LIQUID MEDICINAL FORMS

1. CHARACTERISTIC OF LIQUID MEDICINAL FORMS

Liquid medicinal forms (LMF) are drugs made by mixing or dissolving of active substances in a solvent, and by extracting of active substances from plant raw materials as well.

By the physical–chemical nature they are free thoroughly dispersed systems where a medicinal substance (disperse phase – ***solvendum*)** evenly distributed in a liquid disperse medium (solvent – ***solvents***).

Medicinal substances in LMF can be in various physical states:

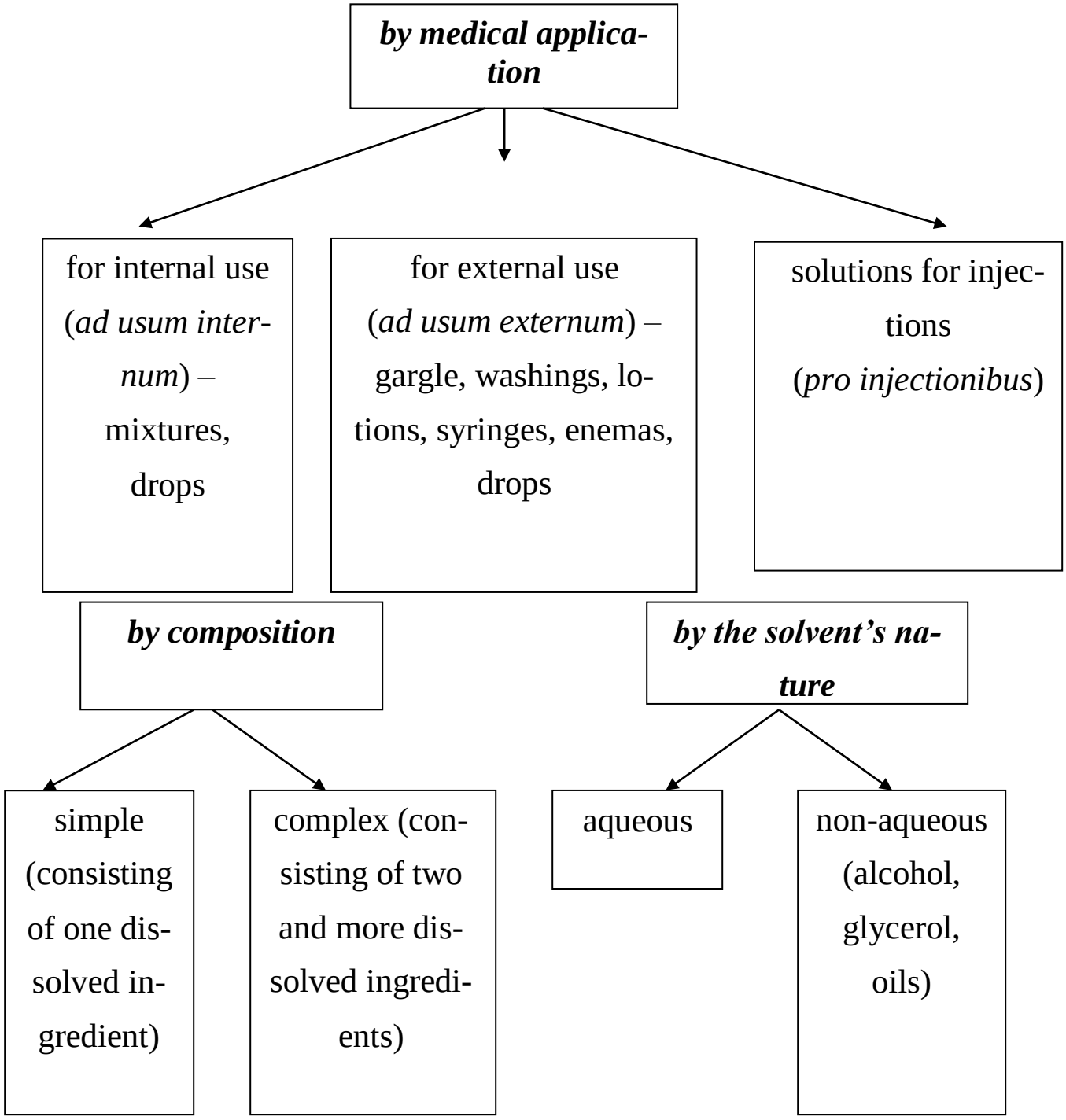
- solid;
- liquid;
- gas.

