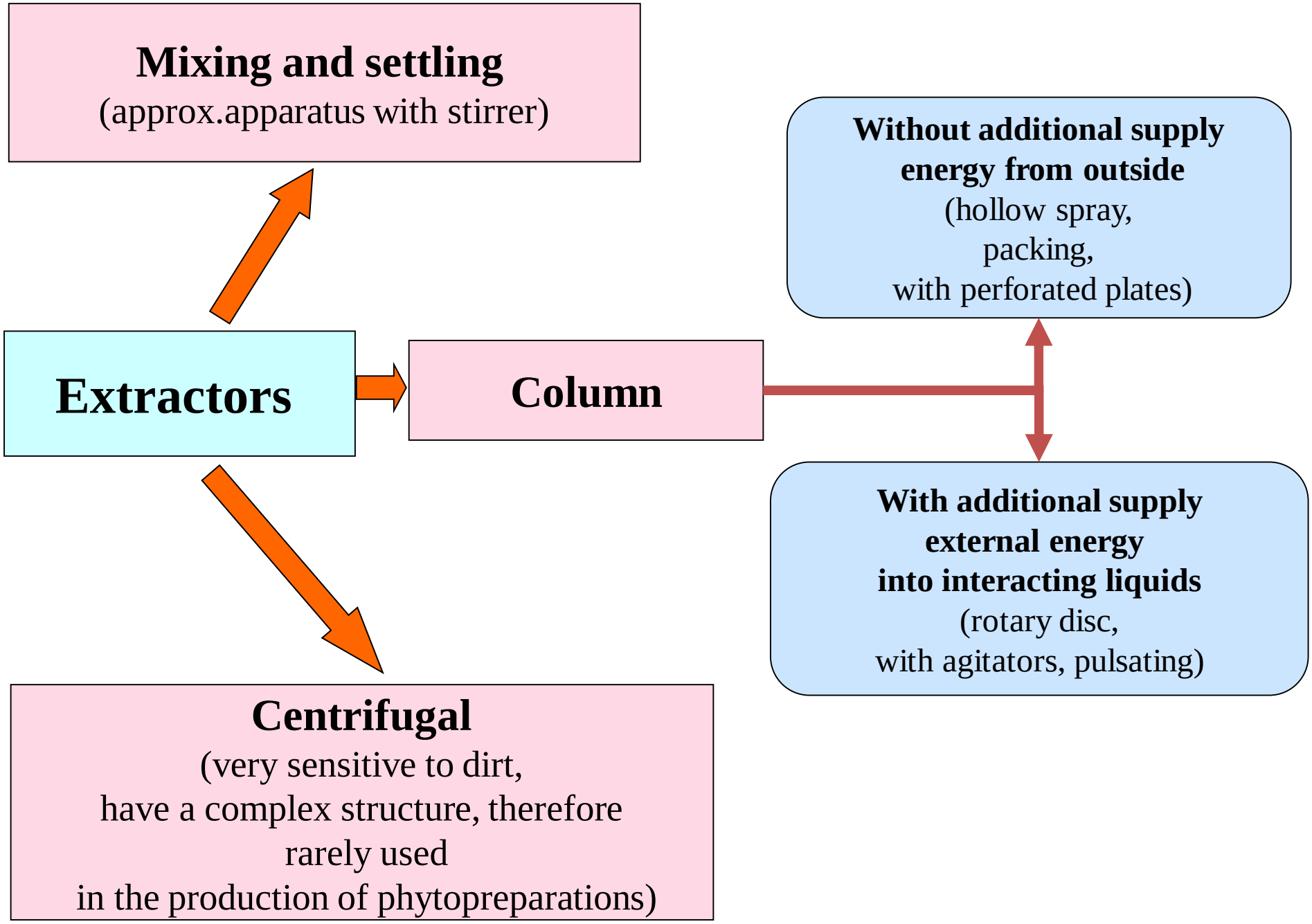
- Stepped (graduate).

Staged extraction can be single-stage (one apparatus) and multi-stage (several apparatus); Besides , it can be direct-flow and counter-flow.

