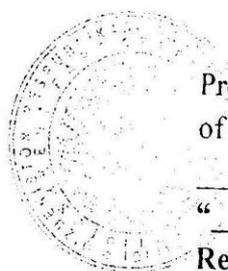


MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN

TASHKENT PHARMACEUTICAL INSTITUTE



«APPROVED»

Pro-rector on educational process
of the institute c.pharm.science,

S.U. Aliev

S.U. Aliev

“ ” 2017

Record №

“PRODUCTION OF MEDICINAL PREPARATIONS”

Education-methodical manual for laboratory lessons
for the students of the third course faculty “Industrial pharmacy”

Part I

Tashkent – 2017

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Education-methodical manual was discussed and approved at the meeting of CMC of the Institute (record № 5 from “5” 01. 2017.) and Academic council of the institute (record № 6 from “10” 01. 2017)

Scientific Secretary, assistant professor:



A handwritten signature in black ink, appearing to read "Khaydarov V. R.", written over a horizontal line.

Khaydarov V. R.

INTRODUCTION

Industrial production of medicinal preparations became the choiceless method of mass provision with available medical aid for population of industrially developed countries. Share decreasing of individual production of medicinal preparations according to physicians' prescribing naturally increases the role of industrial provision with available medicinal means the population of any country. Extract preparations are the most spread medicinal means that is why mastering the principles, technologies and study the equipment for production, quality control of these medicinal forms are always topical when training specialists.

Educational material is given according to logical structure of the theme: objective of the lesson, ability and skills, which must be acquired after doing the tasks, information material, control questions to find out the students' initial level of knowledge and methodical recommendations for carrying out practical tasks. For consolidation students' knowledge on each theme control questions which can be used in conduction seminars are given.

In this section in detail are given theoretical extraction processes, description and principal nomenclature of the produced tinctures and extracts, methods of their preparing, basic methods of purification, technological and instrument production schemes.

In appendix there are general pharmacopoeia articles, technological and instrument production schemes of medicinal forms of industrial production, tests for self-control, creative tasks for students.

**THEME: OINTMENTS AND THEIR INDUSTRIAL PRODUCTION.
TECHNOLOGY FOR PREPARING DICLOFENAC SODIUM**

Objective. Ointment – is a soft medicinal form intended for application to skin, wounds or mucous membranes, and consisting of ointment base and medicinal agents, evenly distributed in it. In recent years there is the tendency of more wide use of medicines in the form of ointments in various branches of medicine. Ointments are widely used in *используются* ophthalmology, otolaryngology, surgery, obstetrics, gynaecology, proctology and other branches of clinic medicine. It is considerably extended the range of both medicinal substances applied in the form of ointments and auxiliary substances playing active role in displaying pharmacological properties of this medicinal form. Ointments are irreplaceable medicinal form for external use and form 15-20% of extemporal formulation.

Studying theoretical bases and technologies of ointments are of great importance for practical activity of pharmacist-technologist. Knowledge and skills, acquired by students on this theme will be used during the next study of the theme “Suppositories”.

Importance of the theme. Production of soft medicinal forms (SMF) is specialized in production conditions and nowadays among finished medicinal forms they have the special place. That is why there is the need to study all necessary conditions and correctly rationalize the production of soft medicinal forms.

For conduction of this practical lesson pedagogical technological method

«MILL» is used

<i>Nº</i>	Name of medicinal substances	Soft medicinal forms		
		Ointment of zinc oxide	Streptocide ointment	Xeroform ointment
1	Zinc oxide			
2	Vaseline			
3	Xeroform			
4	Streptocide			
5	Lanolin			
6	Sulphur			
7	Mercury			
8	Boron			
9	Starch			
10	Camphor			

Situational tasks and theoretical questions

1. Give definitions to soft medicinal forms and their importance in production.
2. Comparative assessment of soft medicinal forms.
3. What bases are used for ointments production?
4. Technology characteristics of ointments production.
5. Classification of ointments on disperse phase.
6. Preparation technology of creams and paste and their application.
7. Technology characteristics of gels production.
8. Calculate consumption coefficient 40.0 g of 10 000 packings of soft medicinal form having total loss of 3.2%.

Ointments consist of a base and medicinal agents evenly distributed in it. Besides, ointments can comprise other auxiliary substances: stabilizers, antioxidants, preservatives, SAS, absorption activators and etc.

Nowadays in the form of ointments are used medicinal substances, related practically to all pharmacopoeia groups.

1. Classification of ointments

Ointments are classified according to different features:

Depending on purpose and application ointments are divided into: 1) dermatological (derma - skin): medical, protective, cosmetic; 2) ointments applied to mucous membranes: nose, eyes, rectum, mouth cavity, vagina (correspondingly – nasal, ophthalmological, rectal, stomatological, vaginal ointments); 3) ointments for curing wounds– surgical and burn.

According to the action ointments can exert local and resorption action, i.e. penetrate deeply into the skin под or mucous membranes, reach blood stream and have general action to the body.

According to disperse system type ointments are divided into homogeneous, i.e. smooth not having separation surface between medicinal agents and the base, and heterogeneous, being two- or multi-phase systems.

According to consistency ointments are divided into pastes, ointments, creams, gels, liniments.

1. Description of ointments as disperse systems

Taking into consideration distribution type of medicinal substances in the base and base origin, ointments are divided into two groups: homogeneous and heterogeneous.

Homogeneous ointments consist of inter-soluble, mixing ingredients and divided into: ointments-solutions, ointments-alloys, extraction ointments.

Ointments-solutions are formed in dissolution of camphor, menthol, phenyl salicylate and other liposoluble substances in lipophilic bases – Vaseline, wax, lanolin, or water-soluble substances – novocaine, dimedrol, ephedrine hydrochloride in hydrophilic bases (gels MC, PEO, Na-CMC and etc.). Concentration of medicinal substance must not exceed the limit of its solubility in this base. The example is camphor ointment 10% on hydrophobic base with composition of: Vaseline (54%), paraffin (8%), lanolin waterless (28%).

Ointments-alloys are obtained by alloying hydrocarbons, fats, resins, waxes and etc. They include spermaceti ointment, naphthol ointment with composition of: naphthol oil (70%), paraffin (18%), and petrolatum (12%).

Extraction ointments are obtained by extraction with vegetable oil of medicinal plant raw material further thickening with aerosil, wax, paraffin, lanolin waterless up to necessary consistency.

Heterogeneous ointments are divided into suspension, emulsion, combined. Suspension ointments include medicinal agents, soluble neither in the base nor in water. Examples are: zinc oxide ointment 10%, methyluracyl ointment 10%, streptocide ointment 10%, sulphur ointment 33% and etc.

In suspensions form are introduced water soluble medicinal substances, prescribed in the amount of more than 5%; substances are decomposed in presence of water (penicilin and etc.), and also zinc sulphate, resorcin (except eye ointments).

Emulsion ointments are characterized by presence of liquid disperse phase not soluble in the base. As disperse phase can be both liquids (tinctures, hydrogen peroxide, Burov's liquid, adrenaline hydrochloride and etc.), and solutions of

medicinal substances (salts of alkaloids and etc.). Such substances as collargol, protargol, plant extracts are surely introduced into ointments in the form of water solutions, or they don't exert therapeutic effect. The example of emulsion ointment is «Calendula» ointment with composition of: Calendula tincture 10.0, emulsion consistency water / Vaseline 90.0.

Combined ointments contain different in their nature medicinal and auxiliary substances. When prepared them the principles for preparing ointments of individual types are followed.

Characteristics of industrial production of ointments:

- 1) Multi-tonnage;
- 2) Possibility of using bases' complex compositions (up to 12 components);
- 3) automation and mechanization of production;
- 4) high quality of produced products.

Control for realization of production is carried out at each technological stage that promotes increasing the quality of released products, prevents material losses.

Production of ointments in pharmaceutical conditions consists of the following stages:

- preparing medicinal substances and the base;
- introducing medicinal substances into the base;
- homogenization of ointment;
- prepacking, packing, labeling.

Preparing medicinal substances is in their grinding, sifting, mixing, if it is necessary. For this purpose grinders of different construction, sieve mechanisms, mixers are used.

Preparing of base include processes of dissolution and alloying of its components with further filtration. Melting bases and their components /Vaseline, lanolin, wax and others are melted in electro-boilers or boilers with steam jacket, with the help of steam needle or electro-panel. Filtration of bases is carried out through the druck-filters.

When prepared emulsion bases SAS are introduced into the phase where it is more soluble. Emulsifying is carried out in the reactor with mixer or nitrogen-burst

processing of filtered air. Introduction of medicinal substances into the base is carried out depending on their physico-chemical properties. Addition of solid medicinal substances or their solutions is carried out at gradual mixing in reactors with steam jacket or electric heating. Reactors have mixers: anchor, orbital, block-type square, which provide good mixing.

In small productions doughing machines are used.

Homogenization of ointments. When mixed large amounts of ointments in boilers often can not be tried for necessary dispersion degree of medicinal substances in ointments. That is why ointments in industrial conditions are subjected to homogenization.

For homogenization of ointments in the production burr mills, roll crusher ointment grates are used. To intensify considerably the processes of preparing emulsions, suspensions, combined ointments it is possible applying the method of RPA - rotor-pulsating apparatus. In work of RPA are combined the processes of grinding, dispersing, mixing, homogenization that leads to considerable save of time, electro energy, decreasing material losses.

Laboratory work -1

10% ointment of zinc oxide

Unguentum Zincci oxydi 10%

Task

1. Prepare 10 g of zinc oxide ointment
2. Draw the scheme of technological process
3. Quality assesment.

Composition:

Zinc oxide - 10.0 g

Vaseline - 90.0 g

Devices and auxiliary materials

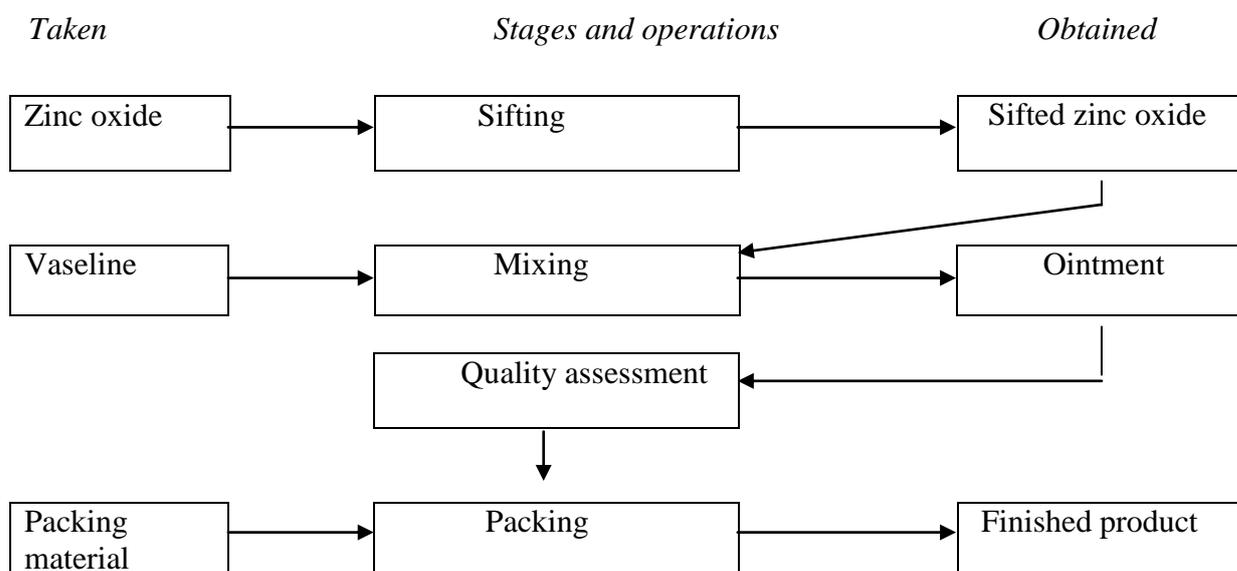
1. Pin, scales and weights
2. Zinc oxide and vaseline
3. Container for finished product

4. Towel, medical gauze and soap
5. Mica, paper for label
6. Electric cooker and 50-100 mcm sieves

TECHNOLOGICAL PROCESS

Zinc oxide is taken (beforehand sifted through 100 mcm sieve) in required amount and in the mortar little by little triturated with Vaseline (10-20 g) using a pestle up to obtaining white mass. Finished product is assessed according to appearance and packed in the beforehand prepared container.

SCHEME OF TECHNOLOGICAL PROCESS



ANALYSIS OF FINISHED PRODUCT

Description of finished product. Ointment of white light-white colour.

Authenticity. To 0.5 g of ointment is added 2 ml of diluted hydrochloric acid, heated when mixed. After cooling 8 ml of water is added and filtered. Filtrate gives quality reactions to zinc (SP XI 1-volume, p.165.)

Quantitative determination. 0.3-0.5 g of ointment in 100 ml flask is taken, added 5 ml of diluted hydrochloric acid, 25 ml of water and heated within 5 minutes. Then it is cooled and neutralized with 1 drop of red methylene. Добавляем 10 ml of chloroform, 5 ml of ammonia buffer solution are added and titrated with c 0.05 mole/l trilon B solution up to appearing dark blue colour in water layer (indicator acid erychrome black). 1 ml of 0.05mole/l of trilon B solution

corresponds to 0.004069 g of zinc oxide. Ointment should include 9.5-10.5% of zinc oxide.

Packing. It is packed in glass dark cups and tubes.

Storage. In dry and cool place.

Application. It is applied as drying remedy in skin diseases.

Laboratory work - 2

10% streptocide ointment

Unguentum Streptocidi 10%

Task

1. Prepare 100 g of 10% streptocide ointment
2. Draw the scheme of technological process
3. Quality assessment.

Composition:

Streptocide - 10.0 g

Vaseline - 90.0 g

Devices and auxiliary materials

1. Pin, scales and weights
2. Zinc oxide and Vaseline
3. Container for finished product
4. Towel, medical gauze and soap
5. Mica, paper for label
6. Electric cooker and 50-100 mcm sieves

TECHNOLOGICAL PROCESS

In the beforehand heated mortar grinded streptocide is triturated by parts with 5-6 g of Vaseline up to obtaining homogeneous mass. Finished product is assessed according to quality parameters and packed.

ANALYSIS OF FINISHED PRODUCT

Description of finished product. White or yellowish ointment.

Authenticity. 0.5 g of ointment with 10 ml of water within 10-15 min is heated

on water bath, cooled and filtered. Filtrate gives quality reactions to streptocide (SP X. p.646).

Quantitative determination. 3.0 g of ointment (accurate sample) in flat-bottomed flask is heated with the help of diluted hydrochloric acid 4 times by 10 min up to separation streptocide. Separated mass is cooled. Then it is filtered into 200 ml flask. Filter paper is washed twice by 15 ml of purified water. Solution is led with water up to the mark. 50 ml is taken from solution and streptocide content is determined.

Packing. It is packed by 50 g in glass dark cups and tubes.

Storage. In dry and cool place.

Application. It is applied as antiseptic remedy in skin diseases.

SCHEME OF TECHNOLOGICAL PROCESS

See laboratory work - 1.

Laboratory work -3

Diclofenac sodium ointment

Unguentum Diklofenaki natrii

Task

1. Prepare 10 g of Diclofenac sodium ointment
2. Draw the scheme of technological process
3. Quality assessment.

Composition:

Diclofenac sodium (100% according to dry residue, BP)	- 3.0 g
Glycerine (PA 42-Uz-0035-2007, SSt 6824-96)	- 8.0 g
Propeleneglycole (TPA 42-1594-86, BP)	- 7.5 g
High-purity 96% ethyl alcohol (SSt 5962-67, PA 42-Y3-0171-2010)	-8.0 g
Carbopol 934 P, 974 P, EP	- 1.0 g
Menthol or racemic menthol (SPX, p.387 PA 42-1866-90, USA P, EP)	- 0.5 g

15% ammonia solution (SSt 3760-79)	- 0.6 g
Formaldehyde solution (SP P, p.628)	- 0.1 g
Purified water (PA 42-Uz-0511-2007)	-up to 100.0 g

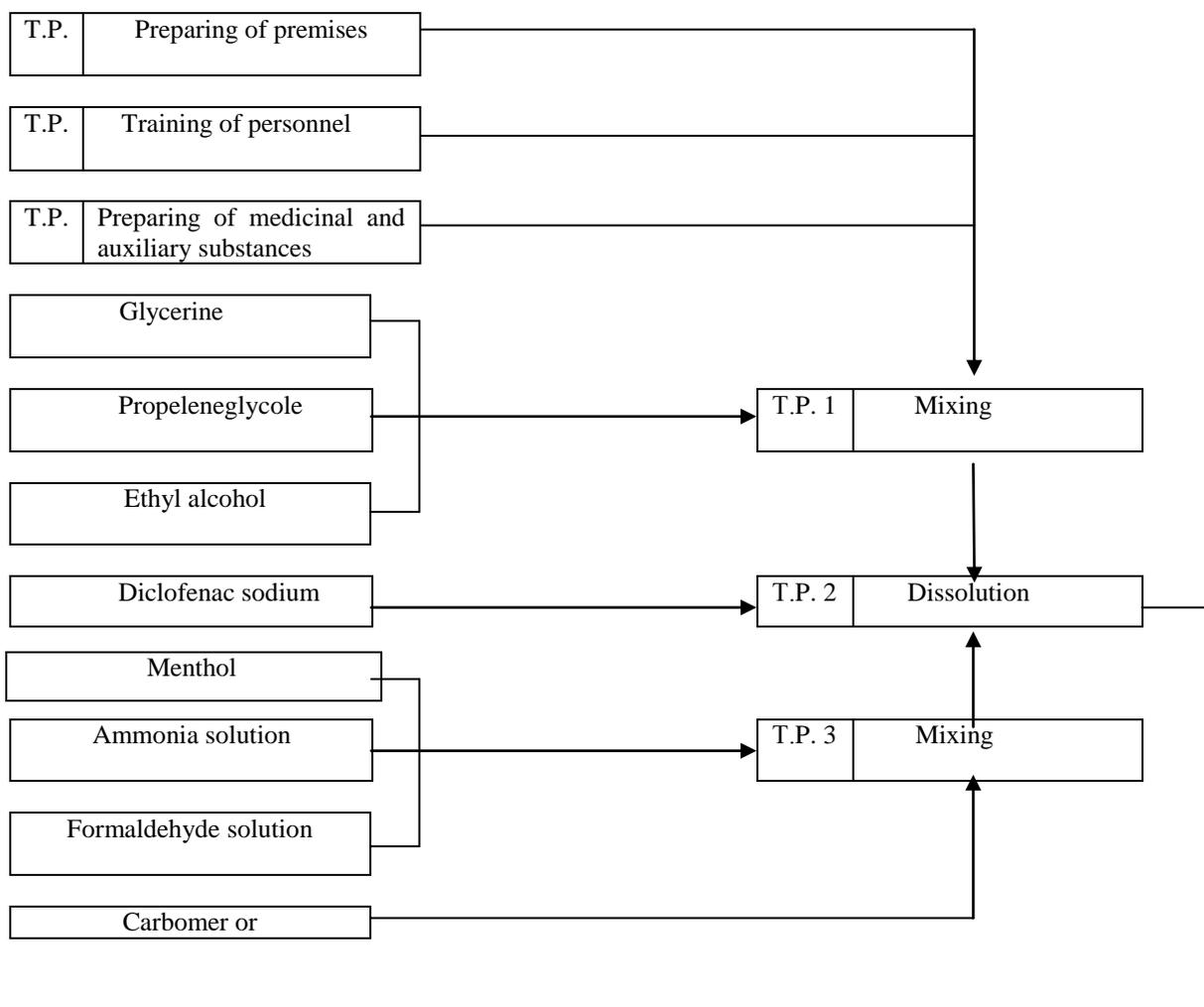
Application: 15% ammonia solution is prepared from concentrated ammonia solution (SSt 3760-79).

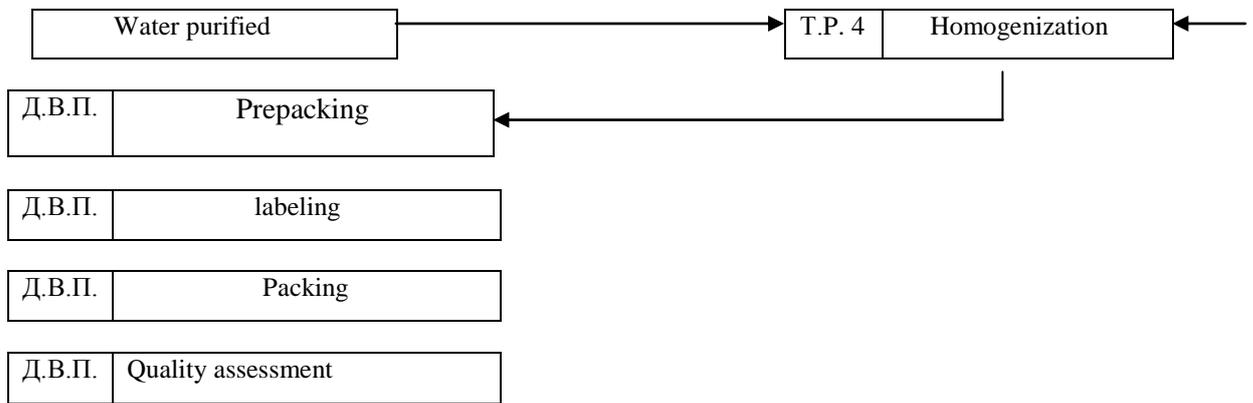
TECHNOLOGICAL PROCESS

Preparations of the first suggested diclofenac sodium ointment was carried out in ointment series production of JV «REMEDY GROUP».

To prepare the ointment glycerine, propeleneglycole and ethyl alcohol are taken in necessary amounts, mixed thoroughly and dissolved diclofenac sodium in it. In separate container are mixed solutions of menthol, ammonia and formaldehyde and added into diclofenac sodium solution. The mass is transferred to homogenizator and homogenized with carbomer and purified water.

SCHEME OF TECHNOLOGICAL PROCESS





THEME: SUPPOSITORIES AND THEIR INDUSTRIAL PRODUCTION.