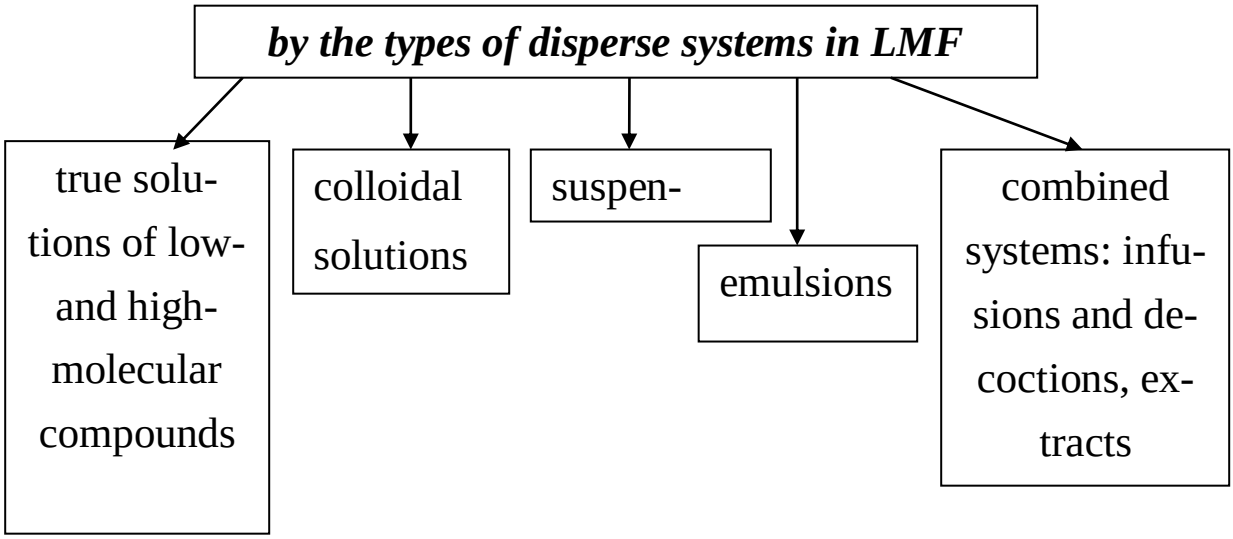
Table 1

The distribution of extemporal medicinal drugs by the types of medicinal forms

Medicinal form	**% from the total amount of extemporal drugs**
Powders	0.4
Herb collections	29.9
Liquid medicinal forms	23.7
Soft medicinal forms	3.1
Intrachemist's product	42.9

CLASSIFICATION OF LIQUID MEDICINAL FORMS





ADVANTAGES OF LIQUID MEDICINAL FORMS

- Variety in medical application.
- Reduction of irritating properties of some officinal drugs (bromides, iodides).
- Simplicity and comfort of using in pediatrics and geriatrics.
- Possibility to mask an unpleasant taste.
- When using internally they absorb and act faster than solid medicinal forms (powders, tablets, etc.) because they act after dissolving in the organism.
- Softening and enveloping action of medicinal substances.