- Continuous.

The extraction process in liquid - liquid consists of the following stages: mixing the original solution with extractant to create close contact between them, the separation of the two non-miscible liquid phases, regeneration extractant, i.e., removing it from the extract and raffinate.

For extraction in liquid systems - liquid use the following main types of extractors[-], mixing and settling, columnar, centrifugal.


Mixing and settling
(approx.apparatus with stirrer)
Extractors
Column
Without additional supply
energy from outside
(hollow spray,
packing,
with perforated plates)
With additional supply
external energy
into interacting liquids
(rotary disc,
with agitators, pulsating)
Centrifugal
(very sensitive to dirt,
have a complex structure, therefore
rarely used
in the production of phytopreparations)

- **TP - 7. Standardization**... Allnew halenspreparations are standardized according to such indicators as substances obtained by chemical synthesis. Some quality indicators, in turn, depend on the consistency of the drug (liquid or solid). The main indicators are:
- - the content of the active substance;
- - solubility (if dry powder);
- - authenticity;
- - impurities;
- - residual amount of organic solvent;
- - pyrogenicity (if the drug is intended for an injection route of administration);
- - microbiological purity or sterility (depending on the purpose of the drug).
- **UMO - 8. Packing, packaging, marking.** Depends on the type of drug (liquid or dry) and is preliminary, since LF is subsequently made.
- **PO - 9. Waste processing.** As a rule, it consists in the recovery of ethyl alcohol and other organic solvents.

Obtaining dosage forms

Novogalenic drugs can be used for the manufacture of various dosage forms administered in the following ways:

- oral route of administration (tablets, granules, drops);
- rectal route of administration (suppositories, rectal ointments);
- injectable route of administration (solutions in ampoules).
-

Examples of Novogalenic drugs

Adonisid - liquid new halen a preparation from the spring adonis containing the sum of cardiac glycosides of the adonis spring.

Biroxan - liquid new halen parsnip preparation containing the amount furocoumarins...

Mukaltin - dry new halen marshmallow herb preparation containing the amount of polysaccharides.