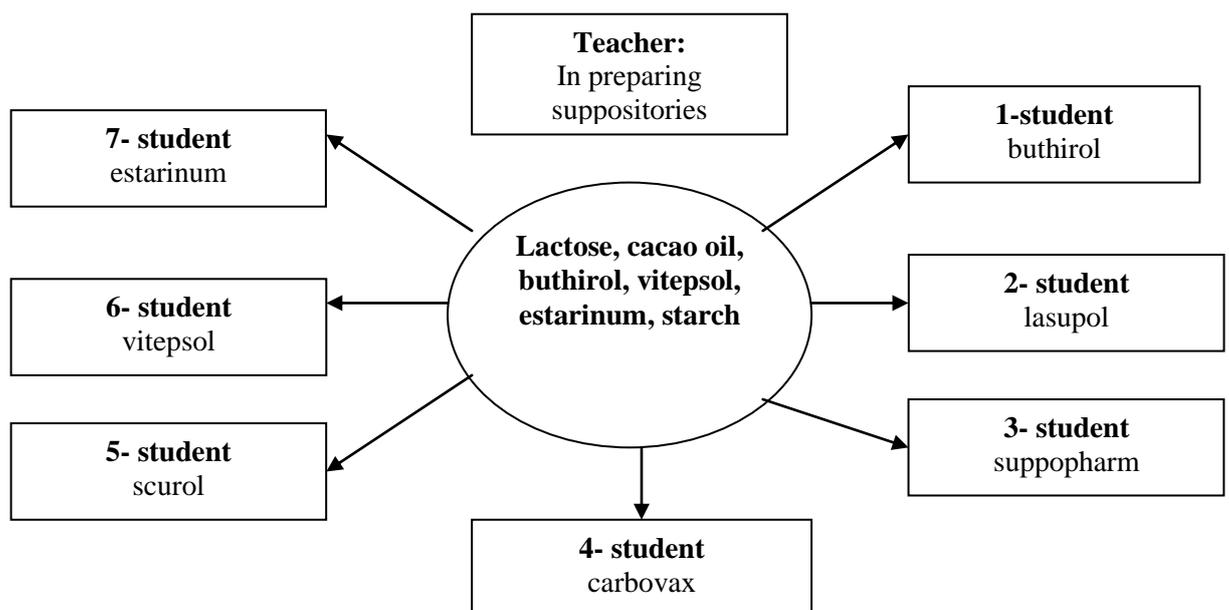
TECHNOLOGY FOR PREPARING DICLOFENAC SODIUM

SUPPOSITORIES

Objective. Learning of preparation technology and quality assessment methods of suppositories.

Importance of the theme. On the account of wide spectrum of action and rate, and also simplicity of use suppositories have special importance among finished medicinal forms. Correct organization of production of suppositories in industrial conditions can completely provide the necessity in this medicinal form.

For conduction practical lessons pedagogical technology «A pen is on the table»



Theoretical questions

1. Give definitions to suppositories and their importance in production
2. Advantages and disadvantages of suppositories among other finished medicinal forms
3. Classification of suppositories according to application
4. Classification of suppositories according to disperse system
5. What are the requirements for suppositories?
6. Bases for preparing suppositories and their classification
7. Methods of introduction medicinal substance into suppository base.
8. Quality assessment of suppositories according to the requirements of SP.

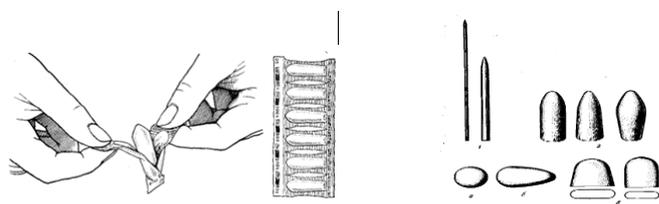


Fig.1. Types of suppositories

Suppositories – are single medicinal preparations for rectal application which have solid consistency at room temperature and melt at body temperature.

Suppositories are intended for rectal (suppositories), vaginal (pessaries, pellets) and other ways of use (rods).

Advantages of suppositories as medicinal form:

- ingress of medicinal substances directly into the general blood stream. Substance in rectal not too deep introduction of suppository passes through venous and lymphatic systems of small pelvis and, passing liver, enters blood circulation. For all that inactive action of digestive juices is eliminated. In the result in the form of suppositories can be introduced the substances damaged by digestive juices;

- high absorption rate of many medicinal substances (MS) which in some cases can be equal to the rate of entering the general blood circulation during injection;

- decreasing of allergic degree of preparation action;

- decreasing or disappearing side effect of MS;

- self-sufficiency of absorption effect on filling digestive tract;

- introduction of substances having unpleasant organoleptic properties, incompatible in other medicinal forms;

- it is noted high efficiency of use of suppositories in pediatry, geriatry, in damages of liver, digestive tract system, impairment of swallowing processes, absorption, in toxicosis of pregnant women;

- simplicity and painlessness of introduction the preparation, absence of bringing in infection;

- possibility of combining in suppositories of ingredients with different pharmacological and physico-chemical properties;

- compactness of medicinal form;

- availability of production;

- rectal introduction do not require special instruments and carried out without damaging skin layer.

Disadvantages:

- instability at storage;

- laboriousness in production;

- discomfort in use.

Depending on introduction ways there are:

Rectal suppositories (Suppositoria rectalia) can have the form of:

- cone, cylinder with acute end, different form with maximum diameter of 1.5 cm.

Vaginal suppositories (Suppositoria vaginalia) can have the form of:

- spherical (pellets, globules), oval (ovuli), in the form of flat body with round end (pessaries).

Rods (Bacili) have the shape of cylinder with acute end and not larger than 1 cm.

- the base should be physiologically indifferent;

- the base should be chemically indifferent;

- the base must not interfere with release and therapeutic action of MS.

Pharmacopoeia requirements for suppositories

1. Homogeneity of mass (tested on lengthwise cut must not be inclusions, particles of various color, crystal tinsels, presence of air rod is permissible).

2. Similar form.
3. Solidity providing convenience of use.
4. Declination in mass from average value must not exceed $\pm 5\%$. Only two suppositories can have declination not more than $\pm 7,5\%$. Average mass is determined weighing 10 or all suppositories.
5. Melting temperature of suppositories on hydrophobic base must not exceed 37°C . If determination of melting temperature is difficult, then is determined the time of complete deformation, which must not exceed 15 min.
6. Dissolution time of suppositories prepared on hydrophilic bases must not exceed 1 hour (it is determined in water).

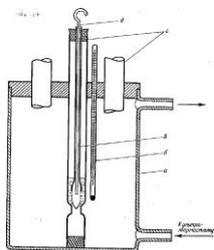


Fig.2. Device for determination the time of complete deformation of suppositories.

7. MS in suppositories must be dispensed accurately. The rule of high single and daily doses for internal application of substances according to letters A and B is spread.
8. Preparations for rectal application according to microbiological purity of SP are related to 3A category and must include in 1 g or 1 ml not more than 1000 aerobic bacteria and 100 fungi in absence of *Escherichia coli*.

Suppository bases. Requirements for suppository bases. Classification.

Requirements for suppository bases are substantiated from biopharmaceutical point of view:

- temperature of melting or dissolution of the base must be close to human's body temperature;

According to water bases are classified into:

- hydrophobic;

- hydrophilic;
- diphilic.

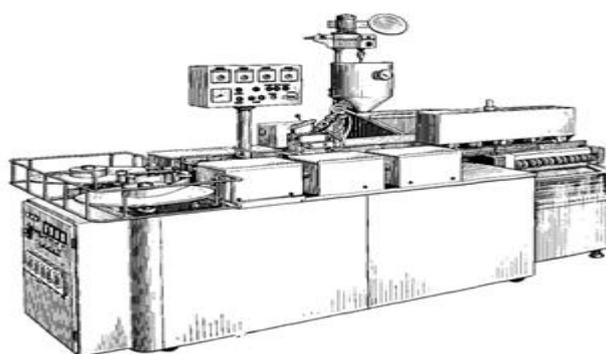


Fig. 3. Device for molding and packing suppositories by molding method

Laboratory work - 1

Suppositories of Diphenhydramine hydrochloride 0.01 g

Suppositorii Dimedrolum rectali 0.01 g

Task

1. Prepare 10 pieces of 0.01 g of Diphenhydramine hydrochloride suppositories by molding method
2. Draw the scheme of technological process
3. Quality assessment.

Composition:

Diphenhydramine hydrochloride - 0.01 g

Fatty base -1.12 g up to obtaining suppositories

Devices and auxiliary substances

1. Diphenhydramine hydrochloride and fatty base
2. Scales and set of weights
3. Chemical glass, porcelain cup, water bath and molds
4. Mixture of soapy alcohol, fridge
5. Towel, medical gauze and glassware for finished suppositories
6. Device for determination of time of suppositories deformation
7. Stopwatch

TECHNOLOGICAL PROCESS

The base is weighed in necessary amount, transferred into the glass or porcelain cup, kept on water bath within 3-4 min up to dissolution of the base. Diphenhydramine hydrochloride is added into the base. Finished mixture is stirred with glass rod on water bath up to obtaining homogeneous mass. The mass is poured into beforehand prepared molds. Molds are put for 20-30 minutes into the fridge then suppositories are taken out. Before using the molds are treated with the mixture of soapy alcohol and put for 15-20 min into the fridge. Molds shouldn't be put into the freezer as can have negative effect on quality of suppositories.

Laboratory work - 2

Suppositories of Diclofenac sodium 0.1 g

Suppositorii Natrii diklofenaki 0.1 g

Task

1. To prepare 6 pieces by 0.1 g of diclofenac sodium suppositories by molding method
2. To draw the scheme of technological process
3. Quality assessment

Composition:

Diclofenac sodium - 0.1 g

Cetyl alcohol - 0.02 g

Suppository base (estarinum, vitepsol or suppocyr) - up to obtaining suppository base of 2.0 g

Devices and auxiliary substances

1. Disintegrator (volume of 3000 cm³)
2. Set of sieves with diameter of pores of 0.16; 0.25; 0.315 mm
3. Electron scales working on scale of 100 g
4. Electron scales working on scale of 10 kg
5. Electron scales working on scale of 100 kg
6. Mixer with steam jacket (volume of 200 l)

7. Automatic device of «SARONG-PA6-H» brand – suppositories producer. It consists of the following parts:

- device forming cells from polyvinylchloride film;
- dosing of suppository mass;
- cooling;
- heat sealing;
- cutting of contour packing and encoding;
- packing.

Preparing of rectal suppositories of diclofenac sodium by 0.1 r consists of the following technological stages:

1. Preparing of raw and auxiliary materials
2. Weighing of raw material
3. Melting of the base
4. Introduction to the base diclofenac sodium and cetyl alcohol
5. Preparing of polyvinylchloride film and cells
6. Filling of cells
7. Cooling of suppositories
8. Heat sealing of polyvinylchloride film (primary pack)
9. Second pack

TECHNOLOGICAL PROCESS

1. Preparing of raw and auxiliary materials

2. Weighing of raw material

The necessary amount of diclofenac sodium is weighed, crushed and sifted through the sieve with diameter of pores of 0.16 mm.

According to technological regulations raw material is weighed in necessary amount:

- | | |
|-------------------------------------|------------|
| 1. Diclofenac sodium | - 0.10 kg |
| 2. Cetyl alcohol | - 2.0 kg |
| 3. Suppocyr (vitepsol or estarinum) | - 188.0 kg |

3. Melting of the base

The necessary amount of suppcyr is melted (vitepsol or estarinum) in the mixer supplied with steam jacket 50-55⁰C.

4. Introduction of diclofenac sodium and cetyl alcohol into suppository base.

The part of melted suppository base is mixed with 2.0 kg of cetyl alcohol and diclofenac sodium up to obtaining homogeneous mass. Finished mass is combined with the rest part of melted base reducing temperature up to 37,5-38,0⁰C. The sample from the finished product is sent for analysis to laboratory. Having obtained positive results the mass is transferred into the bunker dosing into cells.

5. Preparing of polyvinylchloride film and cells for suppository mass.

Two-layer heated polyvinylchloride film is transferred through the matrix forming suppository cell and divided into two parts.

6. Filling the cells with suppository mass.

With the help of dosing unit the mass by 2.0 g is poured out into suppository cells.

8. Cooling of suppository mass.

Poured out into the cells suppositories are transferred into the cooling b area and left for hardening at 17-19⁰C.

8. Heat sealing of polyvinylchloride film.

The upper part of suppository cells heat sealed using the special device at high temperature. Number of series and expiry date of medicinal agent are also sealed into the film.

Polyvinylchloride film is divided by 6 suppositories using special cutter.

9. Secondary packing

Divided by 6 pieces suppositories are packed in special cardboard boxes with annotation for use.

Finished product is transferred into quarantine area and after obtaining positive results with normative document transported to storehouse for storing finished medicinal preparations.

**THEME: DETERMINATION METHODS OF SOLIDITY AND DILUTION OF
ETHYL ALCOHOL. RECORDING OF USED UP ALCOHOL.
ETHYL ALCOHOL (SPIRITUS AETHYLICUS)**

Objective. To consolidate material according to calculation methods used for dilution and strengthening medical solutions. To learn how to use alcoholmetric tables of SP XI. To learn how to use various alcoholmetric tables in solving production tasks on dilution of ethyl alcohol; to apply mathematic formulas and the rule of «ellipsis» in solving production tasks on dilution and strengthening medical solutions; to determine density of liquids with pyknometer and areometer.

Importance of the theme. To determine using aerometer the density of solution suggested by the teacher and dilute it in accordance with required concentration. To solve situational tasks on dilution and mixing solutions. To answer the questions on the theme of the lesson.

Description of finished product. Colourless, transparent, lightly mobile liquid with characteristic odour and burning taste. It is very hygroscopic, mixed with water, ether and chloroform in any ratios. Ethyl alcohol used in medicine is obtained only by fermentation of starch-containing raw material (potato, grain, molasses). According to SSt 5962-67 to pharmacy network, chemical plants ethyl alcohol comes with concentration not less than 96,20%. In production are often used alcohols of 95%, 90%, 70%, 40% concentration which according to SP X are officinal preparations. Ethyl alcohol (Spiritus aethylicus, Spiritus vini) is a good solvent for a large group of medicinal substances, easily mixed with other solvents – water, glycerine, chloroform, dimexide, diethyl ether and etc. Ethanol can be related to anhydrous solvents conditionally – more often are used hydro-alcoholic solutions of different solidity, which is usually expressed in volumetric percent. When alcohol is mixed with water it is observed certain increasing of temperature, elimination of air bubbles and volume decreasing (contraction phenomenon), in each case depending on the ratio in mixture volumes of alcohol and water. In this connection for easing various calculations on dilution alcohol in SP are given corresponding alcoholmetric tables (p.1013, 1014,

1015 and 1016 SP X), with the help of those can be prepared «working» alcohol of different concentration.

Authenticity. Authenticity and purity of ethyl alcohol is tested according to SP X. When adding to ethyl alcohol the solution of icy acetic acid and concentrated sulfuric acid and when heated characteristic ethylacetate odour appears.

When adding to preparation solutions of caustic soda and iodine there appears the odour of iodoform and gradually forms yellow sediment.

Density should be of 0,8066—0,8054, that corresponds to the content of alcohol 96,20—96,50% (on volume).

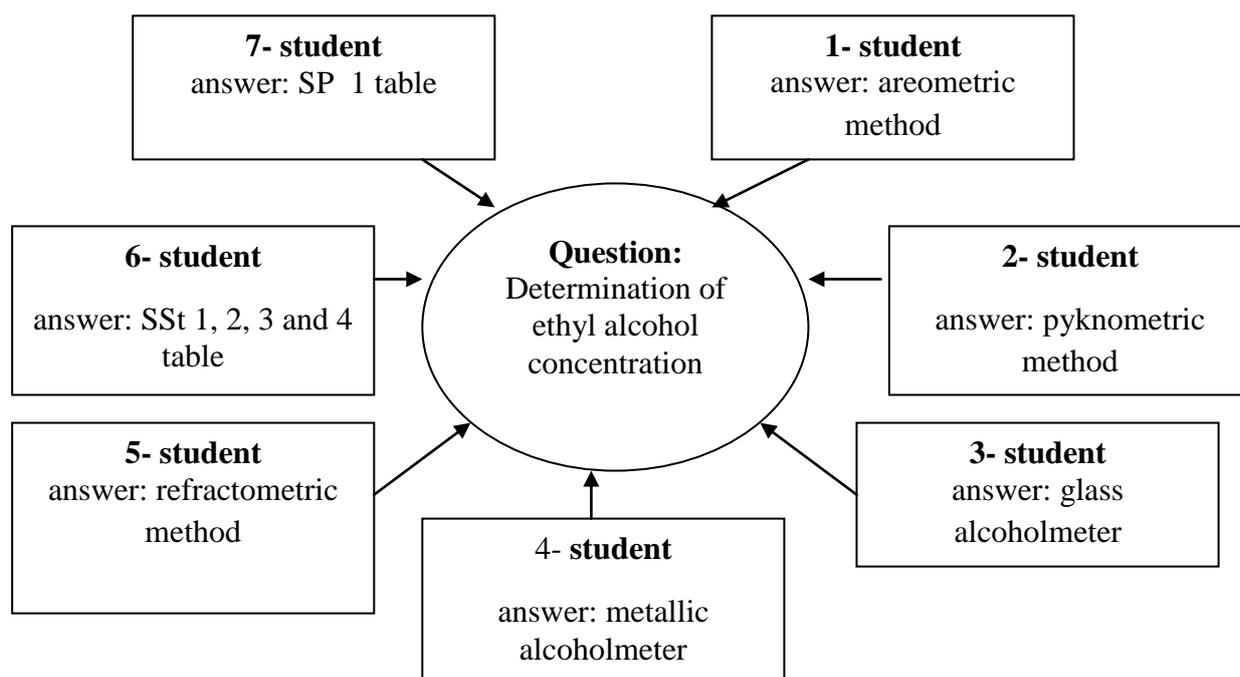
Boiling temperature - 78,3°; freezing temperature - 114°.

Purity. In preparation are tested mechanical impurities, acidity, organic bases, chlorides, sulphates, heavy metals, aldehydes, restoring substances, fusel oils, tanning, extractive and non-volatile substances, methyl alcohol, furfural, which shouldn't be or contained in the range of norms permissible by SP X.

Storage. In well-sealed container in a cool place.

Application. Leach for obtaining galenic and new galenic preparations, for dissolution of medicinal agents and as antiseptic remedy.

For conduction practical lessons pedagogical technology «Boomerang» is applied



Situational tasks.

1. To calculate what amount of alcohol 95 % and water should be taken for preparing 90 ml of alcohol 80%?
2. How much litres of water should be added to 25 l of Burov's liquid with density of 1,060, in order to obtain solution with density of 1,036?
3. How much litres of anhydrous ethyl alcohol at $T=20^{\circ}$ C is contained in 421 l of alcohol 54 %?
4. It is required to obtain 150 l of alcohol 52 %. How much alcohol 70 % and 80 %? should be mixed for this purpose?
5. To obtain 100 kg of alcohol 69 % from alcohol 72 % and 45 %.
6. Readout of areometer at $T=23^{\circ}$ C for hydrochloric acid is equal to 1,1600. Determine density and concentration of this acid at 20° C.
7. To calculate what amount of water should be poured to 2 l of 95 % alcohol in order to obtain 70 % alcohol?
8. To calculate what amount of 95 % alcohol and water should be taken for preparing 40 ml of 80 % alcohol?
9. How much water should be added to 14 kg of aluminum acetate basic solution with density of 1,049 in order to obtain solution with density of 1,036?
10. How much litres of anhydrous ethyl alcohol at $T=20^{\circ}$ C is contained in 100 l of 58 % alcohol?
11. It is required to obtain 150 l of 42 % alcohol. How much alcohol 90 % and 22 % should be mixed for this purpose?
12. To obtain 180 kg of 35 % alcohol from 80 % and 15 % alcohol.

Laboratory work - 1

DETERMINATION OF ETHYL ALCOHOL CONCENTRATION AND ITS DILUTION

Task

1. To determine concentration of initial alcohol using areometer.
2. To determine concentration of initial alcohol using glass (class I) or metallic

alcoholmeter.

3. To dilute strong alcohol according to mass up to required concentration (according to teacher's instructions).
4. To check concentration of diluted alcohol using glass alcoholmeter of class I taking into account temperature of alcohol-water mixture.

Determination of alcohol concentration using glass alcoholmeter (class I)

Glass cylinder of 250 or 500 ml is washed with warm purified water and dried with towel. In such way for work are prepared alcoholmeter, thermometer and glass mixer. Then to cylinder alcohol is poured out and, taken alcoholmeter by upper end of the rod, is carefully dipped into solution. Alcoholmeter in solution should float freely, not touching the walls and bottom of cylinder. After 3-4 min is observed what place in the level of solution crosses the scale of alcoholmeter. Counting is produced by lower edge of meniscus, temperature of alcohol is determined using thermometer.

Readouts of glass alcoholmeter at 20°C corresponds to volumetric percent. If temperature of alcohol is higher or lower than 20°C at metering moment, then concentration of alcohol at 20°C is determined using table 3 of SSt.

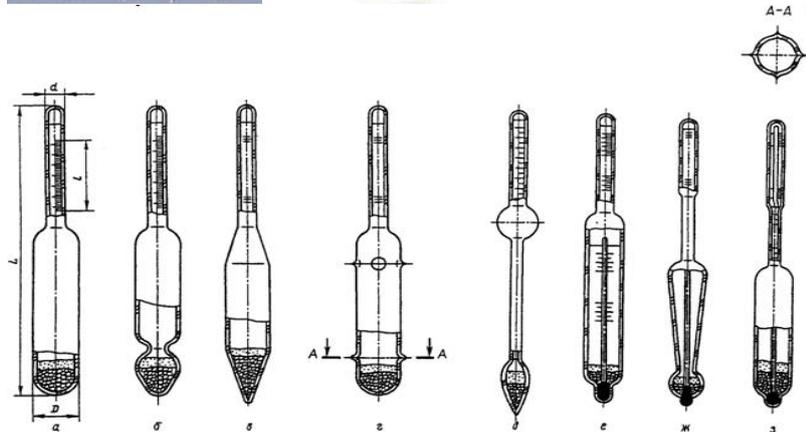
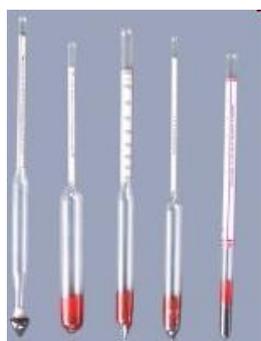


Fig.3. Glass alcoholmeter.