DISADVANTAGES OF LIQUID MEDICINAL FORMS

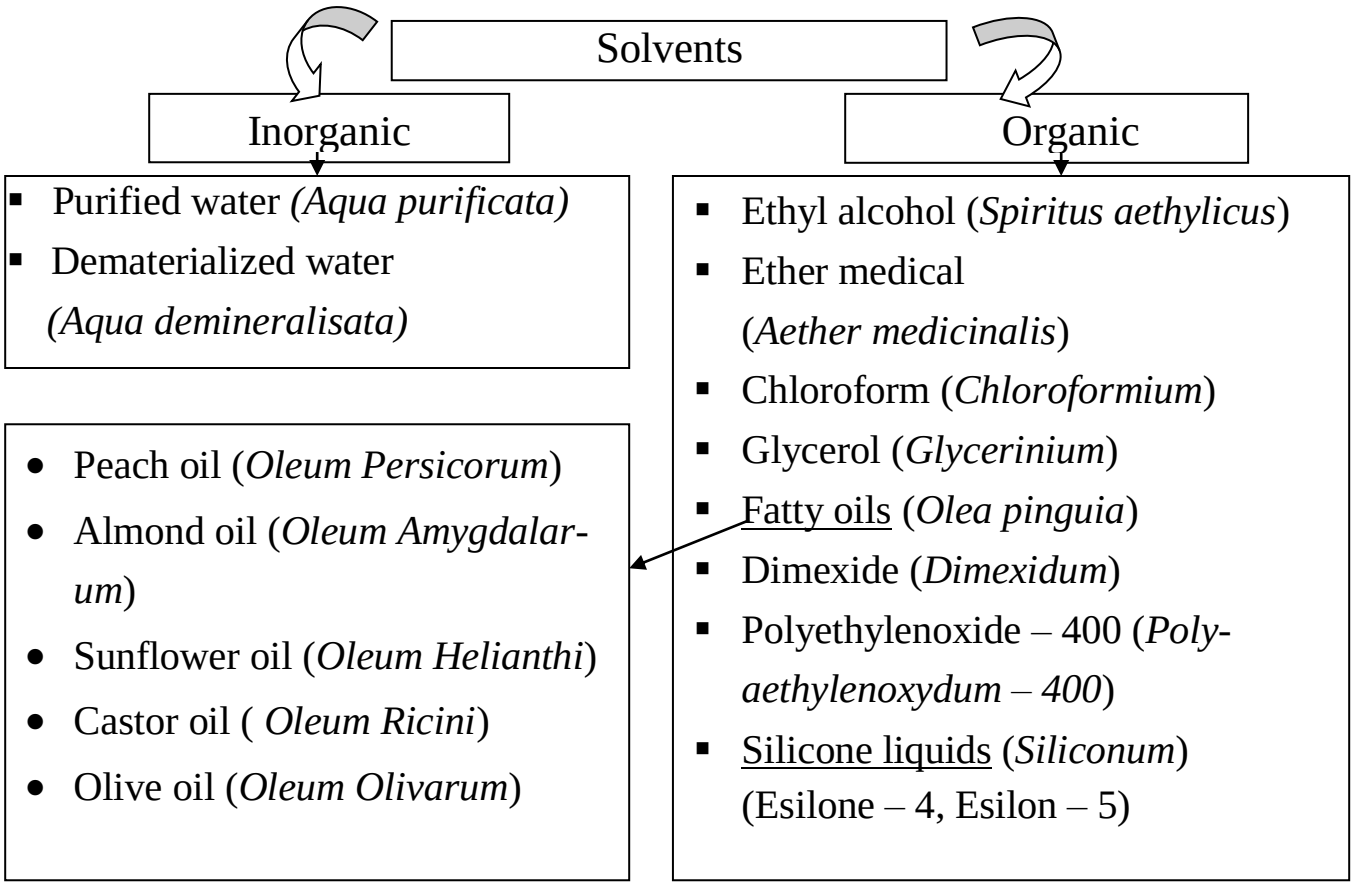
- Solutions are poorly kept because substances in a dissolved state are easily subjected to hydrolysis and oxidation than in a dry state.
- Solutions are favorable environment for development of microorganisms that is why storage of LMF is not more than 3 days.
- Uncomfortable transportation requires more time for preparation and special packing.
- In exact dosage, they are less exact than solid drugs. For example, the dose of powders is out in the chemist's, but mixtures are measured by a tablespoon, drops.

2. SOLVENTS IN TECHNOLOGY OF LIQUID MEDICINAL FORMS. CLASSIFICATION AND REQUIREMENTS FOR THEM

Solvents are individual chemical compounds or mixtures that can dissolve different substances, and form homogeneous systems as solutions that consist of two or more components.

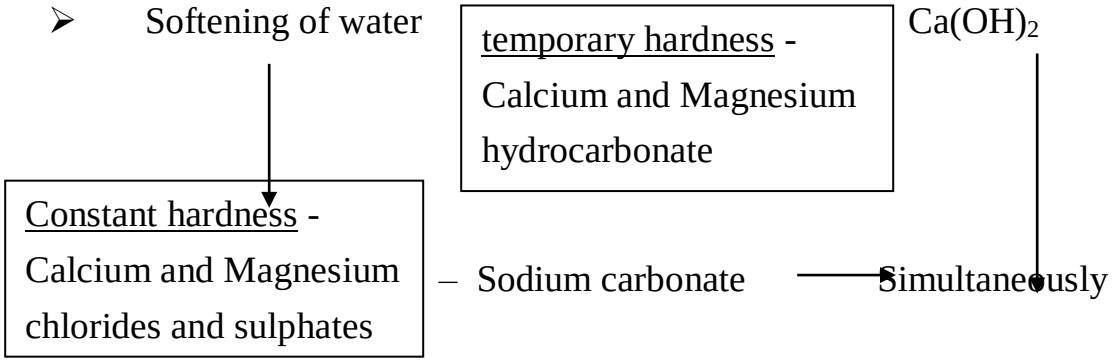
REQUIREMENTS TO SOLVENTS:

- ✓ should be stable when storing, chemically and pharmacologically inert;
- ✓ should have a high solubility;
- ✓ should have a pleasant taste and smell;
- ✓ should be cheap, generally available and have a simple method of obtaining;
- ✓ should not be inflammable and volatile;
- ✓ should not be an environment for growth of microorganisms.