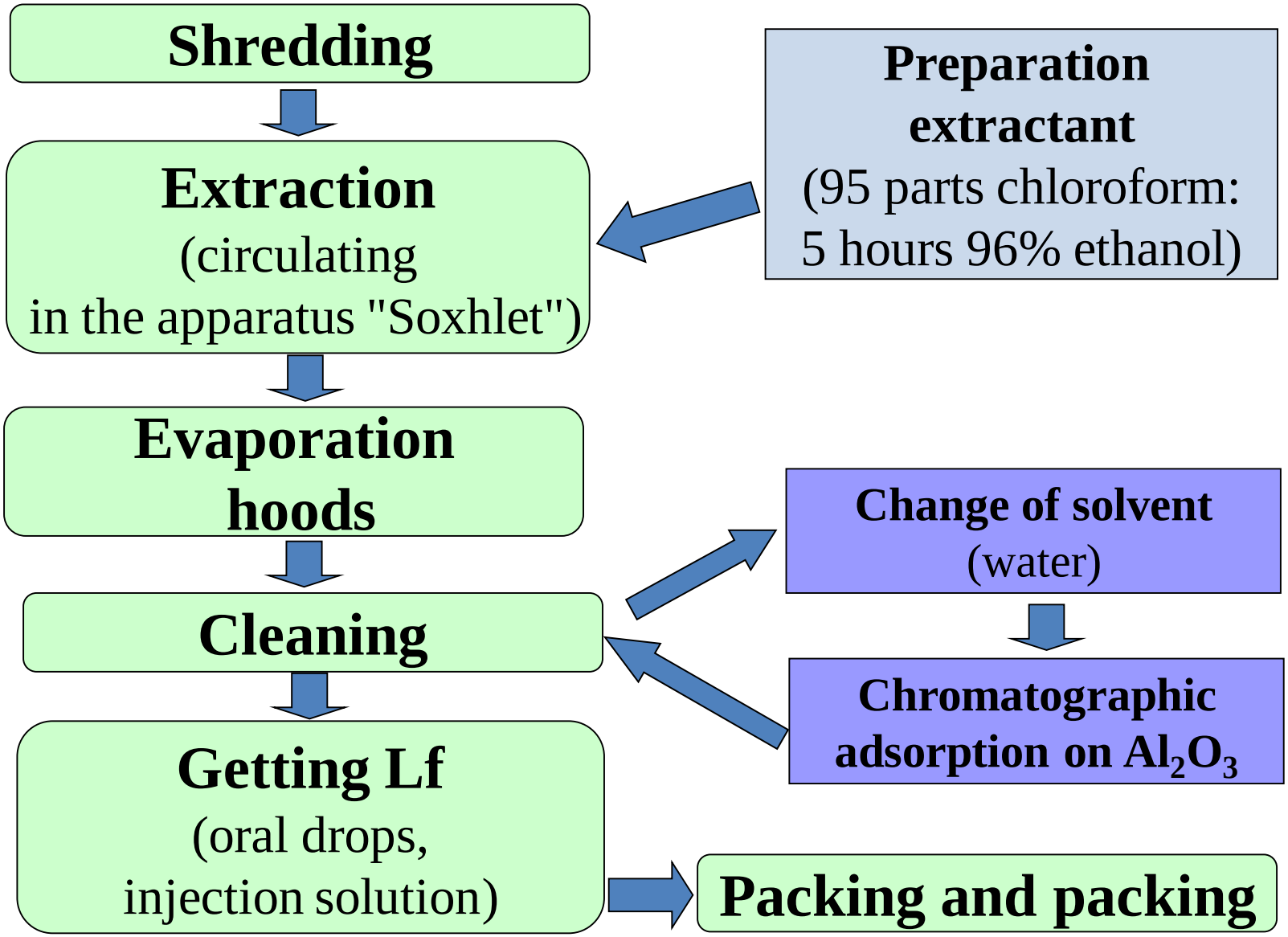
Plantaglucid - dry new halen a preparation from the leaves of the large plantain, containing the sum of the polysaccharides of the plantain large, etc.

Raunatin - dry new halen rauwolfia root preparation serpentinecontaining the sum of rauwolfia serpentine alkaloids.

Flamin - dry new halen preparation of immortelle flowers sandycontaining the sum flavonoid sandy immortelle compounds.

Chlorophyllipt - liquid new halen a preparation from eucalyptus leaves containing the amount of chlorophylls.

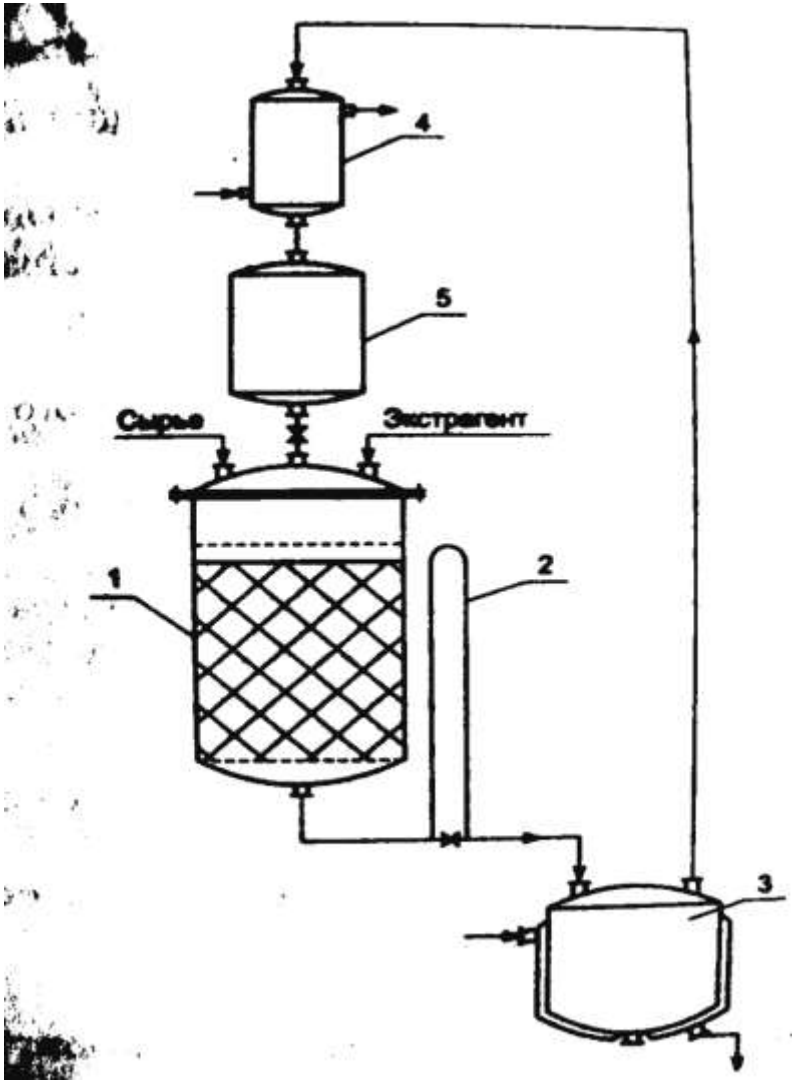
Technological stages of obtaining adonizide