Results of determination

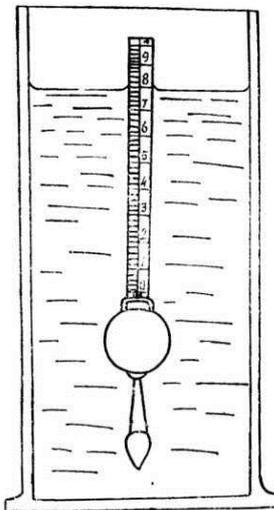
Readout of glass alcoholmeter _____

Readout of thermometer _____

Real concentration of alcohol at 20 °C _____

Determination of alcohol concentration using metallic alcoholmeter

Glass cylinder of 500 or 1000 ml, thermometer are washed with purified water and dried with towel. Alcoholmeter and weights are carefully dried with gauze wipe, beforehand moistened with strong alcohol.



Alcohol-water mixture is poured out into cylinder, mixed thoroughly and dipped alcoholmeter into it and if necessary weighed out weights by its lower rod. When determining concentration of alcohol-water mixture with unknown content of alcohol weighing out of weights is begun with lighter one (90). When alcoholmeter is not dipped up to lower (zero) scale line, the next is weighed out to it, heavier or lighter. If concentration of alcohol-



water mixture is known, weighing out is begun with the weight met to the expected concentration. Thus, having chosen the corresponding weight, at which the level of alcohol-water mixture is between higher and lower scale lines, it is determined alcoholmeter readout, for this purpose to the readout on the scale of the higher alcoholmeter rod is added the number designated on the weight. When alcoholmeter dipped without weight to the scale's readout is added 100. Then using thermometer temperature of solution is determined.

Metallic alcoholmeter even at 20°C shows only conditional concentration, but the accurate concentration of alcohol is found out using table 4 of SSt.



Fig.4. Metallic alcoholmeter.

Results of determination

Readout of metallic alcoholmeter _____

Readout of thermometer _____

Real alcohol concentration _____

Determination of alcohol concentration using areometer

Glass cylinder for 100 ml is washed with warm purified water and dried with a towel. In the same way aerometer and thermometer are prepared for work. Alcohol is poured into cylinder and carefully aerometer dipped in it, which should float freely, not touching the walls and bottom of cylinder. After 2-3 min, when areometer takes alcohol's temperature, it is observed, which place solution's level crosses the scale of areometer. Counting is produced by lower edge of meniscus. At the same time alcohol's temperature is measured. If it is 20°C, than alcohol's concentration is determined using table 1 of SP X.

DILUTION OF INITIAL ALCOHOL ACCORDING TO MASS

Each student dilutes strong alcohol on mass according to teacher's instructions up to the required concentration, which was determined by glass and metallic alcoholmeters.

Calculation on dilution initial alcohol on mass is conducted according to the table of M. U. Usubbaev, where is taken into account real concentration of initial alcohol.

Dilution method. Absolutely clean and dry bottle with ground-in stopper is calibrated on technical scales. Then into the bottle is poured out the calculated amount of initial alcohol, water and weighed, mixed, left for some time up to obtaining room temperature and checked the concentration of diluted alcohol.

Determination of diluted alcohol concentration. Diluted alcohol is transferred to dry and clean cylinder of 250 ml, where is dipped glass alcoholmeter if class I, the scale of which has the expected concentration. Alcoholmeter is left in solution for 3-4 min and then calculation is produced on lower meniscus. At the same time alcohol's temperature is measured. Knowing temperature and readout of alcoholmeter, alcohol's concentration at 20°C is found out using table 3 of SSt.

Results of determination

Readout of glass alcoholmeter _____

Readout of thermometer _____

Real concentration at 20 °C _____

Alcohol is transferred back to the bottle and given to the teacher.

Determination of ethyl alcohol concentration in water-alcohol mixture using pyknometer

With accuracy up to 0,001 clean dry pyknometer is weighed together with the stopper (accuracy of weighting up to 0,0002), filled with the help of small watering can of purified water on lower meniscus, closed with stopper and kept within 20 min in thermostate, where temperature of water is maintained at 20⁰C with accuracy up to 0,1⁰C. At such temperature water level in piknometer is led up to the mark, fastly selecting the excess of water using pipette or rolled up to the tube stripe of filter paper. Pyknometer once again is closed with stopper and kept in thermostat within 10 min, checking meniscus position regarding the mark. Then pyknometer is taken out from thermostat, dried with filter paper the inside surface of pyknometer, and also the whole pyknometer externally, left under the glass of analytic scales within 10 min and weighed with the same accuracy. Pyknometer is freed from water, dried, logically rinsed and filled with the tested water-alcohol mixture and the same operations are conducted, which were conducted with purified water.

Density of water-alcohol solution (g/cm) is calculated according to the formula:

$$g_{20} = \frac{(m_2 - m) * 0.99703}{m_1 - m} + 0.0012$$

m – empty pyknometer mass, g;

m1 – pyknometer mass with purified water, g;

m2 – pyknometer mass with the tested water-alcohol solution, g ;

0,99703–value of water density at 20°C (in g/cm³ accounting air density);

0,0012 – air density at 20°C and barometric pressure of 1011gPa (760 mm mercury column).

According to calculated value ρ_{20} on alcoholmetric table is found the value of concentration of water-alcoholic solution in percent on mass or volume.



Fig.5. Pyknometers.

Examples of task.

1. Readout of density of water-alcoholic solution at temperature of 20°C according to areometer was 0,9736. Determine the concentration of this solution.

Solution:

According to the table №1 SP XI in column «*density ρ_{20}* » we find the given value of density, then in the column «*content of ethanol in water-alcoholic solution in percent on volume*» we find the corresponding to it value of concentration in per: **0,9736–20%.**

Answer: alcohol concentration is 20% (at 20 °C).

2. Alcohol concentration is equal to 20%. Determine the concentration of this alcohol in percent according to mass.

Solution:

According to the table №1 SP XI we find the concentration of this alcohol in percent on volume and the corresponding to it value of concentration in percent on mass: **20% - 16,21% (m/m).**

Answer: concentration of 20% alcohol in percent on mass is 16,21% (m/m) (at 20 °C).

Table №2 SP XI – Amount of (in grams at 20 °C) water and alcohol of various concentration, which necessary to be mixed, in order to obtain 1 kg of alcohol with concentration of 30%, 40%, 50%,60%, 70%, 80%, 90% and 92%

Examples of tasks:

What amount of 96% alcohol and water should be taken to obtain 10 kg of 70% alcohol?

Solution:

According to the table №2 SP XI at the crossing of the line «*strength of the taken alcohol in %*» and the column «*70%*» we find out that for obtaining 1 kg of 70% alcohol 665 g of 96% alcohol and 335 g of water should be taken. According to the conditions of the problem it is necessary to obtain 10 kg of 70% alcohol, which means that, we make up the following proportions:

$$\begin{array}{rclcl} 665 & - & 1 & 335 & - & 1 \\ x & - & 10 & y & - & 10 \\ x = 6650 & & & y = 3350 & & \end{array}$$

Answer: in order to obtain 10 kg of 70% alcohol it is necessary to take 6,65 kg of 96% alcohol and 3,35 kg of water.

Table №4 SP XI – Amount of (in ml at 20 °C) water and alcohol of various concentration, which necessary to be mixed, in order to obtain 1 l of alcohol with concentration of 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 85%, 90%

Example of task:

What amount of 90% alcohol and water should be taken to obtain 500 ml of 40% alcohol?

Solution:

According to the table №4 SP XI at the crossing of the line «*strength of diluted alcohol in %*» and the column «*40%*» we find out that for obtaining 1 l of 40% alcohol 444 ml of 90% alcohol and 581 ml of water should be taken. According to the conditions of the problem it is necessary to obtain 500 ml of 40% alcohol, which means that, we make up the following proportions:

$$\begin{array}{rclcl} 444 & - & 1 & 581 & - & 1 \\ x & - & 0,5 & y & - & 0,5 \\ x = 222 & & & y = 290,5 & & \end{array}$$

Answer: in order to obtain 500 ml of 40% alcohol 222 ml of 90% alcohol and 290,5 ml of water should be taken.

Table №5 SP XI – Amount of (in ml at 20 °C) water and alcohol of various concentration, which necessary to be mixed, in order to obtain 1 l (at 20 °C) of alcohol with concentration of 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%

Table №5 is the same as №4, except the fact that, the strength of diluted alcohol is from 95,1% to 96,5%.

Example of task:

What amount of 96,5% alcohol and water should be taken in order to obtain 2 l of 40% alcohol?

Solution:

According to the table №5 at the crossing of the line «*strength of diluted alcohol in %*» and the column «*40%*» we find out that for obtaining 1 l of 40% alcohol 414,5 ml of 96,5% alcohol and 615,3 ml of water should be taken. According to the conditions of the problem it is necessary to obtain 2 l of 40% alcohol, which means that, we make up the following proportions:

$$\begin{array}{rcl} 414,5 - & 1 & 615,3 - & 1 \\ x & - & y & - & 2 \\ x = 829 & & y = 1230,6 & & \end{array}$$

Answer: in order to obtain 2 l of 40% alcohol 829 ml of 96,5% alcohol and 1230,6 ml of water should be taken.

Table №3 SP XI – Table for obtaining alcohol of various strength at 20°C. Using this table volume of water can be found out which is needed to pour to this volume of strong alcohol in order to obtain water-alcoholic solution of the required concentration.

Example of task:

What amount of water should be added to 50 ml of 95% alcohol in order to obtain 40% alcohol?

Solution:

According to the table №3 at the crossing of the line «*strength of diluted alcohol*» (*1000 volumes*) and the column «*40%*» we find out that for obtaining of 40% alcohol

should be added 1443 ml of water to 1000 ml of 95% alcohol. According to the conditions of the problem volume of 95% alcohol is 50 ml, which means that, we make up the following proportions:

$$1443 - 1000$$

$$x - 0,05$$

$$x = 72,15$$

Answer: in order to obtain 40% alcohol should be added 72,15 ml of water to 50 ml of 95% alcohol.

Dilution of alcohols with different concentration

In industrial production of medicinal forms often are solved practical problems connected with mixing of alcohols with various concentrations.

Example:

It is necessary to obtain 5l of 40% alcohol from 95% alcohol and having in the workshop distillation with concentration of 20% alcohol.

Solution:

We solve the problem according to the rule of «cross»:

$$\begin{array}{rcccl}
 95 & \searrow & & 20 & \text{-----} & x \\
 & & 40 & & & \\
 20 & \nearrow & & 55 & \text{-----} & y \\
 & & & 75 & & 5
 \end{array}$$

We make up proportion: $75 - 20$

$$5 - x \quad x = 1,33 \text{ (l)};$$

$$75 - 55$$

$$5 - y \quad y = 3,67 \text{ (l)}.$$

Then, taking into account contraction phenomenon, after sedimentation of the obtained mixture we lead the volume up to 5 l.

Answer: in order to obtain 5 liters of 40% it is necessary to mix 1.33 l of 95% alcohol, and 3.67 l of 20% alcohol and after sedimentation to bring the volume with water up to 5 l.

In practice, often there is a situation with weighing by weight of alcohol. In this case, you need to convert the concentration of volume percentage into mass, and make calculations according to the rule of "the cross."

Example:

What amount of distillate with alcohol concentration of 20% is required to add to 10 kg of 95% alcohol in order to obtain 40% alcohol?

Solution:

According to alcoholmetric table of №1 SP XI volume percent is converted to mass volume:

% (vol/vol)	%(m/m)
-------------	--------

95,01	92,42
-------	-------

95	—————	x
----	-------	---

<u>94,96</u>	<u>92,35</u>
--------------	--------------

0,05	0,07
------	------

0,01	—————	y
------	-------	---

$$y = 0,014$$

$$x = 92,42 - 0,014 = \mathbf{92,41}(\% \text{ (m/m)})$$

% (vol/vol)	% (m/m)
-------------	---------

40,04	33,33
-------	-------

40	—————	x
----	-------	---

<u>39,91</u>	<u>33,22</u>
--------------	--------------

0,13	0,11
------	------

0,04	—————	y
------	-------	---

$$y = 0,034$$

$$x = 33,33 - 0,034 = \mathbf{33,30} (\% \text{ (m/m)})$$

$$20\% = \mathbf{16,21} (\% \text{ (m/m)})$$

92,41	—————	17,09	—————	10
-------	-------	-------	-------	----

	—————	33,30	—————	
--	-------	-------	-------	--

16,21		59,11	—————	x
-------	--	-------	-------	---

$$17,09 - 59,11$$

$$10 - x$$

$$x = 34,59 \text{ (kg)}$$

Answer: in order to obtain 40% alcohol it is necessary to add 3459 kg of distillate with alcohol concentration of 20% to 10 kg of 95% alcohol.

Determination of content of anhydrous alcohol in water-alcohol mixture

Example:

Which amount of anhydrous alcohol is in 30 l of 65% alcohol?

Solution: Knowing determination of volume concentration the volume of dissolved substance of anhydrous ethyl alcohol is calculated:

$$C \% (\text{vol/vol}) \cdot \text{solution volume}$$

$$\text{Volume of dissolved substance} = \frac{\text{-----}}{100\%}$$

$$v = 0,65 \cdot 30 = \mathbf{19,5 \text{ (l)}}$$

$$m = 19,5 \cdot 0,78927 = \mathbf{15,4 \text{ (kg)}}$$

Answer: 30 l of 65% alcohol contain 19,5 l or 15,4 kg of anhydrous (absolute) alcohol.

THEME: PHARMACEUTICAL SOLUTIONS AND TECHNOLOGIES OF THEIR PRODUCTION IN INDUSTRY PREPARATION TECHNOLOGY OF 5 AND 10% ALCOHOL IODINE SOLUTIONS

Objective: To consolidate theoretical material on questions for self-study and acquire practical skills for the preparation and standardization of aqueous solutions. To consolidate theoretical material for self-study and acquire practical skills in the preparation of syrups and flavoured waters.

Importance of the theme: Liquid dosage forms are free disperse systems in which drugs are distributed in a liquid dispersion medium.

Their advantage compared to solid dosage forms:

- High bioavailability, i.e. rapid absorption and rapid onset of therapeutic effect. This is due to the small size of the dispersed phase.

- Simplicity and ease of use.
- Reduction of irritating effect of drugs on the mucous membrane of the gastrointestinal tract.
- The ability to mask the unpleasant taste and odour of drugs.
- Ease of fabrication.

The main disadvantage of liquid formulations is instability, i.e., microbial contamination in the solutions is possible. Therefore, the liquid dosage forms have a small shelf life (up to 3 days). A second negative aspect of liquid formulations: substances in dissolved form undergo hydrolysis and oxidation processes more than in dry form.

2. Classification of liquid medicinal forms

According to the type of disperse systems:

System description	Disperse phase	Particles' size of disperse phase	Examples of medicinal forms
True solutions of low-molecular compounds	Ions, molecules	1 nm	Solutions of glucose, sodium chloride, magnesium sulphate
True solutions of HMC	Molecules	1-100 nm	Solutions of pepsin, gelatine
Colloidal solutions	Micelles	1-100 nm	Solutions of collargol, protargol
Suspensions	Particles of solid substances	0,1-50 mcm	Suspensions of sulphur, magnesium oxide
Emulsions	Particles of liquids	1-150 mcm	Emulsions of castor, peach oils
Combined systems			Infusions, decoctions, mucilages

II. According to method of application:

- For internal use - mixtures, drops;
- For external use - ointments for rubbing, lotions, enemas, drops;
- For injectable use - solutions.

According to disperse medium:

- Aqueous;
- Non-aqueous: glycerin, alcohol, oil, mixed polymer.

According to applied apparatus:

- Pharmaceutical manufacturing;
- Plant manufacturing.

According to preparation method:

- prepared by mass-volume process (aqueous and hydroalcoholic solutions of solid medicinal substances, drops for internal use, suspensions with the content of solid phase of up to 3%);
- prepared by volume (alcohol solutions with different concentrations, hydrochloric acid and standard solutions prescribed in the recipe under the provisional name);
- prepared by mass (liquid and solid solutions of drugs in a viscous and volatile solvents, emulsions, suspensions with solid phase in an amount of 3% or more, homeopathic liquid medicines).

3. Requirements for solvents:

1. High dissolving ability.
 2. Chemical indifference.
 3. Biological safety.
 4. Absence of unpleasant taste and odour.
 5. Stability to microbial contamination.
 6. Efficiency.
1. High solvency.
 2. Chemical indifference.
 3. The biological harmlessness.
 4. The absence of unpleasant taste and odor.

5. Resistance to microbial contamination.

6. Cost.

Control and theoretical questions:

1. Classification of solutions (water, alcohol, oil, glycerol). Modern range of solutions and the prospects for its expansion.
2. Standardization and storage of medical solutions.
3. Production of medical solutions: basic acetic-aluminum salt, basic acetic lead, alcohol and aqueous iodine solutions, iodinol, iodonate, alcoholic solution of methylene blue, brilliant green.

For conduction practical lesson pedagogical technology

Training «Carousel» is applied

№	Solvents		
		Inorganic	Organic
1	Purified water		
2	Glycerol		
3	Chloroform		
4	Esilon 4		
5	Esilon 5		
6	Diethyl ether		
7	Ethyl alcohol		
8	PEO 400		

Laboratory work - 1

**PA 42-986-72. Camphor alcohol
(SPIRITUS CAMPHORATUS)**

Description of finished product. Transparent, colorless liquid with a smell of camphor. The density of the finished product is 0,882-0,886.

Packing. Produced in bottles of 50 and 500 ml, sealed with plastic caps and plastic screw caps.

Storage. In a well-closed container in a cool, dry, dark place. Shelf life 10 years.

Application. Externally for rubbing both irritating and distracting remedy. It is included in the solution of potassium arsenite.

Task

1. Prepare 20 grams of camphor alcohol.
2. Draw a diagram of the process.
3. To analyze the finished product.

Composition:

camphor 100 g,
ethyl alcohol 700 ml,
purified water 200 ml

Table 1

Description of initial material

Number of pharmacopoeia article and SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art, 128 SSt 5962-67 SP X. art. 73	Camphor Ethyl alcohol Distilled water	Melting point 174-180 ⁰ Not less than 96,2 pH 5,0-6,8	According to SP According SSt According to SP

TECHNOLOGICAL PROCESS

20.0 g of camphor powder introduced into a tared beaker, 14 g of alcohol are added and stirred until complete dissolution of camphor. Then, 4 ml of water are added, and the liquid is mixed again. The product is standardized and passed to the teacher.

ANALYSIS OF FINISHED PRODUCT

Determination of preparation's good quality. To 10 grams of the drug at 20 ° C, slowly is added water at the same temperature until appearing of nonvanishing turbidity. There should not be spent more than 5.3 ml of water. With the further addition of water camphor precipitates.

Quantitative determination is produced by spectrophotometric method. Finished preparation should contain camphor of 9,5—10,5%

Laboratory work - 2

SP X, art. 335. SOLUTION OF IODINE ALCOHOL 5% (SOLUTIO IODI SPIRITUOSA 5%)

Description of finished product. Transparent liquid of reddish-brown color, with a characteristic odor of iodine. The main components in the finished product should be: 4.9-5.2% of iodine, potassium iodide 1.9-2.7%, ethyl alcohol at least 46%.

Packing. In a well-sealed bottles of orange glass by 15-20 kg and in ampoules by 1 ml.

Storage. With caution (letter B) in protected from light place.

Application. Externally as an antiseptic, as well as internally in atherosclerosis.

ISD (internal single dose) internally— 20 drops, IDD (internal daily dose) internally — 60 drops.

Task

1. Prepare 10 ml of 5% alcoholic solution of iodine.
2. Draw a diagram of the process.
3. To analyze the finished product.



Composition:

iodine 50 g,

potassium iodide 20 g,

water and 95% alcohol in equal parts up to 1 l

Table 2

Description of initial raw material

Number of pharmacopoei article and SSt	Technological or trade name of raw material	Content, %	Quality
SP X, art, 354	Iodine	99,5	According to SP
SP X. art. 364	Potassium iodide	99,5	-----
SSt 5962-67	Ethyl alcohol	Not less than 96,2	According to SSt
SP X. art. 73	Distilled water	pH 5,0-6,8	According to SP

TECHNOLOGICAL PROCESS

First, in the cylinder or beaker alcohol-water mixture is prepared consisting of equal volumes of 95% alcohol and purified water. Then to the flask, graduated for 10 ml are placed 0.2 g of potassium iodide and 0.4 ml of the prepared aqueous-alcoholic mixture. After dissolving potassium iodide into a flask 0.5 g of iodine are added and stirred until complete dissolution. Then, the resulting solution is brought up to 10 ml with aqueous alcoholic mixture. The concentrated solution of potassium iodide promotes rapid dissolution of iodine and provides resistance of drug, as thus formed complex compound of the following composition: $KJ + J_2 = KJ_3$

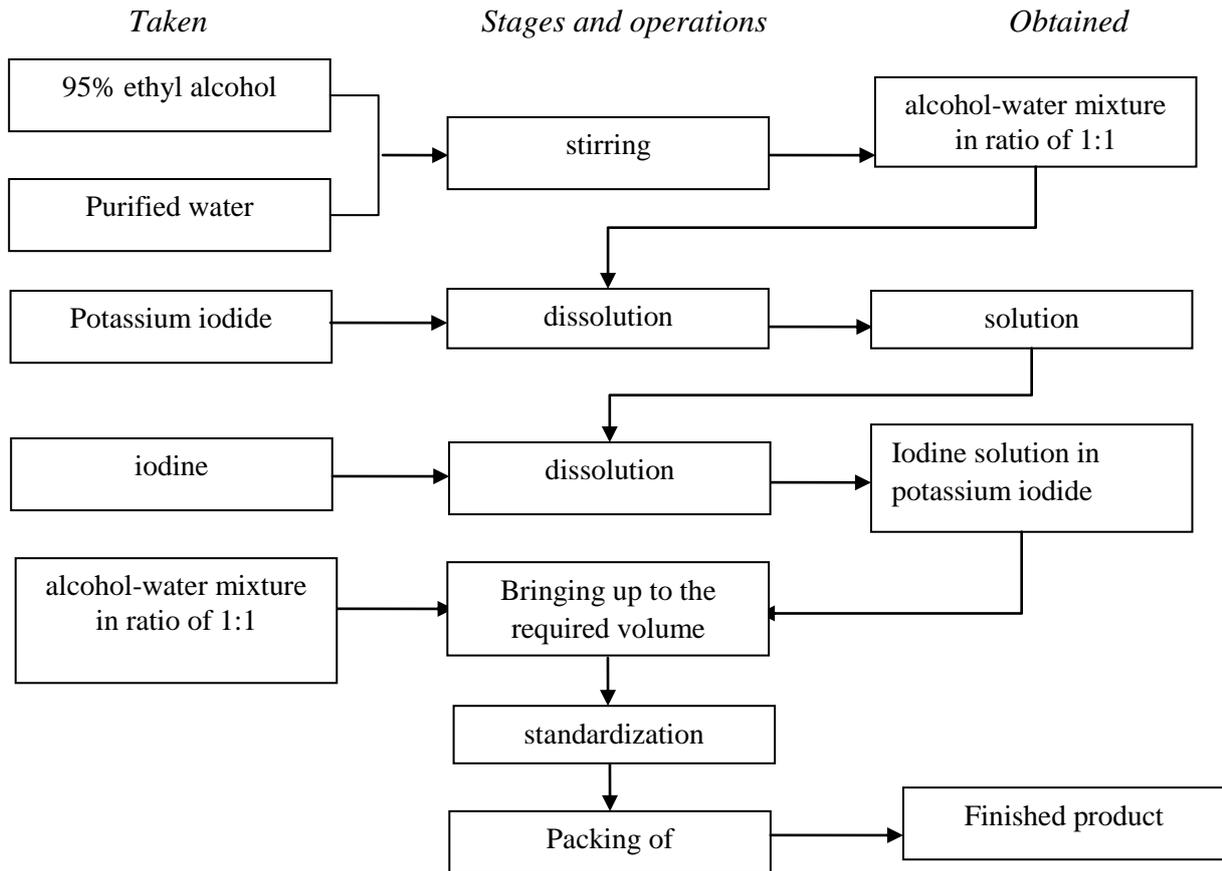
ANALYSIS OF FINISHED PRODUCT

Authenticity. By adding to the preparation of starch solution appears blue-blue color (iodine).