PREPARATION, WAYS OF OBTAINING AND QUALITY CONTROL OF PURIFIED WATER

- Mechanical admixtures separation as infusion decantation;
- Softening of water



- Organic admixtures disintegration – 2.5 g of potassium permanganate per 100 liters of water.
- Binding of ammonia – 50.0 g of alums per 100 liters of water.
- Binding of hydrogen chloride – 35.0 g of sodium phosphate two-substituted

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It is separated after adding of alums (2/3 from alums)

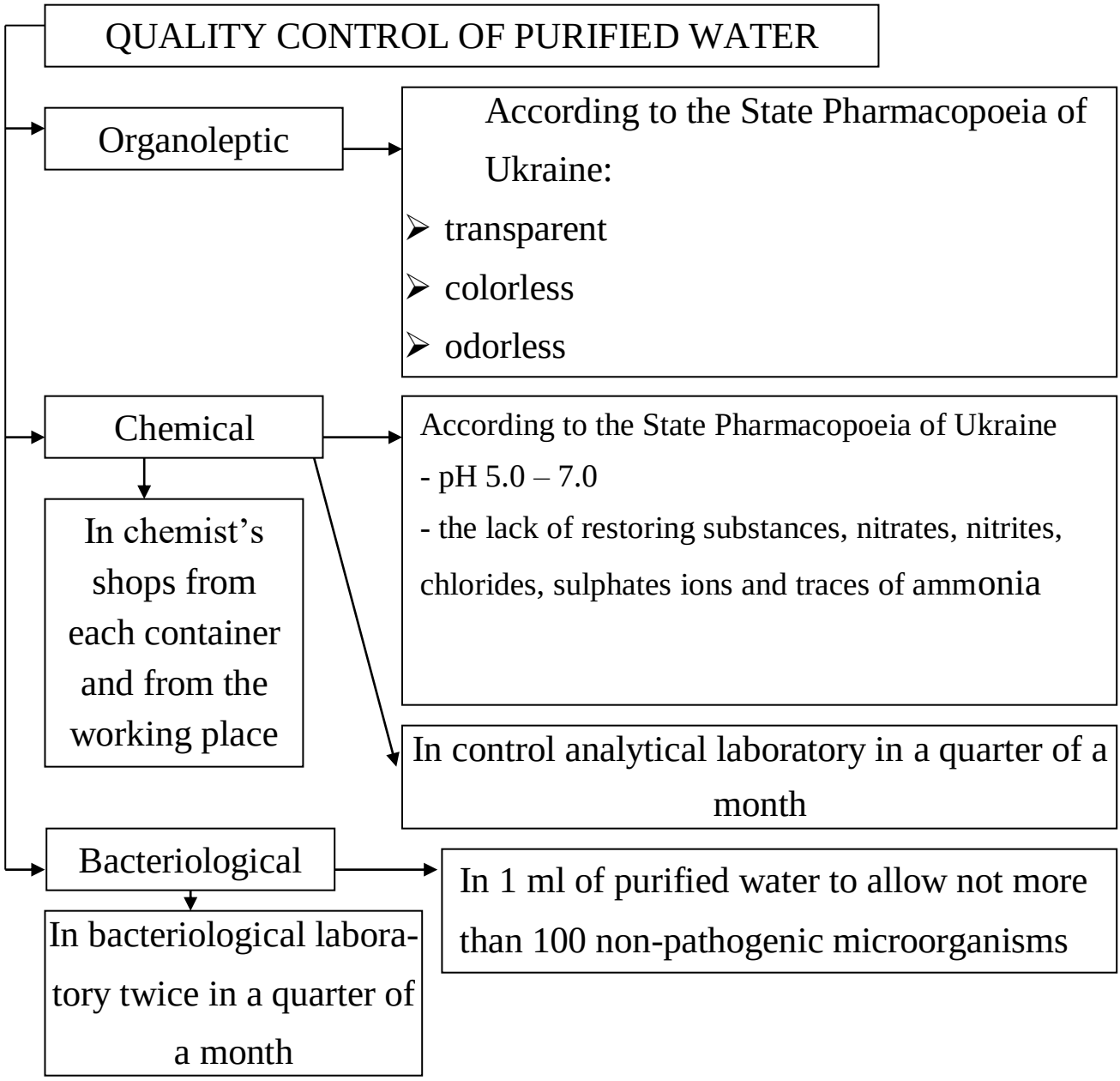
METHODS OF OBTAINING PURIFIED WATER

- distillation → Aquadistillators:
  - Aquadistillators of periodic functioning (warming up by fuel) – DF–10, DTVS–4, etc.;
  - Aquadistillations of uninterrupted functioning (electric) – DE–4, DE–25.
- reverse osmosis
- electric dialysis
- ionic exchange → cationites, anionites