Circulating extraction in the Soxhlet apparatus

- multiple extraction with one portion of the volatile extractant of one portion of raw materials

1 - extractor
2 - siphon
3 - evaporator
4 - capacitor
5 - condensate collector



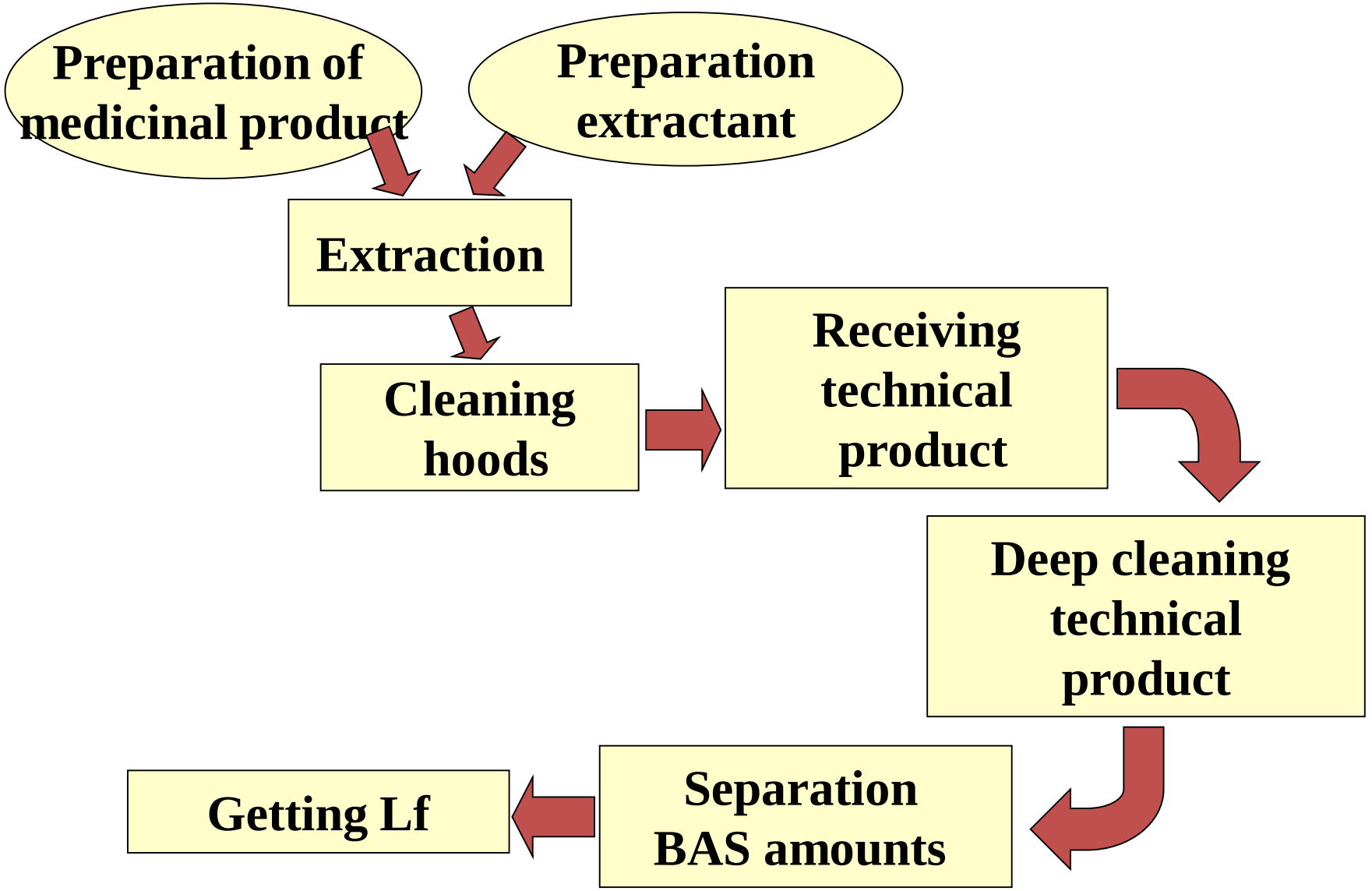
Classification and nomenclature of phytopreparations of individual substances