Quantitative determination. The drug is titrated with sodium thiosulfate until decoloration of solution (without indicator). The preparation should contain 4.9-5.2% of iodine. Titrated solution is diluted with water, added a solution of acetic acid and titrated with silver nitrate solution up to transition of precipitate's color from yellow to pink (the indicator - eosinate sodium solution). The difference between the number of milliliters of silver nitrate and sodium thiosulfate is calculated for potassium iodide, which in a formulation should be 1.9-2.1%.

Ethyl alcohol content in the product should be not less than 46%

SCHEME OF TECHNOLOGICAL PROCESS



Laboratory work -3

SP X, art. 356. SOLUTION OF IODINE ALCOHOL 10%

(SOLUTIO IODI SPIRITUOSA 10 %)

Description of finished product. Liquid of red-brown color, with characteristic odor of iodine. By adding water to the drug fine-grained sediment of iodine precipitates. Finished formulation contains 9.5-10.5% of iodine.

Packing. In a well-sealed containers of orange glass by 15—20 kg.

Storage. With caution (letter B), in protected from light place. Shelf life up to 1 month.

Application. Internally in iodine deficiency. Externally as bactericidal drug. ISD (internal single dose) internally — 10 drops, IDD (internal daily dose) internally -30 drops.

Task

1. Prepare 50 ml of 10% alcoholic solution of iodine.
2. Draw a diagram of the process.
3. To analyze the finished product.

Composition:

iodine 100 g,

ethyl alcohol 95% up to 1 l

Table 3

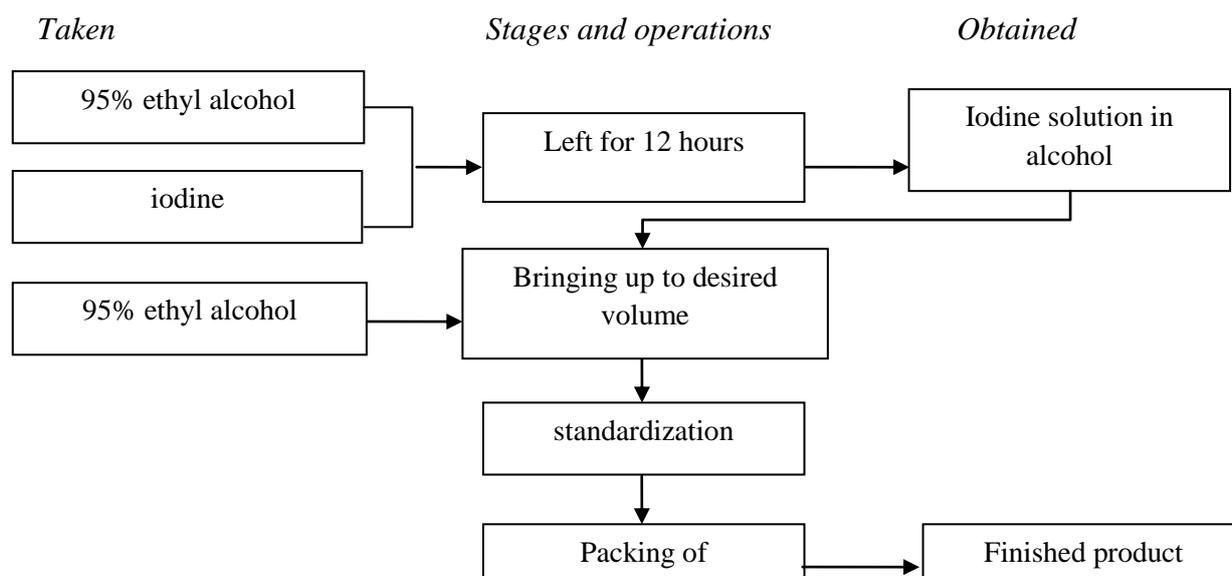
Description of initial raw material

Number of pharmacopoeial article and SSt	Technical or trade name Raw material	Contents, %	Quality
SP X, art, 354	Iodine	99,5	According to SP
SSt 5962-67	Ethyl alcohol	Not less than 96,2	According to SSt

TECHNOLOGICAL PROCESS

Into the glass cylinder of 50 or 100 ml is poured 95% ethyl alcohol in an amount somewhat less than it should be according to the calculation (about 40 ml). Weighed amount (5 g) of iodine are placed in a double-layer gauze bag, which is immersed in the cylinder so that most of its half is in alcohol. The cylinder is stoppered and left to stand for 12 hours. In this way the iodine dissolution proceeds faster as the heavier density of iodine solution is lowered, and the pure alcohol rises, i.e. spontaneous mixing is occurred. Convective motion of the fluid is as long as the iodine is completely dissolved. Then the bag is removed, washed with alcohol, which is adjusted to the desired volume.

SCHEME OF TECHNOLOGICAL PROCESS



ANALYSIS OF FINISHED PRODUCT

Authenticity. To the solution of preparation is added the starch solution, blue-blue coloring appears (iodine).

Hydrogen-iodide acid. To neutralize 2ml of drug should be spent not more than 0.3 ml of 0.1n. of caustic soda solution (permissible limit of hydrogen-iodide acid).

Quantitative determination. The drug is titrated with sodium thiosulfate in the presence of potassium iodide up to the decoloration of solution (without indicator). The finished product should contain 9.5-10.5% of iodine.

THEME: TECHNOLOGY OF SYRUPS AND AROMATIC WATERS

Objective: To consolidate the theoretical material for self-study and acquire practical skills in the preparation of syrups and flavoured waters.

Importance of the theme: Learn how to prepare and assess the quality of the sugar syrup, Althea syrup, licorice root, rhubarb and flavoured waters.

Flavoured waters – are water or water-alcoholic solutions of essential oils. They are transparent or slightly opalescent liquids with a smell of comprising them essential oils. The concentration of essential oils in flavoured waters does not exceed 0.1%.

Flavoured waters should not have a musty smell, contain heavy metals and noticeable dense precipitate. Fragrant waters are used as medicines and as auxiliary agents for the correction of taste and smell in the pharmaceutical technology. Distilled fragrant waters are prepared on pharmaceutical plants by distillation of essential oil plant raw material with water steam. Usually from 1 part of vegetable raw material 10 parts of distillate are obtained. Fragrant waters are prepared from dry comminuted raw materials or pre-digested with water, water-alcohol mixture to facilitate extraction of the active ingredients (alcohol water from the fruit of coriander). Water bitter almond is prepared by distillation with water steam after fermentation of defatted seeds of bitter almonds, and must contain 0.1% of hydrocyanic acid (including free about 0.02% and 0.08% bound), it is stored with caution (list B). Simple aromatic waters are prepared by dissolving of ether oil in water in a ratio of 1:1000 (1:4000 pink water) or dilution of concentrates. Fragrant waters, prepared in different ways, unequal: distilled fragrant waters have more complex composition. Besides the essential oils they contain other volatiles, distillable with steam, which affect the taste and smell of fragrant water. Fragrant waters are susceptible to microbial contamination, isolated sediments.

Syrups - thickish, transparent, sweet taste liquids for internal use, with different taste and smell depending on the composition. They are prepared by mixing a sugar syrup with drug or food (fruit) extracts, tinctures, applying, where necessary, heating. To them as a preservative ethanol is added. Syrups are divided into medicinal and flavoring, standardized by density, sugar content, and medicinal substances.

Control and theoretical questions:

1. General description of syrups. Classification. Nomenclature.
2. Sugar syrup. General description. Production. The use of sugar substitutes.
3. Production of flavor and medicinal syrups.
4. Standardization and storage of syrups.
5. General description of fragrant waters. Classification. Nomenclature.
6. Preparation of fragrant waters by distillation of essential oils with water steam.

7. Preparation of flavored waters by dissolving essential oils.

8. Standardization and storage of fragrant waters.

Laboratory work -1

SP IX, art. 47. WATER BITTER-ALMOND

(AQUA AMYGDALARUM AMARARUM)

Bitter-almond water is prepared from defatted oilcake of bitter almonds by distillation with water steam or by diluting the concentrate with 45% alcohol.

Description of finished product. Bitter-almond water is a colorless, almost clear liquid with an odor of bitter almonds, slightly acidic for methyl orange. The content of hydrogen cyanide is of 0,09-0,11%. The density is of no more than 0.960.

Packing. In glass containers by 15 – 20 kg.

Storage. With caution (list B), in a well-sealed glass bottles of orange glass in a cool place.

Application. As an analgesic, calming the nervous system agent. ISD(internal single dose) - 0.8 ml (30 drops), IDD(internal daily dose) - 1.6 ml (60 drops).

Task

1. Prepare bitter-almond water from 12 g of bitter almond oilcake.
2. Draw a diagram of the process.
3. To analyze the finished product.

Formulation: seeds oilcake of bitter-almond large-crushed powder of 12 g, distilled water 20 g, ethyl alcohol 3,0 g

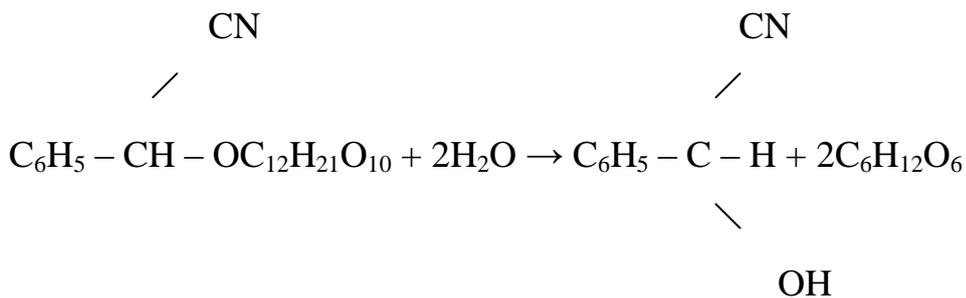
Table 4

Description of initial raw material

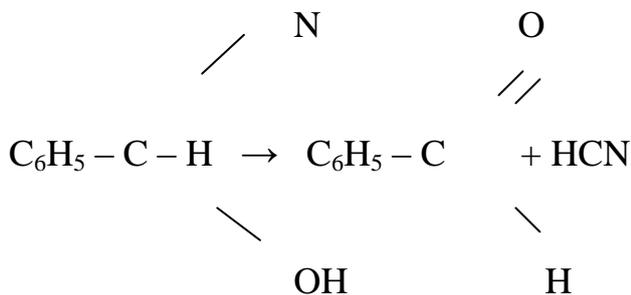
Number of pharmacopoeial article and SSt	Technological or trade name of raw material	Content, %	Quality
SP VIII, art. 498	Seeds of bitter almond	---	According to SP
SSt 5962-67	Ethyl alcohol	Not less than 96,2	According to SSt
SP X, art. 73	Purified water	pH 5,0-6,8	According to SP

TECHNOLOGICAL PROCESS

12 parts of bitter almonds oilcake, converted into a powder, are placed in a jar glass with ground-in stopper, poured over with 20 ml of distilled water, mixed well at room temperature, left for 12 hours. During this time emulsin enzyme located in the seeds of bitter almonds, decomposes the glycoside amygdalin into benzaldehydecyanhydrine and glucose as follows



Benzaldehydecyanhydrine is partially decomposed into benzoic aldehyde and cyanic hydrogen:



After this time the mass is transferred to a flask of the distillation apparatus, which consists of a steam generator, the cube and refrigerator.

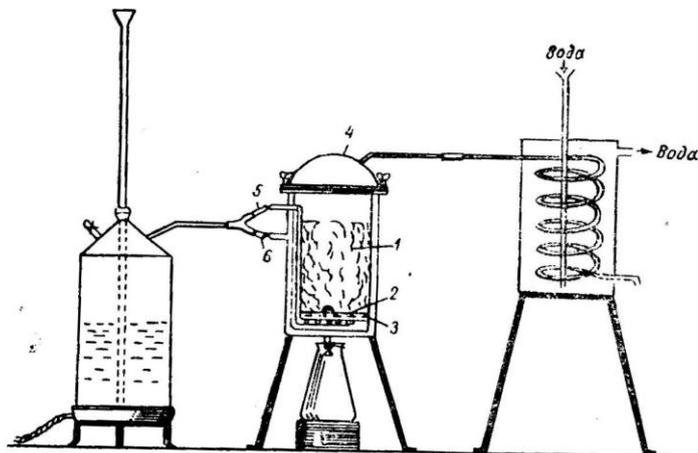


Fig.5. Apparatus for preparing fragrant waters.

Steam from the steam generator passing through the contents of a cube, extracts the volatiles and condensing in refrigerator, is supplied to the receiver, where pre-poured 3 g (3.4 ml) of the alcohol, distilled to obtain 12 parts of distillate. Then, another receiver is substituted and separately collected 3 parts of distillate. Thereafter, the amount of hydrogen cyanide in both distillations and mixed them so as HCN was 0.1% and the alcohol - 20 to 22%. In the case of excessive concentration of hydrogen cyanide in the distillation it is diluted with 20% alcohol, the amount of which is calculated according to the formula:

$$x = \frac{A \cdot (C - B)}{B},$$

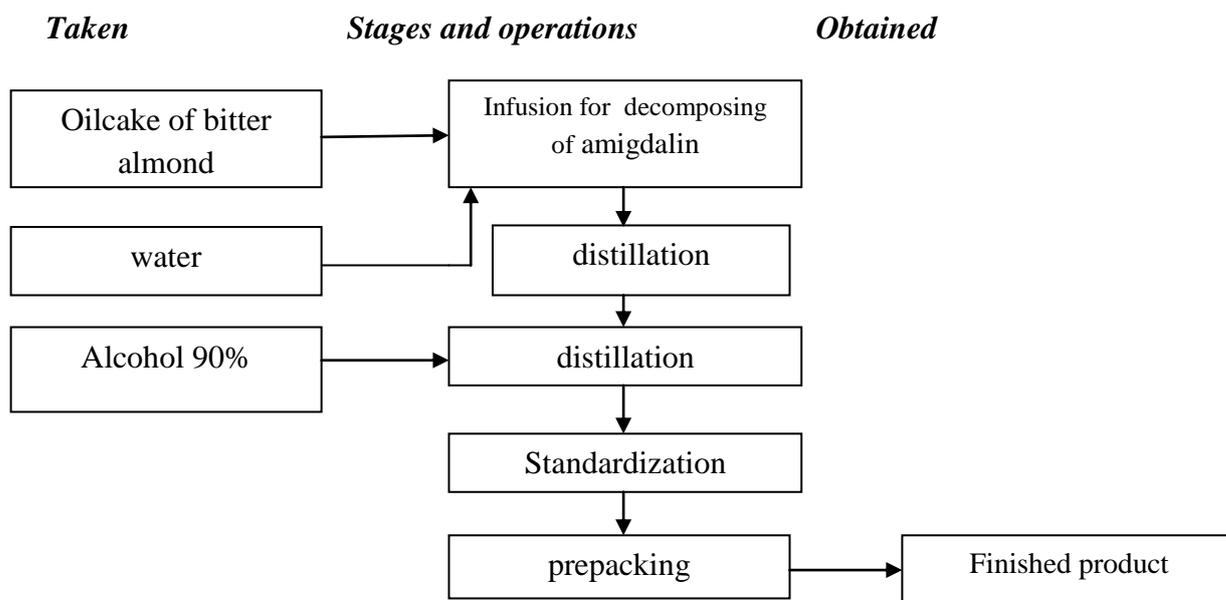
where x — amount of 20% alcohol, necessary for adding to strong distillation, ml;

A – amount of the obtained distillation, ml;

B – percent of hydrogen cyanide according to SP in finished product;

C – real percent of hydrogen cyanide in the obtained distillation.

SCHEME OF TECHNOLOGICAL PROCESS



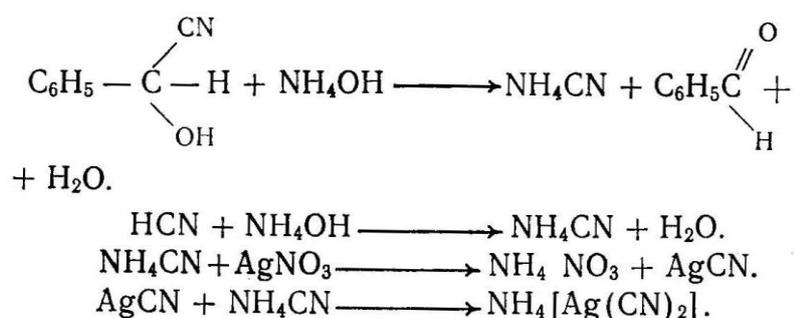
ANALYSIS OF FINISHED PRODUCT

Authenticity. To the preparation are added caustic soda solution, ferrous sulfate, ferric chloride, ferric oxide and diluted hydrochloric acid, resulting in a precipitate of Prussian Blue (hydrogen cyanide).

Purity. The content of heavy metals should not exceed 0.00025%, free hydrogen cyanide should be not more than 0.02% (determined argentometrically in acidic medium).

Quantitative determination. 10 ml of the preparation are diluted with 40 ml of water, added 0.4 ml of ammonia, 0.8 ml of a potassium iodide solution. The liquid is slowly titrated with 0.1N. solution of silver nitrate and strongly shaken up until opalescent yellowish, not disappearing with shaking.

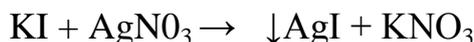
The reaction is as follows:



From one extra drop of 0.1N. solution of silver nitrate the complex is decomposed as follows:



The end of titration according to this turbidity is difficult to detect, that is why potassium iodide solution is added (indicator).



Calculation of percent content of hydrogen cyanide is made according to the formula:

$$X_{\text{HCN}} = \frac{V \cdot N \cdot \mathcal{E} \cdot 100}{1000 \cdot \text{sample}}, \quad \mathcal{E}_{\text{HCN}} = 2 \cdot 27 = 54$$

Note. Bitter-almond water can be prepared from the concentrates diluting 45% alcohol

in the ratio of 1:16; from oilcake of peach seeds and etc. Instead of bitter almond water is allowed to dispense cherry laurel water containing 0,1 % of hydrogen cyanide.

Laboratory work - 2

SP VIII, art. 64. DILL SEED WATER

(AQUA FOENICULI)

Description of finished product. Clear, colorless or slightly not quite clear liquid, neutral, with the smell and taste of fennel.

Packing. In glass containers by 15 - 30 kg.

Storage. In cool place in well stopped up glass containers filled up to the top.

Application. For the improvement of bowel function and reduce flatulence. Administered internally by 1 tablespoon 3-6 times a day.

Task

1. Prepare 100 ml of dill water by dispersion method.
2. Draw a diagram of the process.
3. To analyze the finished product.

Formulation: dill oil 1 g, pure talc 10 g, water heated up to 50 - 60° 1000 ml.