CONDITIONS FOR OBTAINING OF PURIFIED WATER

(Order of MPH of Ukraine № 391 from 03.08.2005)

- A separate premise (walls and floor must be covered with tiles);
- Carrying out of any other work in this premise is forbidden;
- Containers for water must be made of steel or glass (as an exception);
- The cover of the container should have two openings: first – for a collecting tube, second – for a cotton filter.



Ethyl alcohol (*Spiritus ethylicus*)

- Obtained by fermentation of the plant raw materials containing starch (potatoes and grain)
- It has the bactericidal activity;
- Is a hydroscopic, volatile and easy inflammable
- Cause coagulation of proteins, enzymes, mucilages
- It is a non-inert substance in relation to the organism
- It is oxidized by oxidizers
- When mixing with water contraction is observed
- Alcohol solutions of medicinal substances is more stable than water solutions

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Chloroform (*Chloroformium*)

Medical Ether (*Aether medicinalis*)

- It is a volatile liquid with a specific odor
- It is a strong-effective substance with the narcotic action
- It is prescribed in the mixture with alcohol, fatty oils, usually in liniments
- Dosed by weight (density of chloroform is 1.47 – 1.48, density of ether – 0.713 – 0.714)

Glycerol (*Glycerinium*)

- A dense liquid like a syrup with the neutral reaction
- The ability to dissolve is the same as for purified water
- Dissolution of drugs is carried out by heating on the water bath
- Anhydrous glycerol “ch.p.” is hydroscopic and irritates the skin
- Glycerol used should contain 15 % of water with the density of 1.225 – 1.235

Fatty oils *(Olea pinguia)*

- Oils obtained by cold pressing are used
- The quality is regulated by the acid number (not more than 2.5)
- Easily oxidized, the acid number increases, peroxide compounds appear

Vaseline oil
(Oleum vaselini)

- A colorless oil liquid; it is a product of petroleum processing
- The ability to dissolve is the same as for fatty oils
- It does not penetrate via skin
- It is used as an auxiliary liquid in ointments more often

Dimexide
(*Dimexidum*)

- Mix with water, alcohol, glycerol and other non-aqueous solvents
- Easily dissolves medicinal substances
- Quickly conducts medicinal substances through the skin
- It has the anaesthetic, febricide, anti-inflammatory and antimicrobic activity

Polyethylene-oxide–400 (*Polyethylene-oxydum–400*)