Alkaloids preparations
raunatin, vinblastine, aymaline, ergometrine

Glycoside preparations
celanide, strophanthin-K, digitoxin, digogsin

Preparations of other groups
rutin, glyceram, alpizarin

Technological stages of obtaining drugs individual substances



Technological scheme of obtaining preparations of individual substances

BP - 1. Sanitary preparation of production

BP - 1.1. Preparation of industrial premises

BP - 1.2. Processing equipment

BP - 1.3. Sanitary preparation of technological clothing

BP - 1.4. Sanitary training of personnel

BP –2. Preparation of raw materials and extractant

VR-2.1. Grinding raw materials

VR-2.2. Preparationextractants

TP - 3. Extraction (obtaining extraction)

TP - 4. Concentration of extraction

TP - 5. Purification of extraction and production of technical product

TP - 6. Purification of technical product (isolation of individual substances)

TP - 7. Standardization

UMO - 8. Packing, packaging, marking

PO - 9. Waste processing

TP - 5. Purification of technical product (isolation and separation of individual substances)...

IN As a result of the purification step, a solution of individual substances is obtained in any solvent with a minimum content of related substances (technical product).

The extract purified at the previous stage is evaporated under vacuum at a residual pressure of 6666.1-10665.76 N / m^2 and a total preparation is obtained.

To divide the amount and isolate individual substances at the final stage, use:

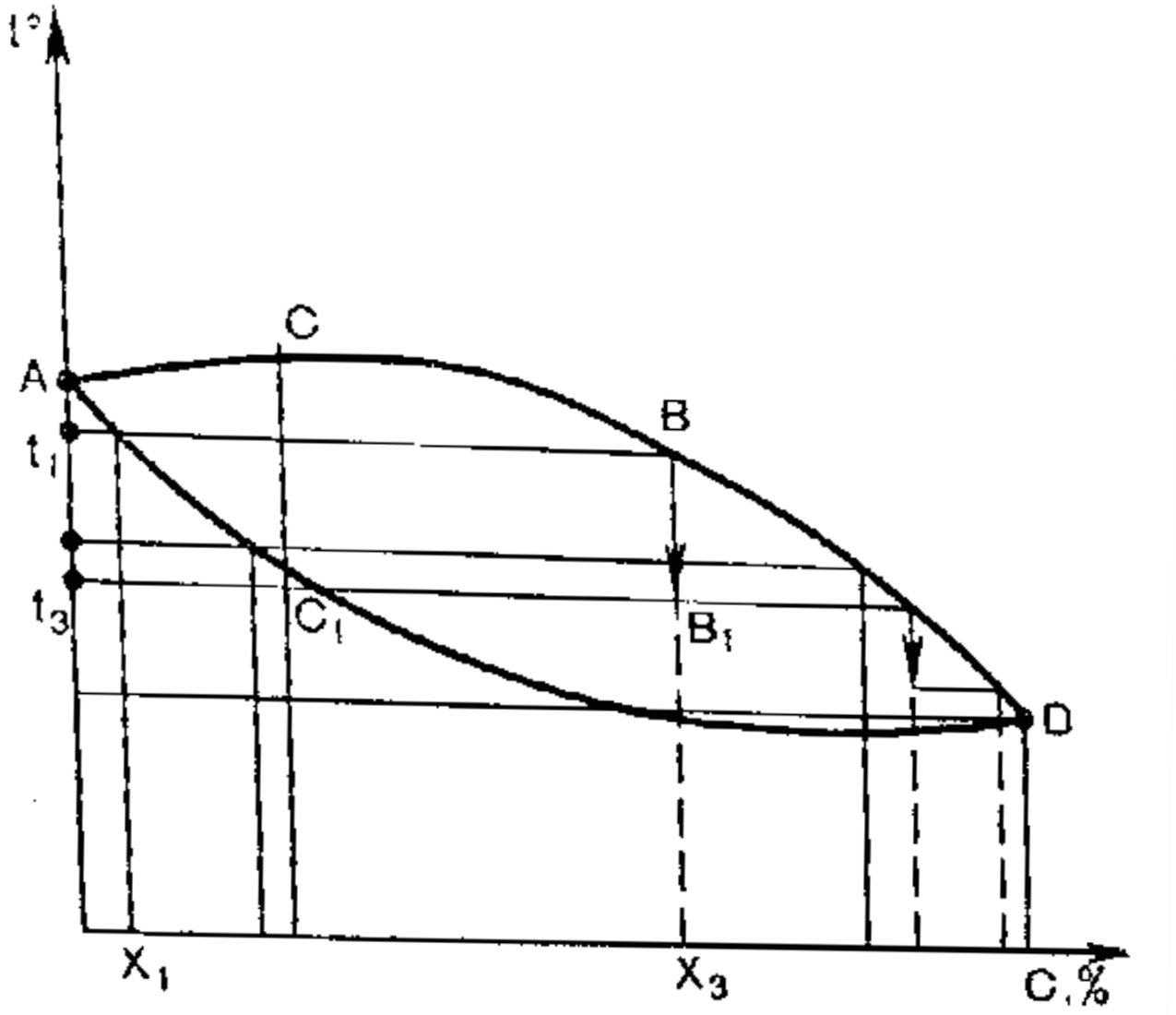
- Combination chromatographic method with crystallization.
- Combination of liquid extraction with crystallization.
- Concentration.
- Crystallization.

The final stage in obtaining individual preparations is always crystallization, which, as a rule, is carried out repeatedly, and it is called recrystallization.

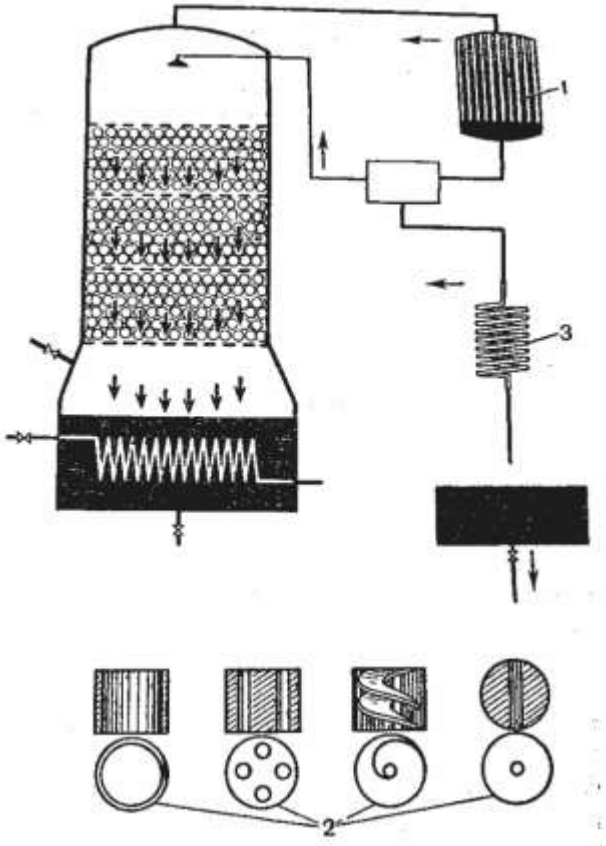
List of some individual phytopreparations
(preparations of individual substances)