Table 5

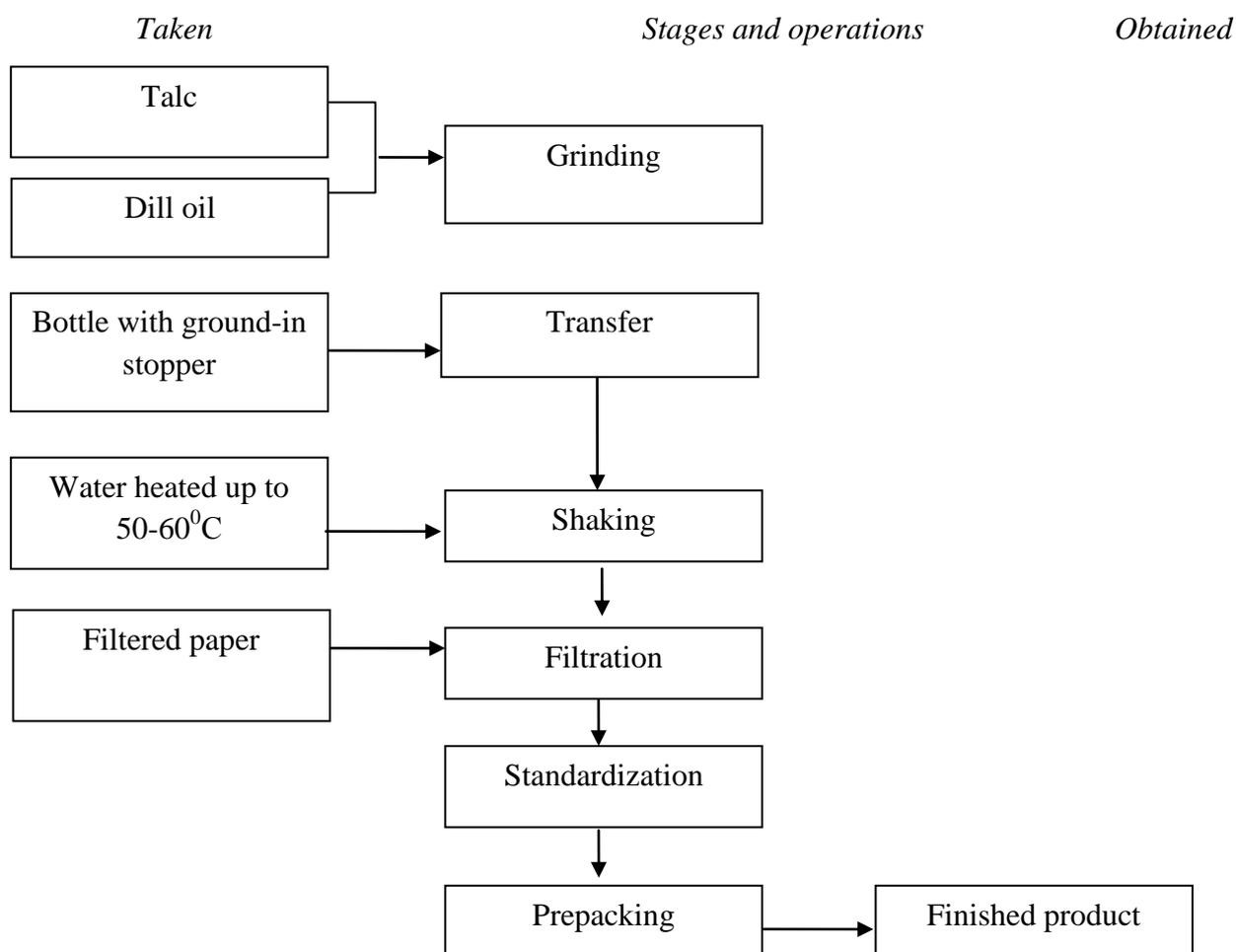
Description of initial raw material

Number of pharmacopoeial article and SSt	Technological or trade name of raw material	Content, %	Quality
SP IX, art, 345	Fennel oil	density 0,960 refraction indicator 1,535 -	According to SP
SSt 879-52	Talc	pH 5,0-6,8	According to SSt
SP X, art, 73	Water purified		According to SP

TECHNOLOGICAL PROCESS

The porcelain mortar is charged with 1 g of talc, added 0.1 g of fennel oil and triturated carefully. The mass is transferred to a flask with ground-in stopper, added 100 ml of warm water, stirred for 15 minutes and filtered through a moistened filter into the bottle for dispense.

SCHEME OF TECHNOLOGICAL PROCESS



ANALYSIS OF FINISHED PRODUCT

Purity. The drug should not give response to heavy metals; 20 ml of the product are evaporated and the residue is calcined. The balance must not exceed 0.005%. To prepare 100 ml of dill water. To carry out the quality test of the obtained product on organoleptic characteristics. To give opinion on the compliance to the requirements of ND. To arrange the data of the experiment in the form of a table.

Name of indicator	Meaning of quality indicator	
	ND	Experimental
Description		
Color		
Taste		
Odour		

Conclusion:

**SP VIII, art. 62. ALCOHOL WATER OF CORIANDER FRUITS
(CORIANDER)
(AQUA CORIANDRI SPIRITUOSA)**

Description of finished product. Colorless, transparent or slightly opalescent liquid with odour of coriander or alcohol, with pleasant taste. Density - 0,950 - 0,980.

Packing. In glass containers by 15 - 20 kg.

Storage. In well stopped up bootles in cool place.

Application. The agent improving the taste and odour of drugs.

Task

1. To prepare 100 ml of coriander water by steam distillation method or by dissolving coriander oil in alcohol.
2. To draw the flow diagram of the process.
3. To conduct the analysis of the finished product.

Formulation: coriander fruits (coriander) pounded 1g, ethyl alcohol 1 g, water purified— sufficient amount.

Table 6

Description of initial raw material

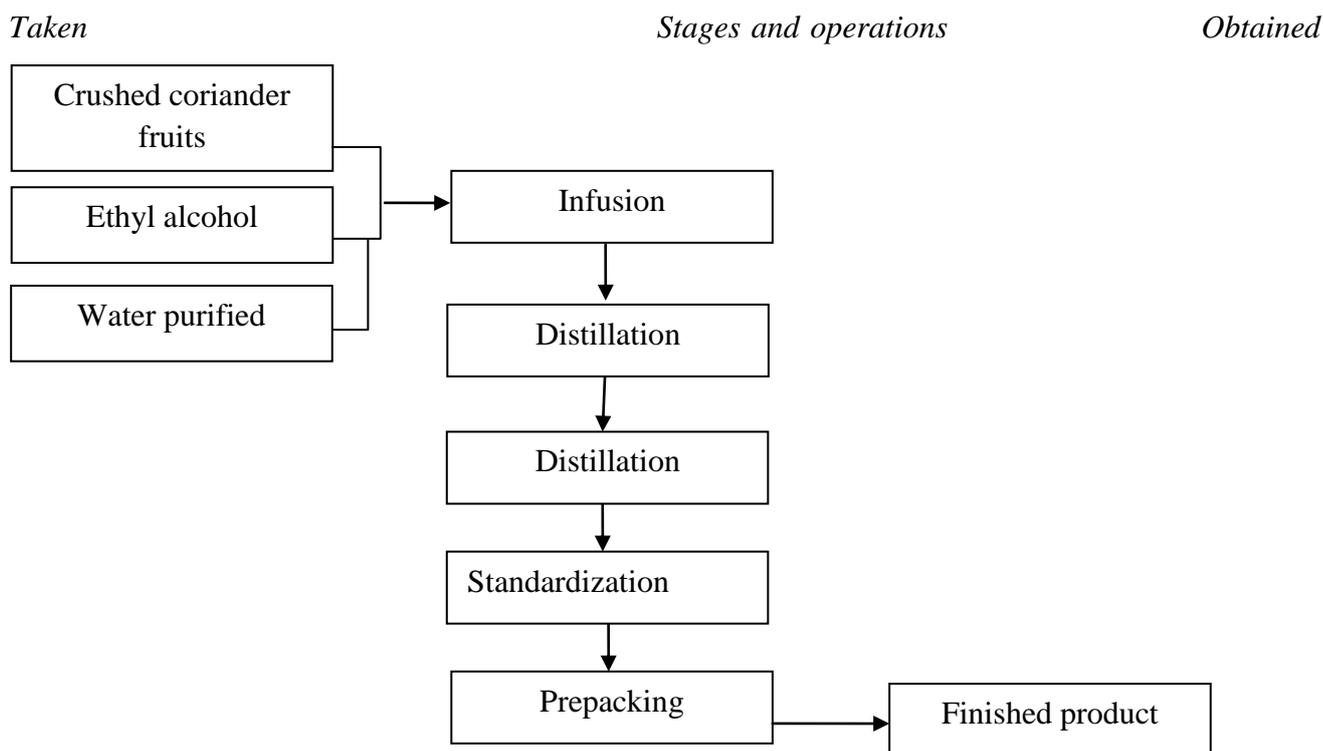
Number of pharmacopo article and SSt	Technological or trade name of raw material	Content, %	Quality
SP IX, art, 214	Coriander fruit	Ether oil not less than 1,5	According to SP
SP IX, art, 343	Coriander oil	not less than 65,0	----
SP X, art, 73	Water purified	pH 5,0-6,8	----

TECHNOLOGICAL PROCESS

Preparation from coriander fruits by steam distillation method: 10 g of comminuted fruit of coriander are placed in a glass jar with ground-in stopper, poured into 10 ml of alcohol, 100 ml of water and at room temperature allowed to stand for 12 hours. After the said time the mass is transferred to a distillation apparatus, and with water steam is distilled to produce 100 ml of distillate.

Preparation of coriander oil: 0.2 g of coriander oil is placed in a glass flask with ground-in stopper, added 10 g (11.3 ml) of the alcohol, shaken until complete dissolution of the oil, then added 90 ml of water, shaken within 30 minutes and left for 30 min. After this time, it is filtered, standardized and passed to the teacher.

SCHEME OF TECHNOLOGICAL PROCESS



ANALYSIS OF FINISHED PRODUCT

Purity. The preparation must not give reactions to the salts of heavy metals.

Possible defects during the work and methods of their elimination

Possible defects during the work	Their reasons and methods of elimination
At the stage the ammonia odour is detected in bitter almond water	When obtaining hydrolysis occurred. Distillate must be delivered to the receiver where there is an alcohol
When obtaining bitter almond water from standard raw material the concentration of active substance is understated	The conditions of technological process are not followed. The connecting junctions of the installation are not sealed To strengthen bitter almond water with large amount of hydrogen cyanide
When analyzing the small drops of ether oil in aromatic water are detected	It was passed through the dry filter. To pass through the moistened filter
When obtaining bitter almond water from concentrator the turbidity of solution was observed	Conditions for dilution were violated. It is necessary to dilute the concentrate with 45% alcohol in the ratio of 1:16

Laboratory work - 4

SP X, 615. SUGAR SYRUP (SIRUPUS SIMPLEX)

Description of finished product. Transparent, colorless or slightly yellowish color thick liquid, with sweet taste, without odour. Density - 1,301 - 1,313. Refraction indicator - 1,451 – 4,454.

Packing. In well stopped up glass containers by 15 - 20 kg.

Storage. In filled up to the top and well stopped up containers in a cool, protected from light place.

Application. Corrigent agent; the base for preparing medicinal syrups.

Task

1. To prepare 250 g of sugar syrup.
2. To draw a diagram of the process.
3. To analyze the finished product.

Composition: lump sugar 64 g, water purified 36 g.

Description of initial raw material

Number of pharmacopoeia article	Technical or trade name of raw material	Content, %	Quality
PA 42-37-72	Sugar	99,8	According to PA
SP X, art 73	Water purified	pH 5,0-6,8	According to SP

TECHNOLOGICAL PROCESS

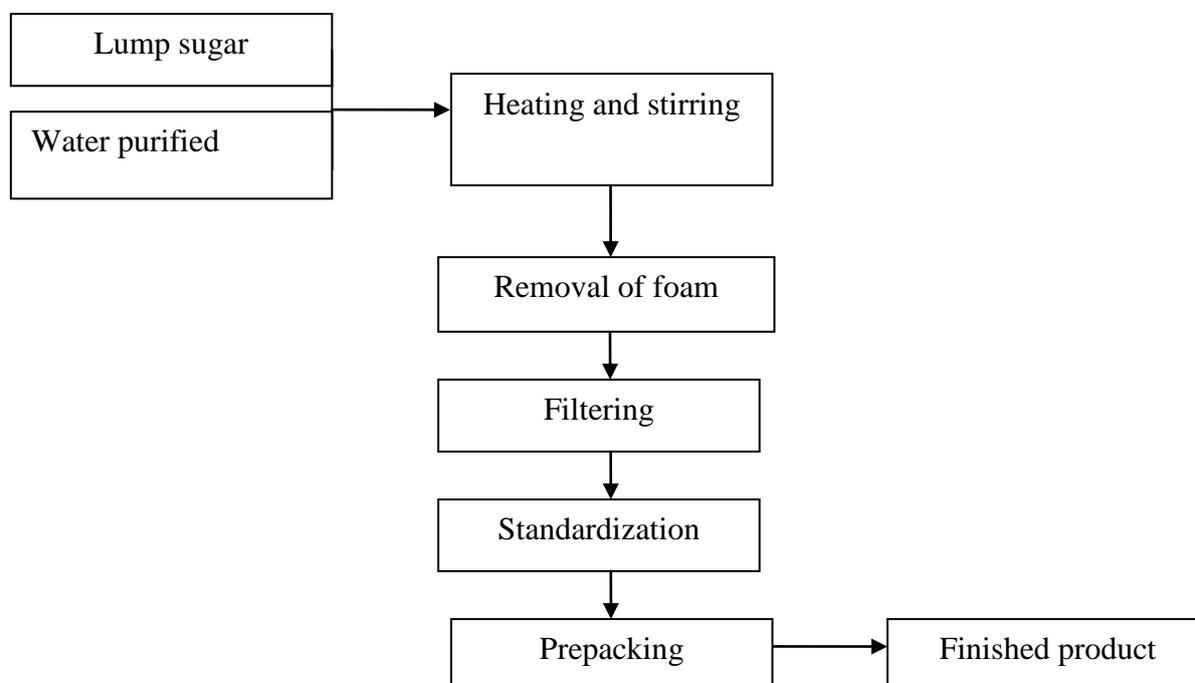
In a tared beaker or a flask with capacity of 500 ml are placed 160 g of refined sugar, added 90 g of hot distilled water. The content of the flask is stirred and put on a hotplate, stirring all the time until sugar is dissolved. Boiled for 5 - 10 min, and with boiling water is led up to 250 g of finished product. Due to the small amount of taken sugar the foam is not removed, the syrup is allowed to cool slightly and filtered hot through the 2 - 3-layer cheesecloth.

SCHEME OF TECHNOLOGICAL PROCESS

Taken

stages and operations

obtained



ANALYSIS OF FINISHED PRODUCT

Density of finished product must be 1,301— 1,313.

Refraction indicator - 1,451—1,454.

Purity. When mixing the equal volumes of syrup and alcohol there must not appear sediment or turbidity (treacle).

When adding to the preparation Feling's liquid within 5 min there must not be observed precipitation of red sediment (invert sugar).

The solution of preparation must not give reactions for chlorides, sulphates and heavy metals.

Laboratory work - 5

SP IX, art. 456. SYRUP OF GLYCYRRHIZA ROOT

(SIRUPUS GLYCYRRHIZAE)

Description of finished product. Liquid of yellow-brown color, with specific odour and taste.

Packing. In well stopped up glass containers by 15—20 kg.

Storage. In a cool, protected from light place.

Application. Expectorant and slightly laxative remedy in the form of mixtures.

Task

1. To prepare 20 g of glycyrrhiza root syrup.
2. To draw the scheme of technological process.
3. To analyze the finished product.

Composition: glycyrrhiza root thick extract 4 g, sugar syrup 86 g, ethyl alcohol 90% 10 g.

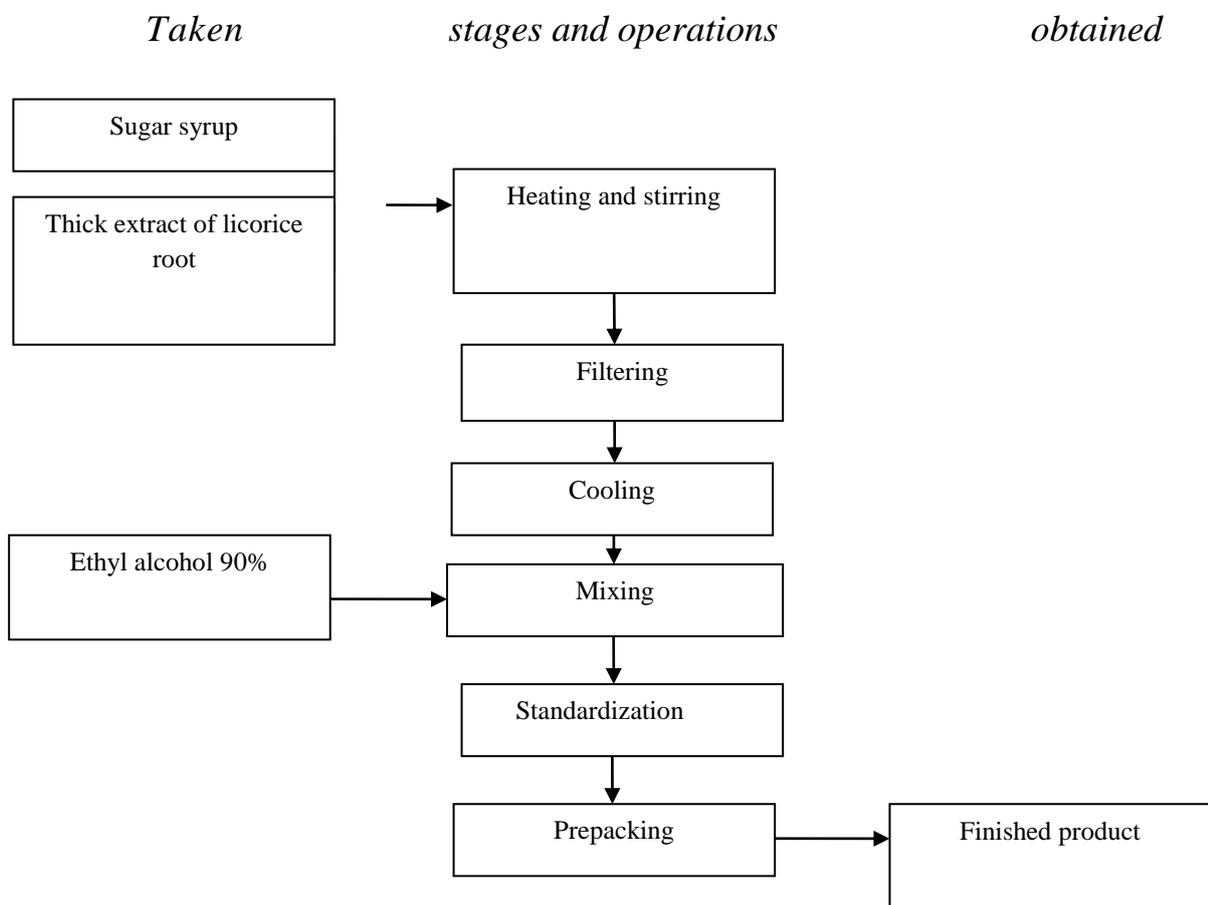
Description of initial raw material Table 8

Number of pharmacopoeia article and SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art, 261	Dry extract of licorice root	Glycyrrhizic acid not less than 14,0	According to SP
SP X, art, 615	Sugar syrup	64,0	----
SST 5962-67	Ethyl alcohol	Not less than 96,2	According to SST

TECHNOLOGICAL PROCESS

In a tared porcelain dish are weighed 17,2g of sugar syrup and 0.8 g of a thick extract of licorice root. The content of the cup at low heat on water bath is stirred with a rod until smooth mass. To the cooled mass is added 2 g (2.24 ml) of 90% alcohol and stirred again. The finished product is standardized and passed the teacher.

SCHEME OF TECHNOLOGICAL PROCESS



ANALYSIS OF FINISHED PRODUCT

Density. 1,290—1,310.

Authenticity. When shaking the preparation with water the foam is formed, it must not disappear within 1 h (saponins).

Note. The syrup must not be dispensed in mixture with acidic liquids.

Laboratory work - 6

SP IX, art. 458. RHUBARB SYRUP

(SIRUPUS RHEI)

Description of finished product. Liquid of red-brown color, with specific odour and taste; mixed with an alcohol to form a transparent solution; with water gives a clear or slightly opalescent solution.

Packing. In well stopped up jars of orange glass by 150-200 g.

Storage. In a cool, dark place.

Application. In pediatry as slightly laxative remedy.

Task

1. To prepare 50 g of rhubarb syrup.
2. To draw the scheme of technological process.
3. To analyze the finished product.

Composition: dry extract of rhubarb 1,25 g, alcohol 2 g, dill water 3 g, sugar syrup 94g

Table 9

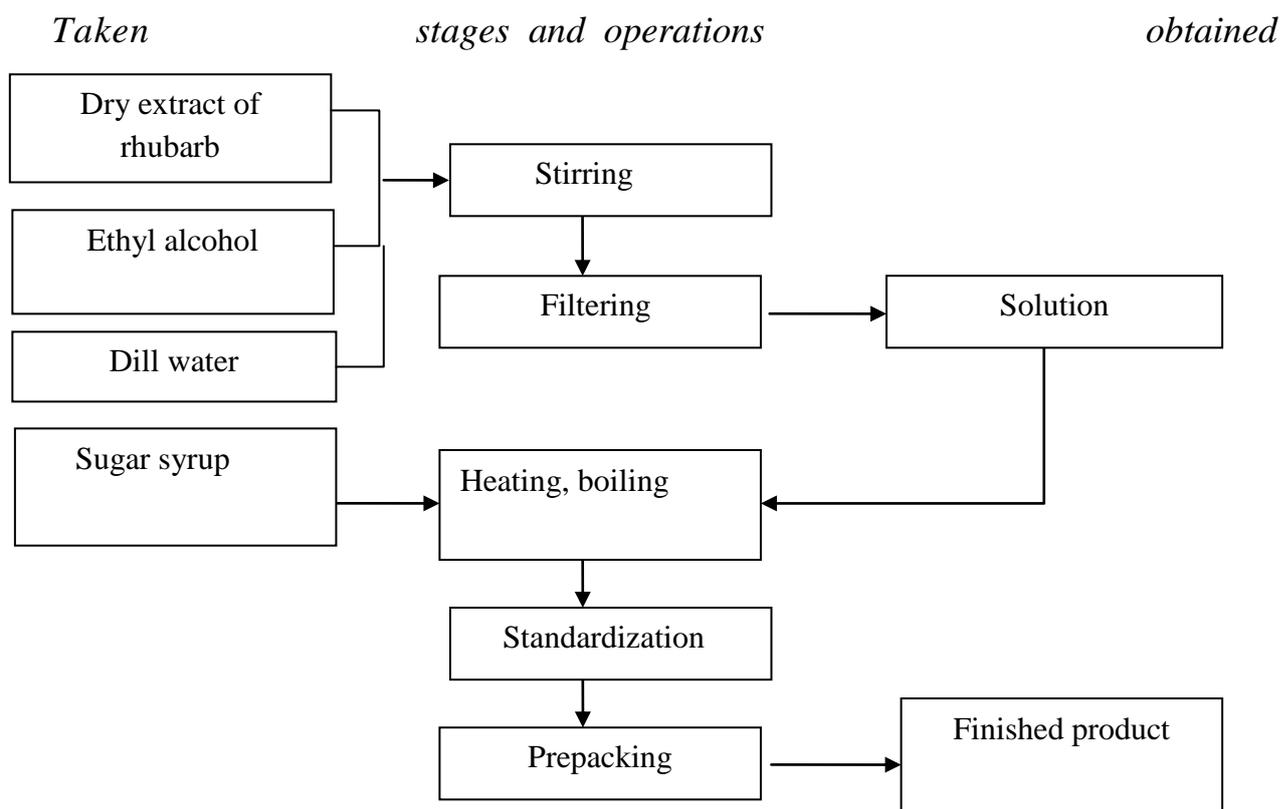
Description of initial raw material

Number of pharmacopoeial article SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art, 264	Dry extract of rhubarb	Anthracene derivatives not less than 3,0	According to SP
SST 5962-67	Ethyl alcohol	Not less than 96,2	According to SST
SP X, art. 615	Sugar syrup	64,0	According to SP
SP VIII	Dill water	-	----

TECHNOLOGICAL PROCESS

In a tared porcelain dish are placed 0.62 g of dry rhubarb extract, 1 g of ethanol, 1.5 g of dill water, stirred until complete dissolution of rhubarb extract and filtered. The filtered solution is again placed in a porcelain dish, added 47 g of sugar syrup, heated and allowed to boil. The formulation in hot form is transferred to the bottle of 50 ml and quickly sealed with a cork.