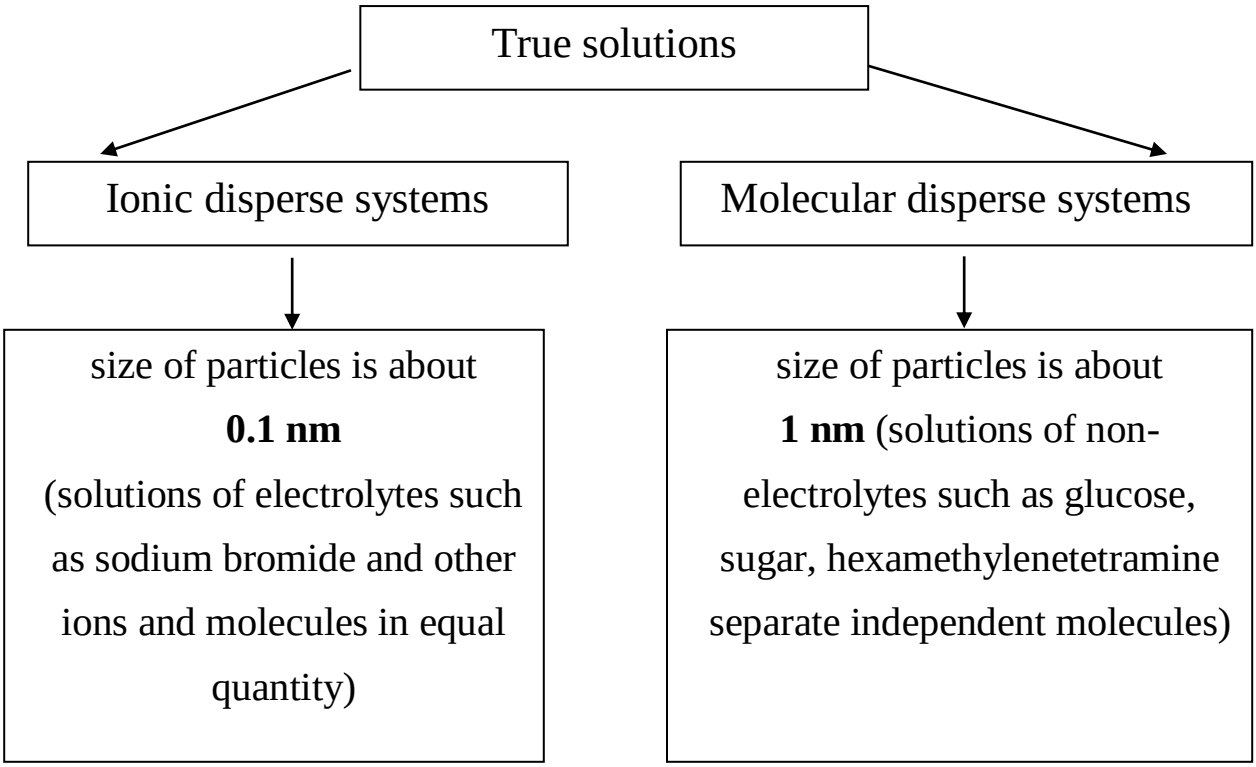
- It is a product of polymerization of ethylenoxide in the presence of water
- It is a viscous hydroscopic liquid
- It has the antimicrobic and high osmotic activity
- It can dissolve: anaesthesin, benzoic acid, salicylic acid, sulphanilamide substances, camphor, furacilin

Silicone liquids
(*Siliconum*)

- They are silicon-organic compounds (polysiloxans)
- They are inert and non-irritate substances in chemical and physiological aspects
- They are readily mixed with different substances; can be easily emulsified

3. SOLUTIONS. WAYS OF PRESCRIBING. METHODS OF FORMULATION. CHECKING OF DOSES

Solutions are homogenous disperse systems (mixtures) of two or more components where molecules of a solute are arranged steady in the volume of a solvent between its molecules.



PROPERTIES OF TRUE SOLUTIONS

- *Diffusion* is expressed very well
  Filtration – their particles pass through paper and ultra-filters
- Their particles pass through a membrane
- They are invisible by general and ultramicroscopic method
- They are visible (the largest molecules) in electronic micro-
- Surface energy is absent; without refraction activity, stable

PRESCRIPTION OF SOLUTIONS

The concentration of solutions in liquid medicinal forms may be expressed by mass-volume percentage in various ways.

For example, in weight percent, molarity, normality, molality, etc.

For readily soluble substances the following parameters are indicated:

1) The concentration of a solute, % (the weight of a solute in grams in 100 ml of the solution):

Rp.: Solutionis Natrii bromidi 2 % 200 ml

D.S.

2) The amount of the solute and the solvent:

Rp.: Natrii bromidi 4.0

Aquae purificatae 200 ml

M. D.S.

3) The amount of the solute and the total volume of the solution achieved by adding of the solvent prescribed:

Rp.: Natrii bromidi 4.0

Aquae purificatae ad 200 ml

M. D.S.

4) The solute-solution ratio:

Rp.: Solutionis Natrii bromidi ex 4.0 200 ml

D.S.

In spite of different prescription of Sodium bromide solution its volume is 200 ml and the amount of a solute is 4.0 g.

For poorly soluble substances

5) The degree of the solute is dilution (1:1000, 1:5000, etc.) and the volume of the solution required is indicated:

Rp.: Solutionis Aethacridini lactates (1:1000) 200 ml

D.S.