Medicinal vegetable raw material	**Dedicated individual phytopreparation**	**Release form, act**
1. Foxglove leaves	Digitoxin (SG), List A	Substance, tablets 0.1 Candles 0.15 (cardiotonic act)
2. Leaves of foxglove woolly	Digoxin (celanide), SG, list A	Substance, tablets 0.1 0.25mg, 0.025% solution in ampoules (cardiotonic action)
3. Ergot horns	Ergotamine hydrotartrate, list A (alkaloid)	Dragee 1mg ampoules 0.05 - 1 ml, solution in bottles 0.1 - 10 ml. Uterotonic drug
4. Ergot horns	Ergometrine maleate, list B (alkaloid)	Substance, 0.2 mg tablets; 0.02% - 1ml in ampoules (uterotonic a drug)
5. Buckwheat herb (Japanese Sophora flowers)	Rutin (flavone)	Substance, packages - 1g. Tablets 20mg. P - vitamin activity, included in the preparationAscorutin
6. Grass glautium (yellow ball) 7. Cinchona bark	Glaucina g / chloride, sp. B (alkaloid) Quinine salts (sulfate, g / chloride, dihydrochloride, iodine bismuthate)	Substance, tablets 50 mg (antitussive drug) Substance, tablets, ampoules Antiplasmodic a drug

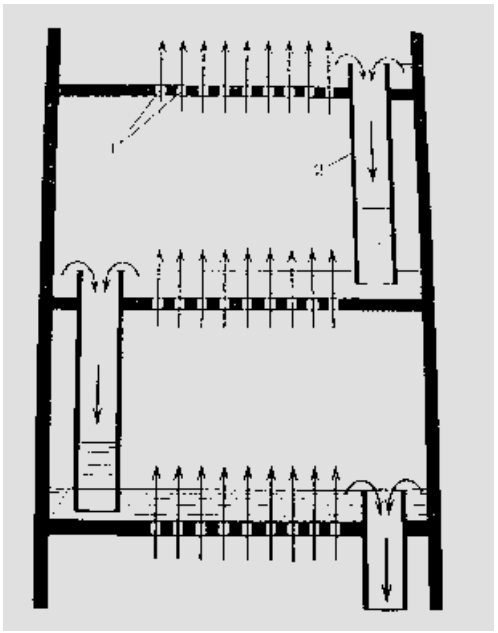
Composition-properties diagram



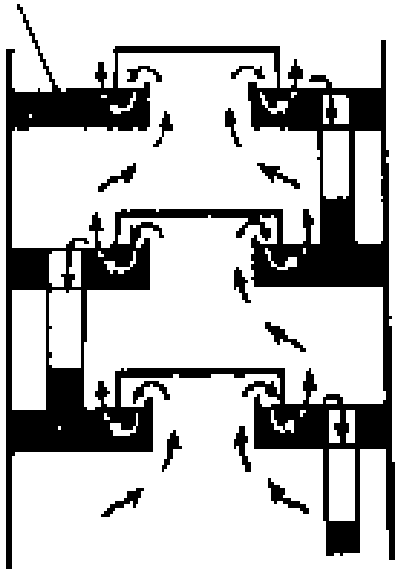
Distillation columns



Rectification plant
with packed column



Bubble, sieve
column



Bubbling, cap column