SCHEME OF TECHNOLOGICAL PROCESS



ANALYSIS OF FINISHED PRODUCT

Density 1,310—1,340.

Authenticity. Preparation is treated with ether. To ether extraction water and ammonia solution are added. For all that water layer is colored in bright cherry-red color (anthracene derivatives).

Possible defects during the work and methods of their elimination

Possible defects during the work	Their reasons and methods of elimination
In production of sugar syrup in analysis the density of 1,225 is ascertained	Sugar concentration is understated. Follow strictly SP X. Density must be 1.301-1.313
In production of sugar syrup the candying is observed	Sugar concentration is overstated. Dilute up to the density of 1,301-1,313
In production of sugar syrup the strange odour is detected	It is not followed the requirement of NTD. The syrup is prepared from nonstandard sugar

THEME: TINCTURES AND THEIR INDUSTRIAL PRODUCTION.

TECHNOLOGY FOR PREPARING VALERIAN TINCTURE

Objective: To acquire skills for the production of tinctures on the basis of theoretical knowledge on the extraction of active ingredients from plants, methods of industrial production of extraction phytopreparations.

Importance of the theme:

- To make up the technological scheme;
- To calculate the amount of raw material, extraction agent and to make up working sample;
- To prepare tinctures in model conditions;
- To make up and calculate the technical and economic balance;
- To carry out the quality control of the product;
- To design the finished product and store it according to the requirements of ND;
- To obtain the recuperator from the extracted raw material.

Tinctures are alcohol extracts from medicinal plant raw materials produced without heating removal of extractant. They are transparent colored liquids having a flavor and odor of plants from which they are prepared.

Tincture is the oldest formulation introduced into medical practice by Paracelsus (1493

- 1541), has not lost its value so far, an official at the SP XI.

Advantages of tinctures:

- comparative simplicity of preparing;
- «mildness» of action (because of presence auxiliary substances);
- Preservation of active substances in native condition;
- Convenience of use.

Tinctures are dyed liquid alcoholic or hydroalcoholic extracts from medicinal plants obtained without heating and removing extractant.

Materials: For tinctures are mainly used the dried plant material, and in some cases - fresh plant material (alcoholators of garlic, lily of the valley, valerian, hawthorn), both aboveground and underground parts.

Extractants: As extractants are used alcohol-water solutions of different concentrations - from 40% to 95%. For tinctures is accepted mass-volume ratio between raw materials and finished product. Generally, from 1 part by weight of non-potent plant raw material 5 volume parts of the finished product are obtained, and from one part of the potent - 10 volume parts.

NB! In some cases tinctures are prepared 1:10 from raw material not containing a potent substances (tincture of arnica, hawthorn, calendula) and in other ratios (mint tincture 1:20).

Tinctures are divided into simple, prepared from one kind of raw materials and compound made from various raw materials, sometimes with the addition of drugs.

According to action tinctures are classified to:

- Tinctures of general list
- Potent tinctures

For their preparation, the dried plant material is mainly used, in some cases - fresh raw material.

Preparation of tinctures

Technological scheme of production tinctures consists of several stages:

1 Auxiliary works

- 2 Extraction
- 3 Purification of extract
- 4 Standardization
- 5 Prepacking, packing, labelling
- 6 Recuperation of extractant from the processed raw material.

Grinding of raw material. It includes raw material preparation (crushing to the desired extent, sifting, weighing). Grinding of the plant material is carried out in a grinder to a varying particle size in different mills, herb cuttings, root cuttings.

Preparing of extraction agent. To carry out the extraction process, the extractant is first prepared, consisting of a mixture of alcohol and water. Alcohol concentration depends on the nature of the active ingredients contained in the plant raw material. If the raw materials contain tannins or alkaloids salts, as extractant 40% ethanol is generally used. In the presence in raw materials of glycosides 70% ethyl alcohol is used.

Extraction process. For preparing tinctures SP XI recommends the use of different methods of extraction: maceration, fractional maceration, maceration with forced circulation of the extractant, vortex extraction, percolation.

Maceration – is a statical method, as the raw material is poured over with extractant and infused within defined time.

The prepared raw material is placed in a maceration tank and poured over with calculated amount of extractant. The container is hermetically closed by a cover. It is infused at a temperature of 15-20 °C and stirring for 7 days, stirred from time to time. Then the extract is poured out, raw material is squeezed. Wrung out raw material is washed with a little amount of pure extractant and raw material is re-squeezed. Wrung out extracts are combined with the main extract and, if desired, with pure extractant is brought to desired volume, again pressed, all extracts are combined, and after infusing for 4-8 days the tincture is filtered, standardized and prepacked or packed into bottles.

Percolation refers to the dynamic methods, consists of passing through the raw material of a continuous flow of extractant, i.e. presents the process of filtering it through a layer of plant material. The extraction is carried out in vessels of various

design, called percolators.

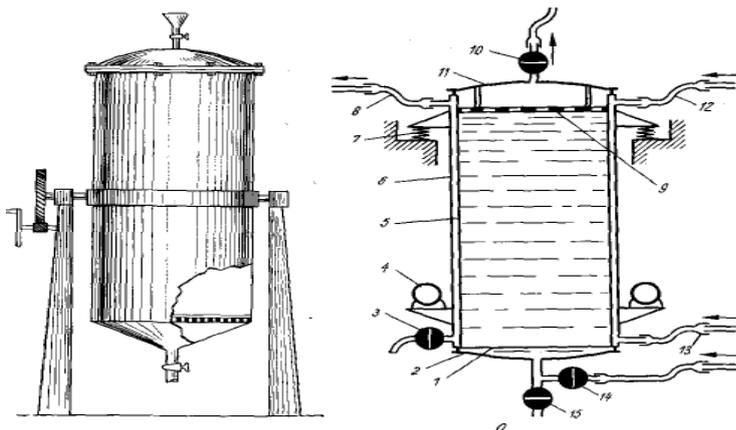


Fig.6. Percolators.

Percolators may be of cylindrical or conical form; with steam jacket or without; overturning or self-dumping.

Percolation method includes 3 serially processing stages:

- Moistening of raw material;
- infusing;
- percolation itself.

Purification of extractions

Tinctures on the degree of purification are one of the most imperfect of drugs. Extracts obtained from the extraction of raw materials, are infused in the precipitation tank at 8-10 °C within the regulated in ND time, but not less than 2 days. Low room temperature reduces the solubility of ballast substances and their precipitation.

Prepacking, packing, labelling are carried out according to the functioning orders or instructions for plants and pharmaceutical enterprises.



Fig.7. Packing of tinctures

Table 9

Nomenclature of tinctures

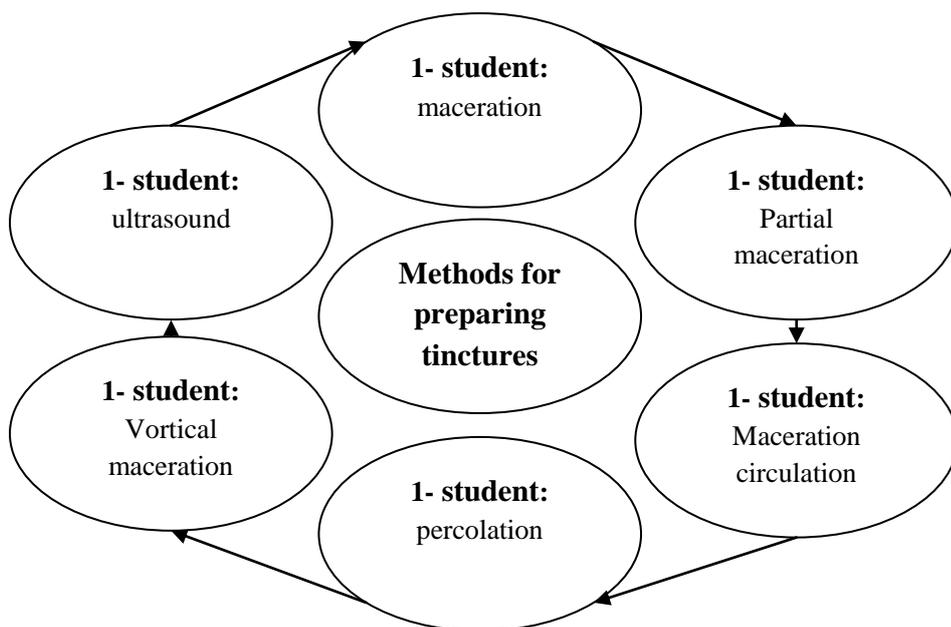
№	Raw material	Extraction agent %	Ratio of tincture's raw material	Basic active substances	Pharmacological action
1	Tincture of aralia – Tincturae Araliae				
	Aralia roots	70	1:5	saponins	tonic
2	Tincture of arnica – Tincturae Arnicae				
	Arnica flowers	70	1:10	Ether oil, caratinoids	Styptic, choleric
3	Tincture of ledum – Tincturae Ledi				
	Ledum sprouts	60	1:10	Ether oil, glycoside (arbutin)	Expectorant, antirheumatic
4	Tincture of barberries leaves – Tincturae foliorum Berberis				
	Barberries leaves	40	1:5	Alkaloids (berberin)	Obstetric-gynaecological practice in post-birth period
5	Tincture of hawthorn – Tincturae Crataegi				
	Hawthorn fruits	70	1:10	flavonoids	Cardiovascular
6	Tincture of Valerian – Tincturae Valerianae				
	Valerian roots and rhizomes	70	1:5	Ether oil	Sedative, spasmolytic
7	Tincture of ginseng – Tincturae Ginsengi				
	Ginseng roots	70	1:10	saponins	Tonic, hypertensive
8	Tincture of wolfberry – Tincturae Echinopanacis				
	Wolfberry roots and rhizomes	70	1:5	saponins	Tonic
9	Tincture of St. John's wort – Tincturae Hyperici				
	St. John's wort herb	40	1:5	Anthracene derivatives	astringent, anti-inflammatory
10	Tincture of calendula – Tincturae Calendulae				
	Calendula flowers	70	1:10	caratinoids	antiseptic
11	Tincture of belladonna – Tincturae Belladonnae				
	Belladonna leaves and herb	40	1:10	alkaloids	cholinolytic
12	Tincture of lagochylus – Tincturae Lagochili				
	Lagochylus herb	65	1:10	lagochylin, ether oil	Styptic
13	Tincture of lilly of the valley – Tincturae Convallariae				

	Lilly of the valley herb	70	1:10	Cardiac glycosides	cardiotonic
14	Tincture of magnolia vine – Tincturae Schizandrae				
	Magnolia vine seeds	95	1:5	phenolic compounds	Tonic
15	Tincture of pepper mint – Tincturae Menthae piperitae				
	Pepper mint leaves	90	1:20	ether oil	spasmolytic, choleric
16	Tincture of silk vine – Tincturae Periplocae				
	Silk vine bark	40	1:10		cardiac
17	Tincture of pepper leguminous – Tincturae Capsici				
	Pepper fruits	90	1:10	alkaloids	irritating, counter-attraction
18	Tincture of peony – Tincturae Paeoniae				
	Roots and rhizomes, herb of peony	40	1:10	alkaloids, ether oil	sedative
19	Tincture of plantain – Tincturae Plantaginis				
	Plantain leaves	70	1:10	mucus	Anti-inflammatory expectorant
20	Tincture of absinth – Tincturae Absinthi				
	Herb of bitter absinth	70	1:5	Bitter taste substances, ether oil	appetizing, choleric
21	Tincture of propolis – Tincturae Propolisi				
	Propolis (bee glue)	80	1:10	ether oil, flavonoids	Anti-inflammatory, Wound-healing
22	Tincture of motherwort – Tincturae Leonuri				
	Leonurus herb	70	1:5	flavonoids	sedative, soothing
23	Tincture of Sophora Japanese – Tincturae Sophorae japonicae				
	Sophora fruits	48	1:10	alkaloids	Wound-healing
24	Tincture of Ononis – Tincturae Ononidis				
	Ononis roots	70	1:5	flavonoids	Laxative, in haemorrhoids
25	Tincture of Sterculia – Tincturae Sterculiae				
	Sterculia leaves	70	1:5	alkaloids	stimulating, tonic
26	Tincture of strophantus – Tincturae Strophanthi				
	Strophantus seeds	70	1:10	glycosides	cardiac
27	Tincture of Veratrum – Tincturae Veratri				
	Veratrum roots and rhizomes	70	1:10	alkaloids	insecticide
28	Tincture of eucalyptus – Tincturae Eucalypti				
	Eucalyptus leaves	70	1:5	Ether oil	Anti-inflammatory
29	Tincture of Eucommia – Tincturae Eucommiae				
	Eucommia bark	30	1:5	acids	hypertensive

Control and theoretical questions:

1. General description of tinctures, methods for their obtaining, ratio of raw material and extraction agent amount.
2. Apparatus for tinctures production.
3. Technological scheme of preparing tinctures.
4. Methods of maceration, repeated maceration.
5. Methods of percolation, dissolution.
6. Techniques for intensification of tinctures production.
7. Infusion and centrifugation of tinctures.
8. Standardization of tinctures.
9. Special cases for production and particular technology of tinctures.

To explain this theme the pedagogical technology «round table» is applied



Case tasks.

Task № 1

Activity I. To calculate and obtain the required amount of raw material and extracting agent for preparing of 30 ml of Valerian tincture 1: 5, accounting the consumed and alcohol-absorption coefficients. Compose a working formulation. You must obtain 30 ml of Valerian tincture.

Tincture is prepared in the ratio of 1: 5 on 70% ethanol, alcohol-absorption coefficient for the roots and rhizomes of Valerian 1.5, consumable coefficient - 1.03. Raw material mass is 6,0g (30: 5 = 6).

1. The volume of the required extractant amount is calculated according to formula: $X=Pc \cdot K+V$, where X – required extractant amount, ml Pc – raw material mass, g. K – alcohol-absorption coefficient V – tincture volume, ml;
 $X=6,0 \cdot 1,5+30\text{ml}= 39 \text{ ml } 70\% \text{ of ethanol.}$

Accounting consumed coefficient: $39 \cdot 1,03 = 40,17 \text{ ml } 70\% \text{ of ethanol}$

2. Prepare 40,17 ml of 70% ethanol, on the basis of presence 96% ethanol.

Taking into account the properties of ethanol, the calculation is made according to:

2.1. Volume percent is converted to percent on mass 70% corresponds to 62,4%; 96% corresponds to 93,86%.

2.2. The volume of 70% ethanol is expressed in measurement on mass $M = V \cdot \rho$,

where: $M = 40,17 \cdot 0,8854 = 35,56 \text{ г.}; \rho$ – ethanol density at 20° C.

2.3. According to formula or in diagram form is determined the mass of initial ethanol (96%) in $X= P \cdot a$

where: X –mass of 96% ethanol, g.; P – mass of 70% ethanol, g

b – concentration of 70% ethanol, in % m

a – concentration of 96% ethanol, in % m,

$X= 35,56 \cdot (62,40:93,83) = 23,64.$

2.4. Amount of water is determined: $35,56 - 23,64 = 11,92 \text{ г}$

2.5. Volume of 96% ethanol:

$V = 23,64:0,8029 = 29,29 \text{ мл.}$

Activity 2. Requirement with indication of volumes of 96% and pure ethanol is written out, laboratory assistant gives ethanol, subscribed beforehand the requirement by the teacher.

Activity 3. Ethanol is diluted with calculated amount of water.

SP X, art. 694. VALERIAN TINCTURE

(TINCTURA VALERIANAE)

Description of finished product. Transparent liquid of reddish-brown color (darkens under the influence of sunlight), of characteristic aromatic odor and bitter-sweet spicy taste.

The dry residue is of at least 3%, alcohol for at least 65%, Valerian acid is not less than 0.2%.

Packing. In glass containers by 20 l and in vials by 25—50 ml.

Storage. In well stopped-up container in a cool, protected from light place.

Application. As sedative remedy nervous conditions, neurosis of cardio-vascular system, insomnia, spasms of gastro-intestinal tract. Internally by 20-30 drops 3-4 times a day.

Task

1. To prepare Valerian tincture:
 - a) according to WRIP (World Research Institute of Pharmacy) method - 25 ml,
 - б) by vortical extraction method - 100 ml.
2. To recuperate alcohol from the treated raw material by washing with water.
3. To draw the scheme of technological process.
4. To analyze the finished product.

Formulation:

Crushed roots and rhizomes of Valerian 200 g,
alcohol 70% - up to obtaining 1 l of tincture.

Table 10

Description of initial raw material

Number of pharmacopoeial article SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art 583	Roots and rhizomes of Valerian	Extraction substances not less than 25,0 Moisture not more than 15,0	According to SP
SSt 5962-67	Ethyl alcohol	Not less than 96,2	According to SSt
SP X, art 73	Water purified	pH 5,0-6,8	According to SP

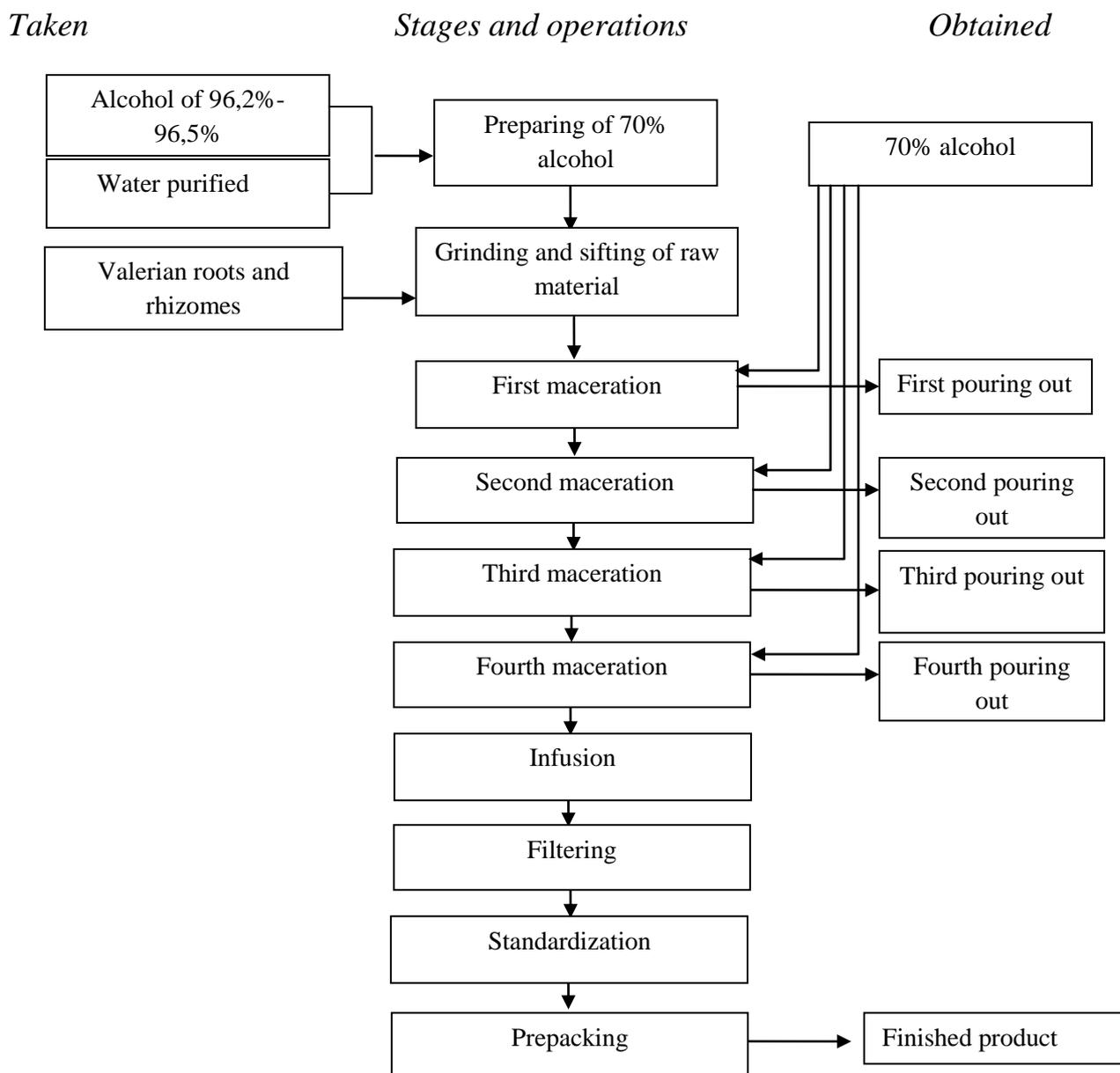
TECHNOLOGICAL PROCESS

Preparing of tincture by the method of WRIP (World Research Institute of Pharmacy)

Before starting work on the bottom of percolator is placed 3-4-layer piece of gauze to prevent clogging of the crane with raw material. The gauze is moistened with extractant.

5 grams of powdered rhizome with the roots of Valerian (1-8 mm) are sifted out of dust and evenly placed in a percolator, lightly tamping with a rod. To prevent floating of plant material is placed on top is placed a circle of filter paper or gauze wipe (4-layer) and the load in the form of porcelain pieces. To remove air from the filling materials loading percolator with extractor is carried out at a slightly open tap of percolator. The extractant is poured slowly through the wall of the percolator. The leaked liquid from the receiver is poured back into the percolator, the tap is closed and added extractant to form a "mirror" of the surface over the raw material with 1-2 cm thick. Percolator is closed with double layer of polyethylene and left for infusion within 24 hours. After this time, tincture is poured into cylinder in an amount of 1.4 parts of the total volume, that is 6.25 ml. After receiving the first drain into percolator for the second time an extractant is added to form a "mirror" of the surface. After 1.5 hours, the second drain of finished products is produced in the same amount as in the first case. Again an extractant is poured and after 1.5 hours similarly produced the third and fourth drains. All collected extracts are combined together in a stoppered flask (their amount should be 25 ml) and left for removal of roughage in a cool place (8-10 °) for 1 day. Then tincture is filtered through a dry folded filter.