Very often the concentration of a solute (%) is used

Ways of preparing solutions

by weight

On viscous solvents – a solute and a solvent are weight out

- Balances (manual, prescription)
- Bottles for dispensing

by weight-volume

A solute is weighed, a solvent is measured or dilute to the volume

by volume

A solute and a solvent are measured

- Flasks for measuring
- Cylinders
- Beakers
- Droppers
- Pipettes
- Burettes (system)

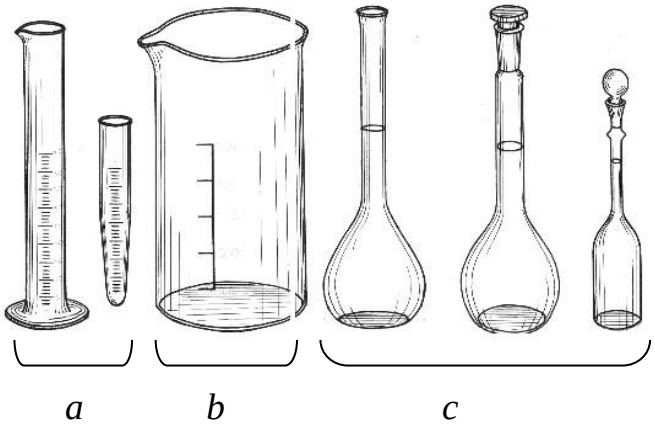


Fig. 1. Measuring tableware:
a – cylinders; b – beakers;
c – flasks.

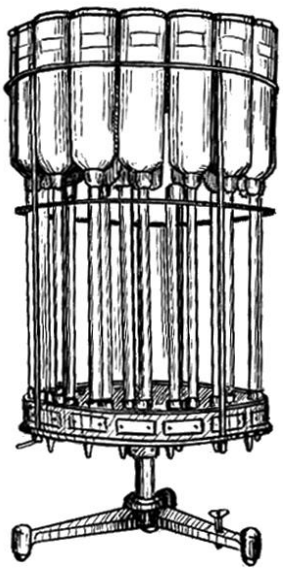


Fig. 2. The burette system

CHECKING OF DOSES FOR POISONOUS, NARCOTIC AND STRONG-EFFECTIVE SUBSTANCES IN MIXTURES

Rp.: Analgini 3.0
Kalii bromodi 4.0
Aquae purificatae 200 ml
Tincturae Belladonnae 5 ml
Tincturae Valerianae 10 ml
M.D.S. 1 tablespoon 3 times a day.

The total volume = 200 + 5 + 10 = 215 ml;
V of 1 tablespoon is 15 ml

↓

Number of doses = 215 ml / 15 ml = 14 times

↓

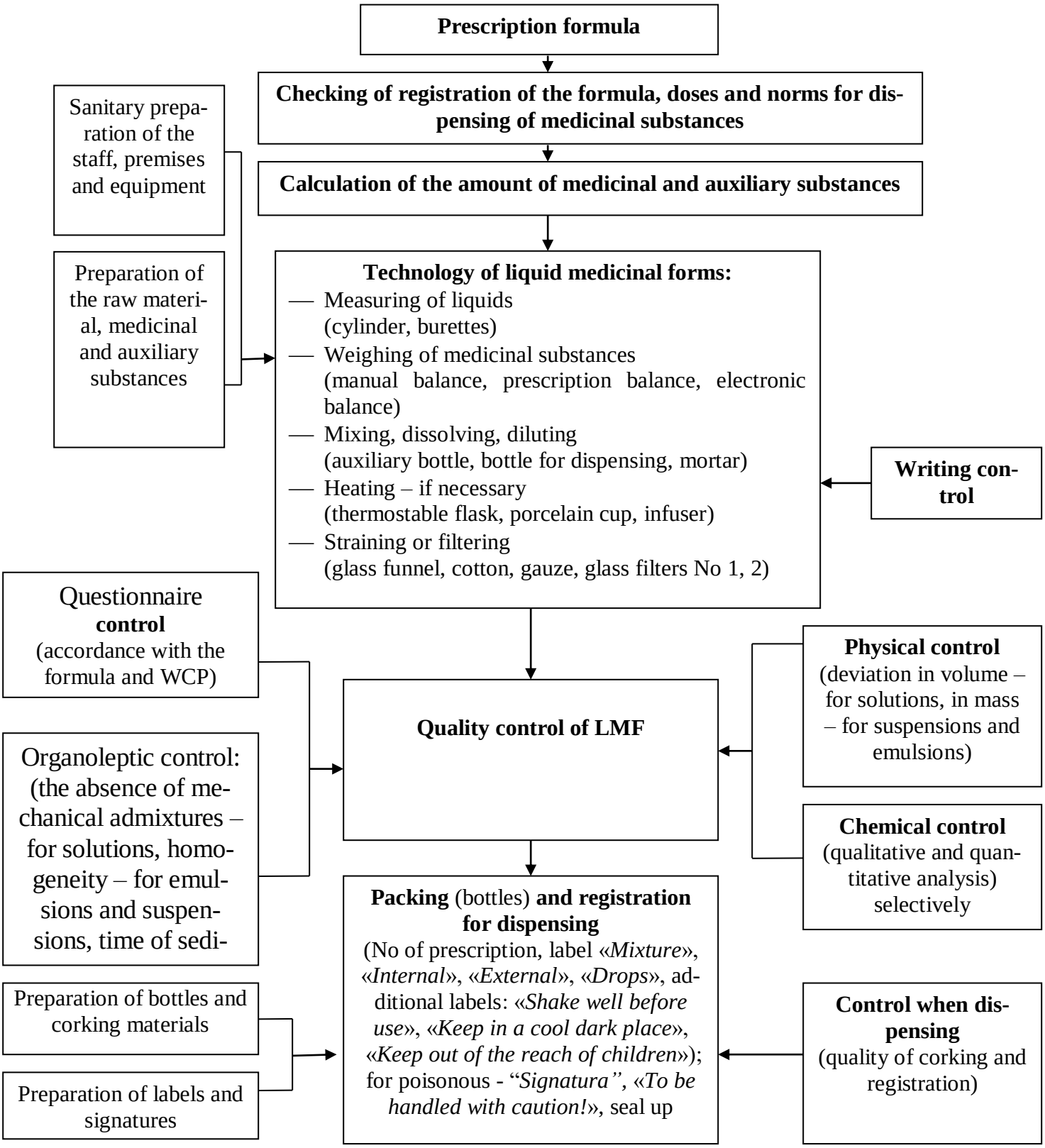
A single dose of analgin:
3.0 / 14 = 0.21 or 215 ml ----- 3.0
15 ml ----- x x = 0.21
A daily dose of analgin:
0.21 x 3 = 0.63
According to the SPU H.S.D. = 1.0; H.D.D. = 3.0
Doses are not exceeded