SCHEME OF TECHNOLOGICAL PROCESS



Preparing of Valerian tincture by vortical method

Extract is obtained in the apparatus of “Tissues microgrinder of PT 2 type”, stirrer speed is of 3000-5000 rev/min (Fig. 20). For preparing 100 ml of tincture 20 g of powdered rhizomes with Valerian roots (1-8 mm) are placed in a beaker of apparatus and poured over with 130 ml of 70% alcohol (considering the absorption coefficient of the extractant by raw material). The mixer is turned on with speed of 5000 rev/min, and extracted for 5 minutes then turned off the apparatus and left for 10 min. Extraction is repeated four times. Thus, vortex extraction (without interruption) is performed within 25 min. Extract is poured into the cylinder through a funnel with

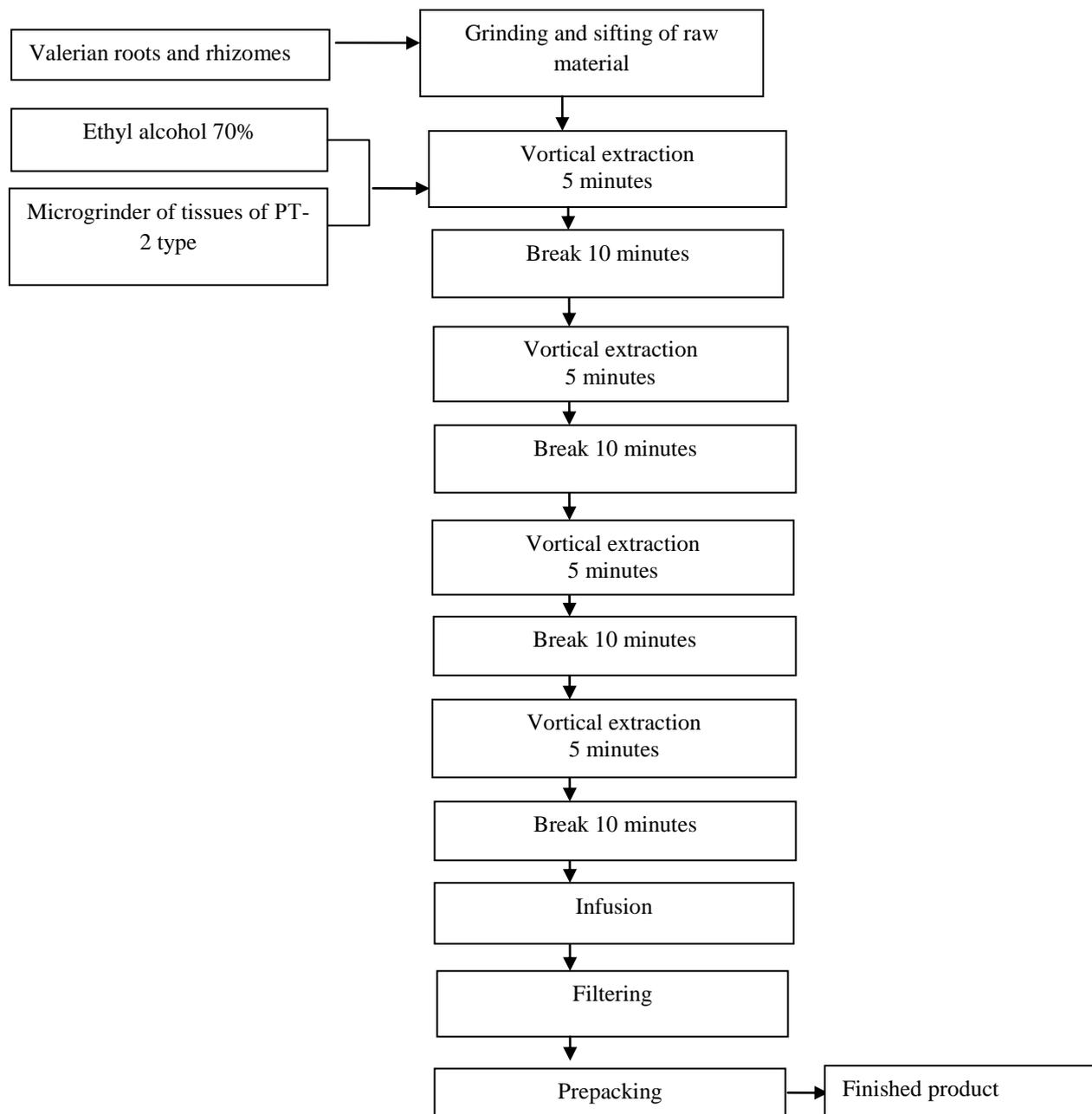
cotton, the raw material is drained through the two-layer gauze and the squeezed liquid is added to the extract. In the case of preparing tincture less than 100 ml raw material is washed with 70% alcohol, squeezed and added to the tincture. The obtained tincture is poured into the stoppered flask and allowed for removal of roughage in a cool place (8-10 °C) for 3-4 days. Then tincture is filtered through a dry folded filter into a dry flask. It is standardized and delivered as a finished product. From waste materials alcohol is recuperated.

SCHEME OF TECHNOLOGICAL PROCESS

Taken

Stages and operations

Obtained



ANALYSIS OF FINISHED PRODUCT

Dry residue should be not less than 3%.

Alcohol concentration is determined according to boiling temperature. Alcohol should be not less than 65%.

Purity. There shouldn't be heavy metals more than 0,001%.

Quantitative determination. To 10 ml of preparation 150 ml of water is added and titrated with 0,1n. of caustic soda solution (indicator - phenolphthalein, 10 drops).

1 ml 0,1 n. of caustic soda solution corresponds to 0,01021 g of Valerian acid, which in preparation must be not less than 0,2%

Laboratory work-2

SP X, art. 686. TINCTURE OF BELLADONNA (TINCTURA BELLADONNAE)

Description of finished product.

Transparent liquid of greenish or reddish-brown color, with specific odor and bitter taste. Alcohol content is less than 35%. Alkaloids (based on hyoscyamine) should be 0,027-0,033%.

Packing. In glass containers by 20 kg.

Storage. In well sealed containers in protected from light place. Letter B.

Application. As antispasmodic and analgesic in gastric ulcer, gallstones and other diseases accompanied by spasms of smooth muscles of the abdominal cavity. For internal use: adults by 5-10 drops; children – by 1-5 drops depending on age. ISD (internal single dose) for adults - 0.5 ml (23 drops). IDD (internal daily dose) for adults - 1.5 ml (70 drops)

Task

1. Prepare 100 ml of Belladonna tincture by ultrasonic extraction method.
2. Recuperate alcohol from processed raw material washing with water.
3. Draw the scheme of technological process.
4. Conduct the analysis of finished product.

Formulation:

Crushed leaves or herb of Belladonna 100 g,
alcohol 40%—up to obtaining 1 l of tincture

Table 11

Description of initial raw material

Number of pharmacopoeia article and SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art 276	Belladonna leaves	Alkaloids – not less than 0,3	According to SP
SST 5962-67 SP X, art 73	Ethyl alcohol Water purified	Moisture – not more than 13,0 Not less than 96,2 pH 5,0-6,8	According to SSt According to SP

TECHNOLOGICAL PROCESS

Preparation of tincture is carried out ultrasonic extraction method. Scoring is carried out using the USP-ZM apparatus (portable ultrasound therapeutic). For obtaining 100 ml of tincture 10 g crushed (1.8 mm) and filtered from dust raw material is placed in a crystallizer and poured over with 40 ml of 40% alcohol. A crystallizer is tightly closed on top with a glass plate and left for 3 hours. Then here is also added another 60 ml of 40% alcohol and produced ultrasonic extraction. Scoring is carried out as follows: lowering an ultrasonic horn so as it tightly touches the liquid or was slightly immersed in it – according to the following regime: intensity - 2.5 W/cm², the ultrasonic wave frequency of 800 kHz, the audio during 20 min. After this time the device is switched off.

Extraction is poured into the cylinder through a funnel with cotton wool, where on top is placed a two-layer gauze, which is placed in the raw materials, and squeezed. Squeezed liquid is added to the extract. In the case of obtaining tincture less than 100 ml raw material is washed with 40% alcohol, squeezed and added to the tincture. The resulting extract is poured into a stoppered flask and for treatment of ballast substances is left in a cool place (8-10 ° C) for 3 days. Then tincture is filtered through a dry folded filter into a dry flask, standardized and delivered as a finished product.

ANALYSIS OF FINISHED PRODUCT

Authenticity. After evaporation of drug to the dry residue is added alcohol solution of caustic soda and acetone, a violet color is appeared (atropine).

Availability chrisothropic acid (as opposed to the tincture of henbane) is proved on blue fluorescence and UV light by adding ammonia solution.

The concentration of alcohol is determined by the boiling point. The alcohol content should be not less than 35%.

Purity. Heavy metals should be not more than 0,001 %

Quantitative determination is carried out by neutralization method on excess of alkaloids content on account of hyosciamin should be 0,027-0,033%.

SP X, art. 685. TINCTURE OF ABSINTH

(TINCTURA ABSINTHII)

Description of finished product. Transparent liquid of brownish-green color, with characteristic odor and bitter taste. A mixture of 2 ml preparation with 1 ml of water gives a turbid solution. The dry residue is of at least 3%, alcohol not less than 64%, the rate of the bitterness not less than 1: 4000.

Packing. In glass bottles by 18 kg and in vials by 15, 25 and 50 ml.

Storage. In well sealed bottles and vials, in protected from light place.

Application. As aromatic bitterness to excite the appetite and increase activity of the digestive organs by 10 to 20 drops 2-3 times a day for half an hour before meals.

Task

1. Prepare 50 ml of absinth tincture by the method of centrifugal extraction.
2. Draw the sheme of technological process.
3. Recuperate alcohol from processed raw material
4. Conduct the analysis of finished product.

Formulation:

Crushed absinth herb 200 g,

Alcohol 70% - up to obtaining 1 l of tincture.

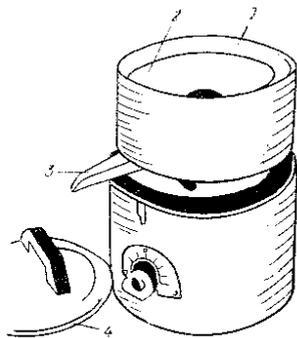
Table 12

Description of initial raw material

Number of pharmacopoeia article and SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art 232 SST 5962-67 SP X, art 73	Herb of absinth bitter Ethyl alcohol Water purified	moisture – not more than 13,0 Not less than 96,2 pH 5,0-6,8	According to SP According to SST According to SP

TECHNOLOGICAL PROCESS

Centrifugal extraction method is based on using of as much as possible crushed materials (particles size of 0.25 mm or less) followed by separation of extract on juicer of type CB-1 (drum rotation speed of 3000 rev/min)

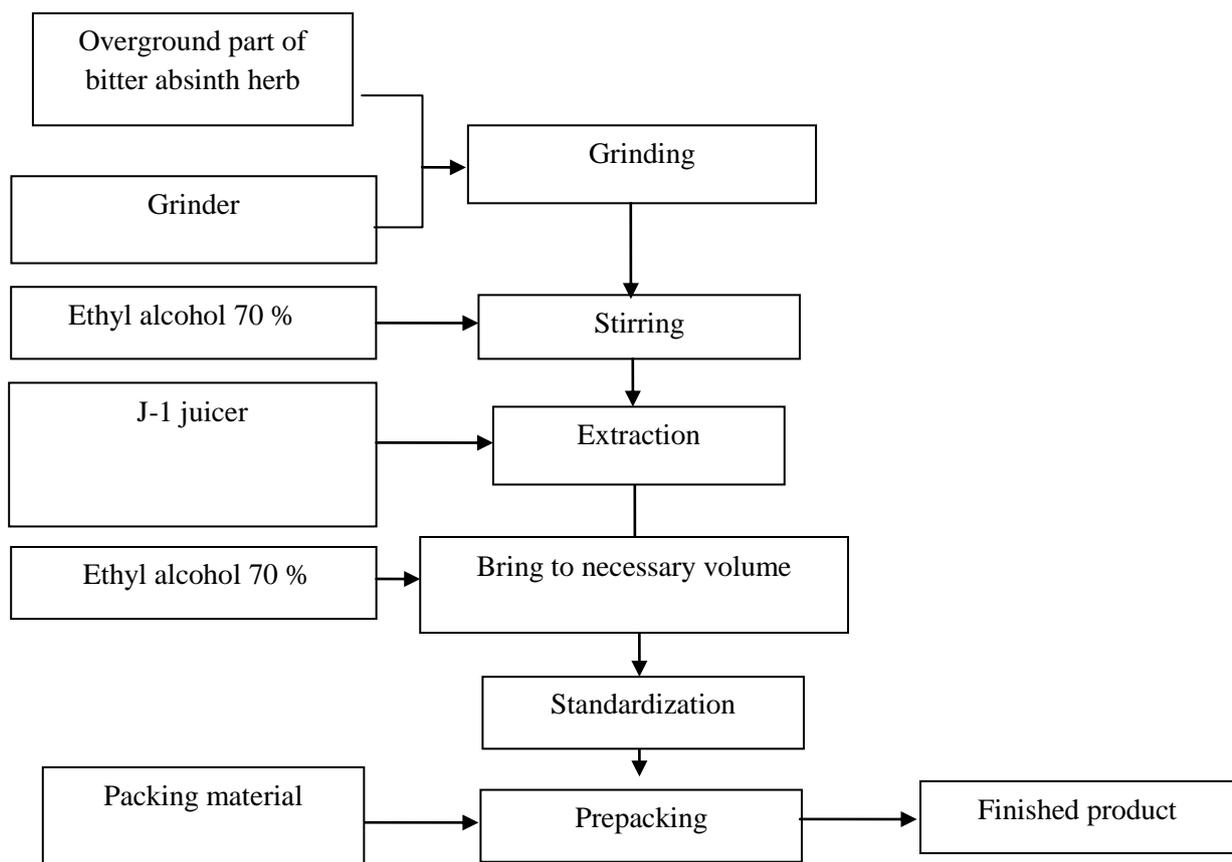


To the grinder is placed 10 grams of bitter absinth herb and turn it on for 45 seconds. This yields to herb powder containing about 70% of particles smaller than 0.25 mm and 30% of particles - larger than 0.25 mm. Then the grinded raw material is poured in a beaker of 100 ml, poured over with 65 ml of 70% alcohol, stirred with a rod and left unopened for 5 min for infusing.

After that the contents of the beaker is stirred again and transferred into a vessel of juicer with filter uniformly laying for preventing vibration of apparatus during rotation of the rotor, and then closed with lid and turned on for 30 sec.

Extract is collected into a beaker through the pouring spout of juicer, volume is measured, poured into a bottle and left for 1 day in a cool place (8-10 ° C) and then filtered through a dry folded filter, standardized and delivered as a finished product.

SCHEME OF TECHNOLOGICAL PROCESS



ANALYSIS OF FINISHED PRODUCT

Authenticity. Preparation with concentrated sulphuric acid forms brownish-red color, turning into violet when adding alcohol (glycosides absinthin and anabsinthin).

Dry residue. It should be not less than 3%.

Alcohol concentration is determined on boiling point of tincture, preparation should contain alcohol not less than 64%.

Purity. Heavy metals should be not more than 0,001 %.

Determination of bitterness. 1 ml of preparation is diluted with water up to 100 ml, 1 ml of the obtained solution is diluted with water again up to 40 ml, 10 ml of this solution at slow mouthwashing causes bitterness (dilution 1:4000).

Possible defects in work and ways of their elimination

Possible defects in work	Reasons and methods of their elimination
The obtained tincture is very turbid, doesn't undergo on transparency	Modern accelerated extraction methods were applied (turboextraction, forced extraction and etc.) To prolong time of infusion at temperature of 8-16 ⁰ C and filter through the thick filter layer – cloth
In production of tinctures the extractant is consumed over the norm	Raw material was soaked beforehand or poorly packed in percolator. It is necessary to pack it and observe during percolation the constancy of «mirror level» over raw material.
At stage control in mint tincture, 4% of ether oil is detected	Lowed concentration of active substance. Bring up to the norm of (5%) according to calculation

Task

1. Calculation of raw material and extractant for preparing tinctures

Calculating of medicinal plants amount, 95% ethanol and purified water to prepare tinctures is carried out on the basis of the correlation between the raw material and the extraction and the formula for calculating the volume of extracting agent.

Calculation example

To calculate the amount of raw material and extractant necessary for preparing 300 l of Belladonna tincture.

Solving the task:

Tincture of Belladonna is prepared at the ratio of 1:10, i.e. from 1 mass part of raw material are obtained 10 volume parts of tincture. An extractant is 40% ethanol, the amount of which is calculated on the account of coefficient of raw material alcohol-water-absorption – $K=2$.

1. The amount of raw material is calculated:

1.0 of Belladonna herb - 10 ml of tincture

x of Belladonna herb - 300 ml of tincture $x = 30$ kg

2. The amount of 40% ethanol is calculated:

V of extractant = $300 \text{ l} + 30 \text{ kg} \times 2 = 360 \text{ l}$

3. It is calculated the amount of 95% ethanol according to the formula of dilution alcohol:

$$x = V * \frac{b}{a}, \text{ where, } V - \text{tincture volume};$$

b – concentration of alcohol in tincture;

a – concentration of strong ethanol.

$$x = 360 * \frac{40}{95} = 151,6$$

4. It is calculated the amount of purified water necessary for preparing 40% ethanol from 95% according to alcoholmetric table №3 (SP XI, ed. 1): from table №3: to 1000 ml of 95% ethanol is necessary to add 1443 ml of purified water in order to obtain 40% alcohol. The proportion is:

1l of 95% ethanol– 1,443 l of purified water

151.6 l of 95% ethanol - x l of purified water

$$x = \frac{151,6 * 1,443 \text{ л}}{1 \text{ л}} = 218,7 \text{ л}$$

Thus, to prepare 300 ml of Belladonna tincture it is necessary to take: 30 kg of Belladonna herb, 151.6 l of 95% ethanol, 218.7 l of purified water.

Tasks for self-study work

1. To calculate the amount of raw material and extractant for preparing 120 l of lily of the valley tincture, if alcohol-absorption coefficient is equal to 1,9. To solve this task it should be taken into account: 1 – the ratio in which lily of the valley tincture is prepared 1:5, 1:10 or others (depending on nature of active substances); 2 - extractant and its concentration; 3 – total volume of extractant is summed from the volume of tincture (in this task 120 l) and ethanol, retained by raw material. 4 – amount of water and 96% ethanol is calculated according to the tables of SP-XI or by calculation method.

2. To calculate the speed of percolation in drops per 1 minute, if the diameter of percolator is 5 cm, the height of working volume is 14 cm, and 1 ml of percolate contains 40 drops.

To solve this task it should be taken into account:

1 – working volume – the volume, taken by raw material and extractant;

2 – calculation formula of percolation speed: $V = \Pi \cdot r^2 \cdot h / 24 \cdot 60$.

3 – obtained result, ml/min – to calculate in drops.

3. It was obtained 150 l of Valerian tincture containing extraction agents of 6% and 2%. Bring the tincture up to the norm - 3%. The task is solved by analogy to solutions – according to calculation formula of "cross" ("star").

5. To calculate the mass of raw material and extractant amount for preparing of 500 l of Valerian tincture from 95% ethanol (K – 1.3).

6. To calculate the mass of raw material and extractant amount for preparing of 350 l of Leonurus tincture from 95% ethanol (K – 2).

7. To calculate the mass of raw material and extractant amount for preparing of 300 l of lily of the valley tincture from 95% ethanol (K – 2.5).

THEME: EXTRACTS. LIQUID EXTRACTS AND THEIR PRODUCTION.

TECHNOLOGY FOR PREPARING LIQUID EXTRACT OF ORIGANUM

Objective: On the basis of theoretical knowledge about obtaining concentrated extracts from medicinal plants, methods of industrial production to acquire skills for the production of liquid extracts.

Importance of the theme:

- To prepare liquid extracts in laboratory conditions according to normative documentation;
- To make up technological scheme for obtaining extracts;
- To calculate the amount of raw material, extractant, to make up the working formulation;
- To prepare liquid extracts in model conditions;
- To obtain and use intermediate products in production;
- To carry out quality control of intermediate and finished product;
- To make up technical-economic balance;
- To design finished products and store it according to ND;

Extracts (*Extracta*) are called concentrated liquid or concentrated by partial or complete removal of the aqueous extractant, hydroalcoholic, alcoholic or ether extracts of biologically active substances of vegetable origin, which are mobile, viscous liquids or dry mass. Extracts form a significant group of galenic preparations.

Classification of extracts. Depending on the amount of the left extractant the extracts of various consistences are obtained:

1. Liquid extracts (*Extracta fluida*), which are liquid concentrated extracts containing extractant – alcohol in the initial concentration;
2. Thick extracts (*Extracta spissa*), which are very viscous liquids usually not pouring out of the vessel, but spreading out in fibers; contain up to 25% of moisture (in some cases - up to 35%).
3. Dry extracts (*Extracta sices*), which are powders or light spongy masses, easily turning into powder; contain up to 5% of moisture.

According to extractant's origin, with the help of which was produced the extraction of biologically active substances, extracts are divided into:

1. Water extracts (*Extracta aquosa*) preparing with the help of water;
2. Alcoholic extracts (*Extracta spirituosa*) preparing with the help of strong or diluted ethyl alcohol;
3. Ether extracts (*Extracta aetherea*) preparing with the help of ethyl ether.

Liquid extracts can be only alcoholic; others can be both alcoholic and hydrous. There are also ether extracts among thick extracts.

Liquid extracts (EXTRACTA FLUIDA) are liquid concentrated extracts from medicinal plants. For their preparation the dried plant raw material and extractant are used. As the extractant only ethyl alcohol of different concentrations is used. Liquid extracts are prepared in the ratio of 1:1, i.e. from one part by weight of not strong effective plant raw material one volume portion of extract is obtained. Liquid ethanol extracts are prepared by methods: percolation repercolation, swift repercolation. The most common method in repercolation is modification of N.A.Chulkov. Liquid extracts are made with 70% ethanol, 40% ethanol (extracts of Viburnum, nettle, burnet, milfoil). With 20-30% ethanol extracts of Bergenia, brotherwort, thyme are obtained. In the production of some liquid extracts (sage, thyme) glycerin is added to ethanol as a peptizing agent, also reducing the surface tension.

However, the liquid extracts are not without serious disadvantages. First of all they are:

1. Their saturation with ballast substances extracted from plant raw material; such a circumstance is the reason of precipitation in liquid extracts at low decreasing of temperature and the partial evaporation of the alcohol;
2. For this reason they require hermetic sealing and storage at a temperature of 15-20 °C. The latter condition is especially difficult to meet during transportation;
3. Liquid extracts contain large amounts of extractant. Dry residue, i.e. the amount of extractants in them can reach 25%. Thus, liquid extracts (although less than the tinctures) are low transportable drugs, especially when taking into account that they are stored and transported in glass bottles. Extract is obtained by officinal (percolation, repercolation and dissolving of dry extracts) or non-officinal methods (WRIP method, vortex extraction, maceration-circulation and subsequent compressing of raw material).

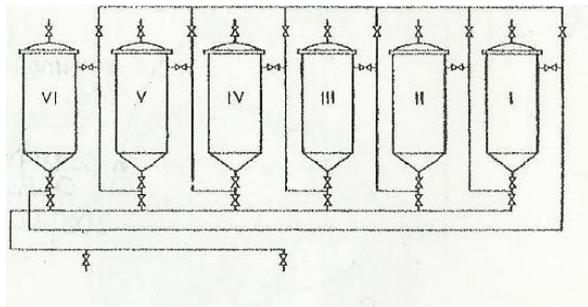


Fig.8. Battery of percolators

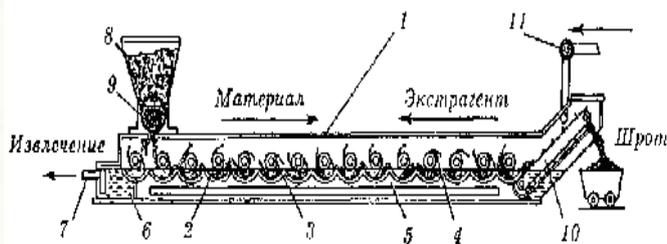


Fig.9. Spring- paddle extractor

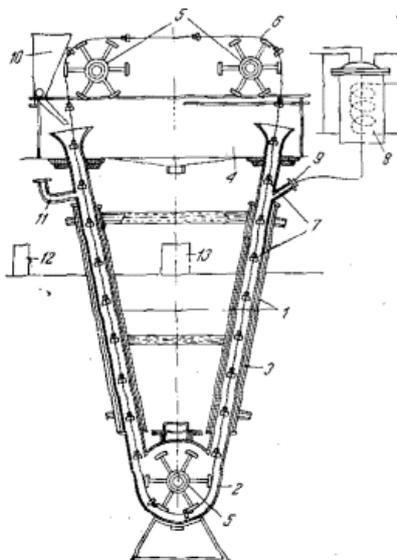


Fig.10. Scheme of disk extractor

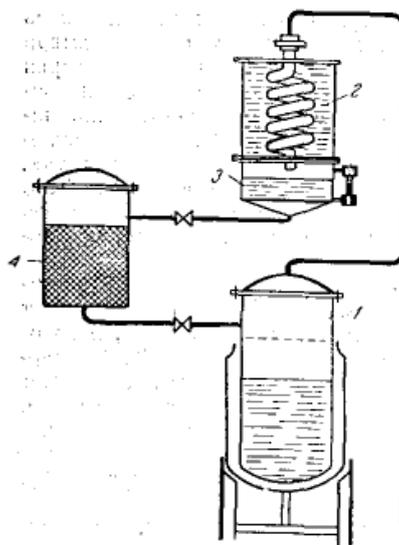


Fig.11. Scheme of circulation apparatus of Soxlet type

Purification of liquid extracts. For this group of drugs, as well as for tinctures the infusing method is used. Extract is infused at a temperature of not higher than +8°C for at least 2 days. At lower temperature the solubility of the substances which are needed to be isolated by infusing is decreasing, slows down the evaporation process of the infused liquid, less of microflora is developed there. Proteins, mucus, crushed colloids and other oxidation products are removed. The infused liquid is poured out from the precipitate by a siphon, with a centrifugal pump, to the end of the suction hose filter- fungus is put on. For the filtration of large quantities of extraction druck-filters, filter-presses are used. Liquid extracts are standardized in appearance, active ingredients and numerical indicators. The taste, color, odor of liquid extract must be characteristic for initial raw material.

Control and theoretical questions:

1. Description of extracts as medicinal form. Classification on consistence and used extractant.

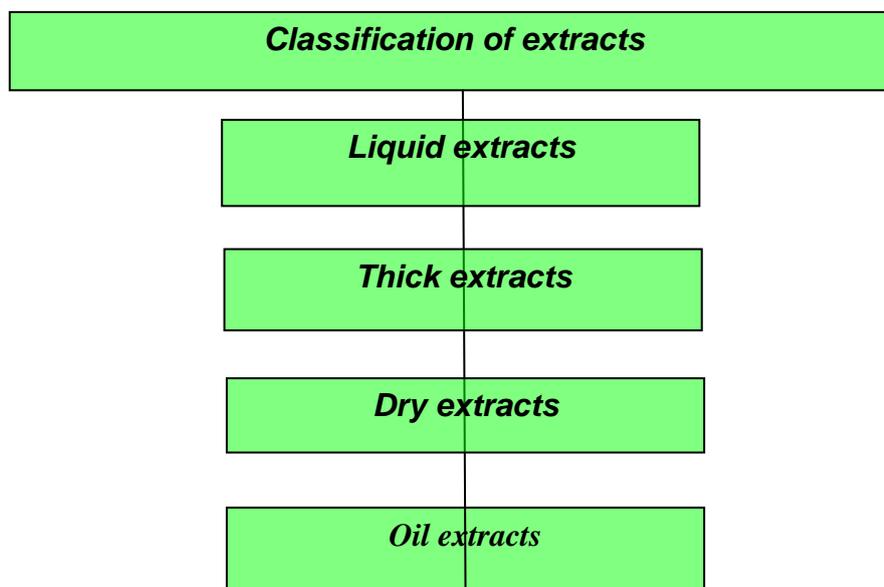
2. Liquid extracts. Preparing methods. Percolation method. Repercolation method according to the method of N.A.Chulkov. Method of swift repercolation.

3. Continuous extraction. Screw device of Bukharov. Vertical screw device. V-shaped device of Natradze-Ryazanceva. Spring-paddle extractor (for tinctures). Extractor (vortical extraction). Extractor with the use of ultrasound.

4. Purification of initial extracts. Standardization of liquid extracts. Organoleptic analysis. Determination of content of active substances.

5. Determination of dry residue. Determination of ethanol content. Determination of heavy metals.

For conduction this practical lesson pedagogical technological method «Cluster» is applied



Case tasks:

Action 1. To calculate and obtain the necessary amount of raw material and extractant for preparing May rose liquid extract of 1:1 60 ml.

1. Liquid extracts are prepared in the ratio of 1:1, to prepare 60 ml of liquid extract is required 60,0 g of May rose bark, crushed up to the size of 1-3 mm and

fourfold amount of 50% ethanol (by volume related to raw material mass). The required ethanol volume 50% $y=60 \times 4=240$ ml.

2. To prepare 240 ml of 50% ethanol based on the presence of 96% ethanol.

Taking into account ethanol properties, the calculation is produced as follows:
The concentration from volume percent is converted to percent by mass.

50% corresponds to 42,50% m

96% corresponds to 93,86% m

The volume of 50% ethanol in measuring on mass is expressed using the formula:

$$P = V \cdot \rho_{20} \quad \text{where: } P - \text{mass, g; } V - \text{volume, ml; } \rho_{20} - \text{density at } 20^{\circ}\text{C.}$$

$$P = 240 \times 0,9300 = 223,20 \text{ g.}$$

According to the formula or graphically the mass of initial ethanol is determined:

$$x = \frac{b}{a} \cdot P$$

where: x – the mass of 96% ethanol; P – the mass of 50% ethanol, g; b – the concentration of 50% ethanol in % m; a – the concentration of 96% ethanol in % m

$$x = \frac{42,5}{93,86} \cdot 223,2 = 101,06 \text{ g}$$

Water amount is determined: $223,20 - 101,06 = 12,14$ g.

2.5. The mass of 96% ethanol is converted to volume:

$$V = \frac{P}{\rho_{96}} = \frac{101,06}{0,8874} = 125,16 \text{ ml}$$

Action 1. The requirement with indication of extract's name, amount, concentration of extractant and volume amount of 96% and pure ethanol is written out. The requirement is signed by the teacher and ethanol is taken from the laboratory assistant.

Action 2. The dilution of alcohol is produced with calculated amount of water.

Laboratory work - 1

**SP X, art. 258. LIQUID BUCKTHORN EXTRACT
(EXTRACTUM FRANGULAE FLUIDUM)**

Description of finished product. Liquid of dark-brown-red color, in the thin layer transparent, of bitter taste. Anthracene derivatives content is not less than 1,2%. Alcohol content is not less than 54%.

Packing. In glass containers by 20 kg or in bottles of 30 ml.

Storage. In well sealed vessels, in protected from light place at 12-15°C.

Application. Liquid buckthorn extract is recommended as laxative remedy by 20-40 drops for single dose. Pharmacological action of anthraglycosides is based on their decomposition in large intestine and strengthening of peristalsis that is why laxative action is moderated and manifested after 8-10 hours after taking the preparation.

Task

1. To prepare 25 ml of liquid buckthorn extract by percolation method.
2. To recuperate alcohol from the processed raw material.
3. To draw the scheme of technological process.
4. To conduct the analysis of finished product.

Formulation:

Crushed buckthorn bark 1000 g,

70% alcohol – up to obtaining 1 l of extract.

Table 13

Description of initial raw material

Number of pharmacopoeia article and SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art. 183	Buckthorn bark	Extractants not less than 20,0 moisture not more than 15,0 anthracene derivatives content not less than 4,5	According to SP
SSt 5962-67 SP X, art 73	Ethyl alcohol Purified water	Not less than 96,2 pH 5,0-6,8	According to SSt According to SP

TECHNOLOGICAL PROCESS

25 g of bark, crushed up to a particle size of 3 mm and filtered from dust is placed in a glass jar with a ground-in stopper, moistened with 50 ml of 70% alcohol, thoroughly mixed and allowed to swell for 4 hours. Then, at the bottom of the glass percolator is placed 3-4-layer piece of gauze and placed on it firmly swollen bark, tamping with a glass rod, on top put a circle of filter paper with a load. To remove the air contained between the particles of raw materials, the drain valve is opened and the extractant is quickly poured on the wall of percolator, the leaked liquid from the receiver is poured back into the percolator. The tap is closed and added with extractant up to the "mirror" surface over the raw material with thickness of 1-2 cm. The percolator on the top is closed with double layer of polyethylene and left for infusion for 24 hours. After this time, the percolation with the calculated rate is started.

Extraction is carried out into 2 receivers. The first is filled with 85% of percolate, calculating from the mass of taken raw material:

$$\begin{array}{l} 25\text{g} \underline{\hspace{2cm}} 100\% \\ X \underline{\hspace{2cm}} 85\% \end{array}$$
$$X = \frac{25 * 85}{100} = 21,25\text{мл}$$

The collected extract is poured into a glass bottle with a ground-in stopper and made the inscription "percolate number 1". In the second receiver is collected the extraction without taking into account the volume of the resulting percolate, until complete bottoming of raw materials. Extraction in the second flask is transferred to a distillation flask and distilled alcohol. The aqueous residue is evaporated in a vacuum-evaporator device up to a thick consistency and after cooling mixed with the first percolate. The resulting extract is poured into a graduated cylinder, measured the volume and adjusted up to 25 ml with 70% alcohol. The prepared liquid extract is left for 5-6 days at a temperature of 8 ° C for the removal of ballast substances and filtered through a dry pleated filter. The alcohol is recuperated from the spent raw materials washing with water.

ANALYSIS OF FINISHED PRODUCT

Authenticity. 0.5 ml of the drug is mixed with 1 ml of alcohol and 10 ml of water, boiled for 1 minute, filtered after cooling. When shaking the filtrate with ether, the ether layer is colored in intense yellow color (chrisophanic acid). In processing the ether layer with ammonia solution the aqueous layer is colored in an intense cherry-red color and ether - does not change its color (oximethylantrachinons).

Alcohol content is determined according to the distillate. Alcohol should be not less than 54%.

Purity. Heavy metals should be not more than 0,01 %.

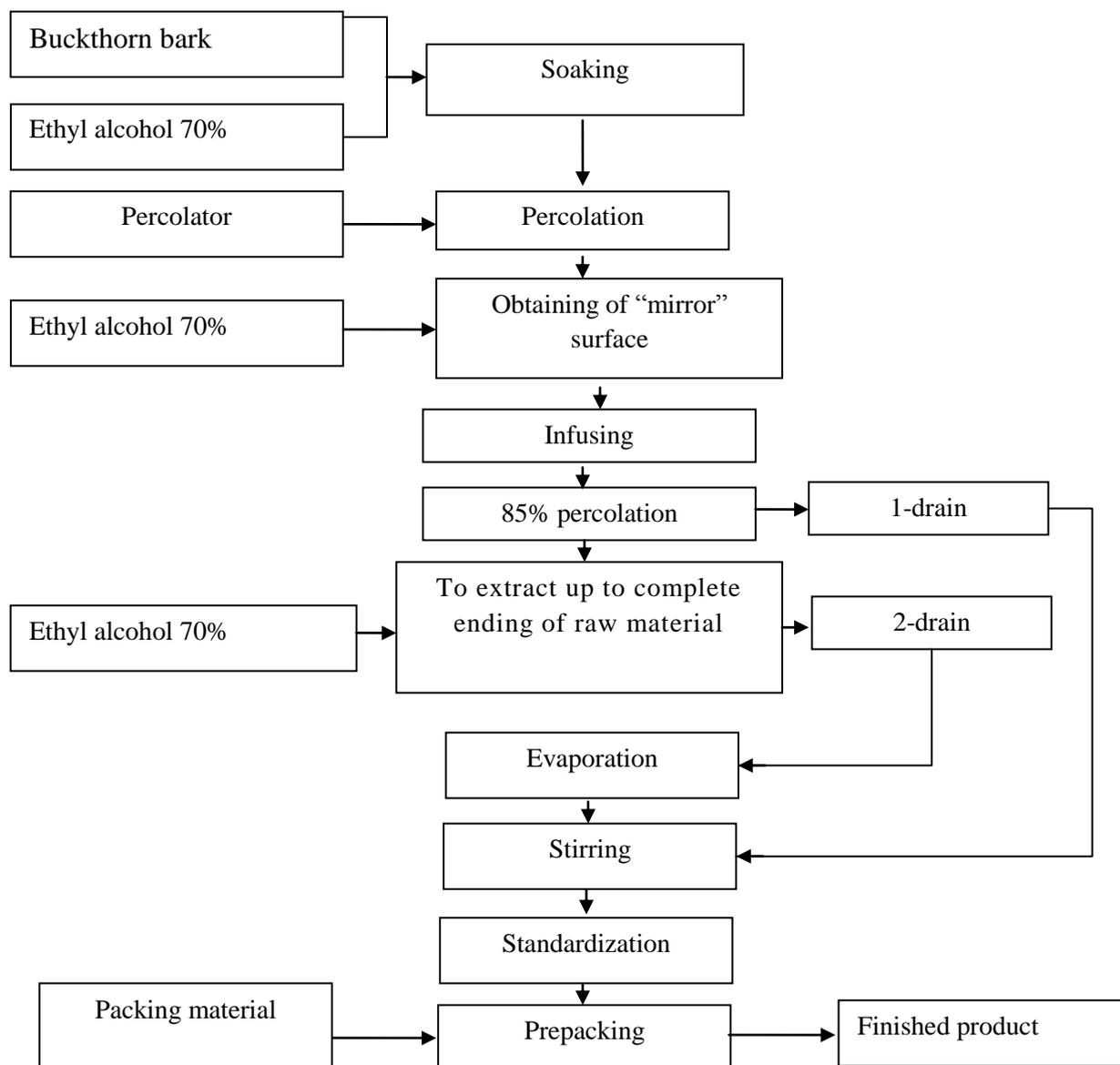
Quantitative determination is carried out by photoelectrocolorimetric method. The content of anthracene derivatives in the formulation should be at least 1.2%

SCHEME OF TECHNOLOGICAL PROCESS

Taken

Stages and operations

Obtained



Laboratory work -2

SPX, art. 266. LIQUID EXTRACT OF VIBURNUM (EXTRACTUM VIBURNI FLUIDUM)

Description of finished product. Transparent liquid of red-brown color, with specific odour, bitter taste.

Content of tanning substances is at least 4%, dry residue -13%, alcohol - 45%.

Packing. In glass containers by 15— 20 kg or in bottles by 10 ml.

Storage. In a dark cool place, at temperature not higher 12°C.

Application. As styptic remedy, mainly in uterine bleedings. Internally by 20 - 40 drops 3 - 4 times a day.

Task

1. To prepare 60 ml of Viburnum liquid extract by vortical extraction method.
2. To draw the scheme of technological process.
3. To conduct the analysis of finished product.

Formulation:

Crushed bark of Viburnum 1000 g,

Ethyl alcohol 50% - up to obtaining 1 l of extract.

Table 14

Description of initial raw material

Number of pharmacopoeia article and SSt	Technical or trade name of raw material	Content, %	Quality
SP X, art 183	Viburnum bark	Tanning substances not less than 4,0, extractants – not less than 18,0, moisture – not less than 14,0	According to SP
SSt 5962-67 SP X, art 73	Ethyl alcohol Purified water	Not less than 96,2 pH 5,0-6,8	According to SSt According to SP

TECHNOLOGICAL PROCESS

The extraction is obtained in the device «Microgrinder of tissues PT-2» (rotation speed of mixer 3000 - 5000 turn/min). To obtain 60 ml of finished product 60 g of Viburnum bark are divided into 4 equal parts by 15 g. Into the glass of device is poured 150 ml of 50% alcohol (taking into account absorption coefficient) and 15 g of cut into pieces Viburnum bark (grinding degree up to 3 mm). The mixer is turned on with speed of 5000 turn/min and extracted within 5 min then the device is turned off and left for 10 min. After some time the extract is poured out, raw material is placed in double-layer gauze tissue, wrung out and toster is thrown out. The obtained extract again poured into the glass of device, placed 15 g of raw material and repeated the above-listed operation three times, each time with new portion of Viburnum bark.

After fourfold treatment of raw material the finished extract is obtained in the amount equal to the mass of treated raw material, i.e. 60 ml.

The obtained extract is left in a cool place within 6 days and filtered through the dry

folded filter. From the treated raw material alcohol is recuperated washing with water.

ANALYSIS OF FINISHED PRODUCT

Authenticity. When the preparation diluted with water (1:10) residue of orange color precipitates, which then is filtered. To one part of filtrate is added 1 drop of solution of iron oxide chloride – green color appears (tanning substances).

To another part of filtrate is added 1 drop of ammonia solution – red color appears (anthracene derivatives).

Dry residue should be at least 13%.

Alcohol content is determined according to distillate. Alcohol should be at least 45%.

Purity. Heavy metals should be at least 0,01%.

Quantitative determination. 5 ml of preparation is placed into measured flask with capacity of 50 ml and brought the volume with 50% alcohol up to the mark. 5 ml of the obtained solution is placed into the flask with capacity of 1 l, added pipette 10 ml of indigocarmine solution and 750 ml of water, stirred and titrated with 0,1 n. solution of potassium permanganate up to converting of dark-blue color of solution through dark-blue-green to light-golden-yellow. Parallel the control experiment is carried out. 1 ml of 0,1 n. potassium permanganate solution corresponds to 0,04157 g of tanning substances which in preparation should be at least 4%.

Laboratory work - 3

PA-42-241-72. THYME LIQUID EXTRACT

(EXTRACTUM SERPILLI FLUIDUM)

Description of finished product. Liquid of brown color, of bitter taste, with specific odour of thyme.

Dry residue is at least 8%, alcohol content - 22%.

Packing. In glass containers by 20 kg.

Storage. In a cool place protected from light. Shelf life - 1 year.

Application. As an expectorant, and also as analgesic in radiculitis and neuritis.

Extract is in the composition of «Pertussin» preparation.

Task

1. To prepare 30 ml of thyme liquid extract by the method of WRIP (World Research Institute of Pharmacy).
2. To draw the scheme of technological process.
3. To conduct the analysis of finished product.

Formulation:

Crushed herb of thyme 1000 g,
 glycerine 100 g,
 alcohol 30% — up to obtaining 1 l of extract.

Table 14

Description of initial raw material

Number of pharmacopoeia article and SSt	Technical or trade name of raw material	Content, %	Quality
OSt 4338 SP X, art 73 SST 5962-67 SST 7482-55	Thymus herb Purified water Ethyl alcohol Glycerine	pH 5,0-6,8 Not less than 96,2 Density not less than 1,2584	According to OSt According to SP According to SST -----

TECHNOLOGICAL PROCESS

30 g of ground thyme herb (particle size 3 mm) is divided into equal portions and charged to three numbered percolators by 10g each. On its bottom a piece of 3 - 4-layer gauze is put. Raw is tamped with a glass rod, placed on top a circle of filter paper and a weight. The first percolator is filled with extractant (30% alcohol containing glycerine) to form a "mirror" surface, displaced air trapped between particles of raw materials, and infused for 2 hours. The extract is decanted and poured with it the raw material of the second percolator. The first percolator is filled with extractant up to "mirror" surface. After displacing the air, both percolators are infused for 2 hours. After this time, the extraction from the second percolator is transferred to the third, from the first - to the second, and to the first is poured a new portion of extractant up to "mirror" surface. All three percolators are left until the next day. Then from the third percolator is obtained the first portion of finished product which is 1/3 component of

the total volume of the finished extract, that is 10 ml.

Extraction from the second percolator is transferred to a third, from the first - to the second and the first is disconnected from the battery. The second and third percolators are left for 2 hours. After the specified time from the third percolator the second portion of the finished product in the amount of 10 ml is collected. Extraction from the second percolator is transferred to the third and left for 2 hours. The second percolator is cut off. Then the last portion of the finished product - 10 ml is collected. All three portions are combined and for purification of ballast substances are left in a cool place for a day. Then they are filtered through a dry pleated filter.

Alcohol is recuperated from the treated raw material by washing with water.

SCHEME OF TECHNOLOGICAL PROCESS ANALYSIS OF FINISHED PRODUCT

Authenticity. The preparation is treated with ether. Ether extract is evaporated to dryness. To the dry residue are added concentrated solutions of acetic, sulfuric and nitric acids, it appears deep red color turning into orange (thymol).

The preparation is treated with charcoal and filtered. The filtrate should discolor mixture consisting of 1N. borax solution and 7% alcohol solution of phenolphthalein (glycerin).

Dry residue in a preparation should be at least 8%. The alcohol content - at least 25%.

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