A single dose of belladonna tincture:
5 ml / 14 = 0.36 ml or 215 ml ----- 5 ml
15 ml ----- x x = 0.36 ml
A daily dose of belladonna tincture:
0.36 x 3 = 1.08 ml
According to the SPU H.S.D. = 0.5 ml; H.D.D. = 1.5 ml
Doses are not exceeded

4. TECHNOLOGY OF LIQUID MEDICINAL FORMS

Scheme 1

The technological scheme of preparation of liquid medicinal forms



DISSOLVING OF MEDICINAL SUBSTANCES

Solvency is a property of substances to dissolve in different solvents (the amount of a solvent per 1.0 g of a substance)

"Like dissolves like" – Similia similibus solventur

- polar substances are dissolved in polar solvents (water, acids, and lower alcohols);
- non-polar substances are dissolved in non-polar solvents (hydrocarbons and others).

Table 2

ACCORDING TO THE STATE PHARMACOPOEIA OF UKRAINE

Conventional terms	**The amount of a solvent (ml) required for dissolution of 1.0 g of a substance**			
Very readily soluble	To	1		
Readily soluble	More than	1	Less than	10
Soluble	–"–	10	–"–	30
Sparingly soluble	–"–	30	–"–	100
Slightly soluble	–"–	100	–"–	1000
Very slightly soluble	–"–	1000	–"–	10000
Practically insoluble	–"–	10000		

Table 3

PROPERTIES OF DIFFERENT DISPERSE SYSTEMS

Properties of particles	***True solutions***	***Colloids***	***Suspensions***
Type	transparent	transparent (opal-escence)	opaque
Size	0.1 nm (0.0001 μm) and less, homoge-neous	1 – 100 nm (0.001 – 0.1 μm) heterogeneous	100 - 1000 nm (0.1 – 1 μm) and more, heterogeneous
Diffusion	Expressed	Poorly expressed	Lacked
Filtration	Particles pass through paper and ultra filters	Particles pass through a paper fil-ter, they are re-tained by an ultra filter	Particles do not pass through a pa-per filter
Penetration through the membrane	Penetrate	Do not penetrate	Do not penetrate
Microscopic vis-ibility	Invisible	Invisible	Visible
Ultramicroscopic visibility	Invisible	Can be found	Visible
Electronic mi-croscope visibil-ity	Only the largest molecules are visi-ble	Visible	Visible
Surface energy	Absent	Reveals abruptly	Reveals weakly
Light refraction	Optical empty	Tindal's cone	Diffuse as a result of reflection and re-fraction
Stability	Stable	Relatively unstable	Unstable

STRAINING AND FILTERING OF SOLUTIONS

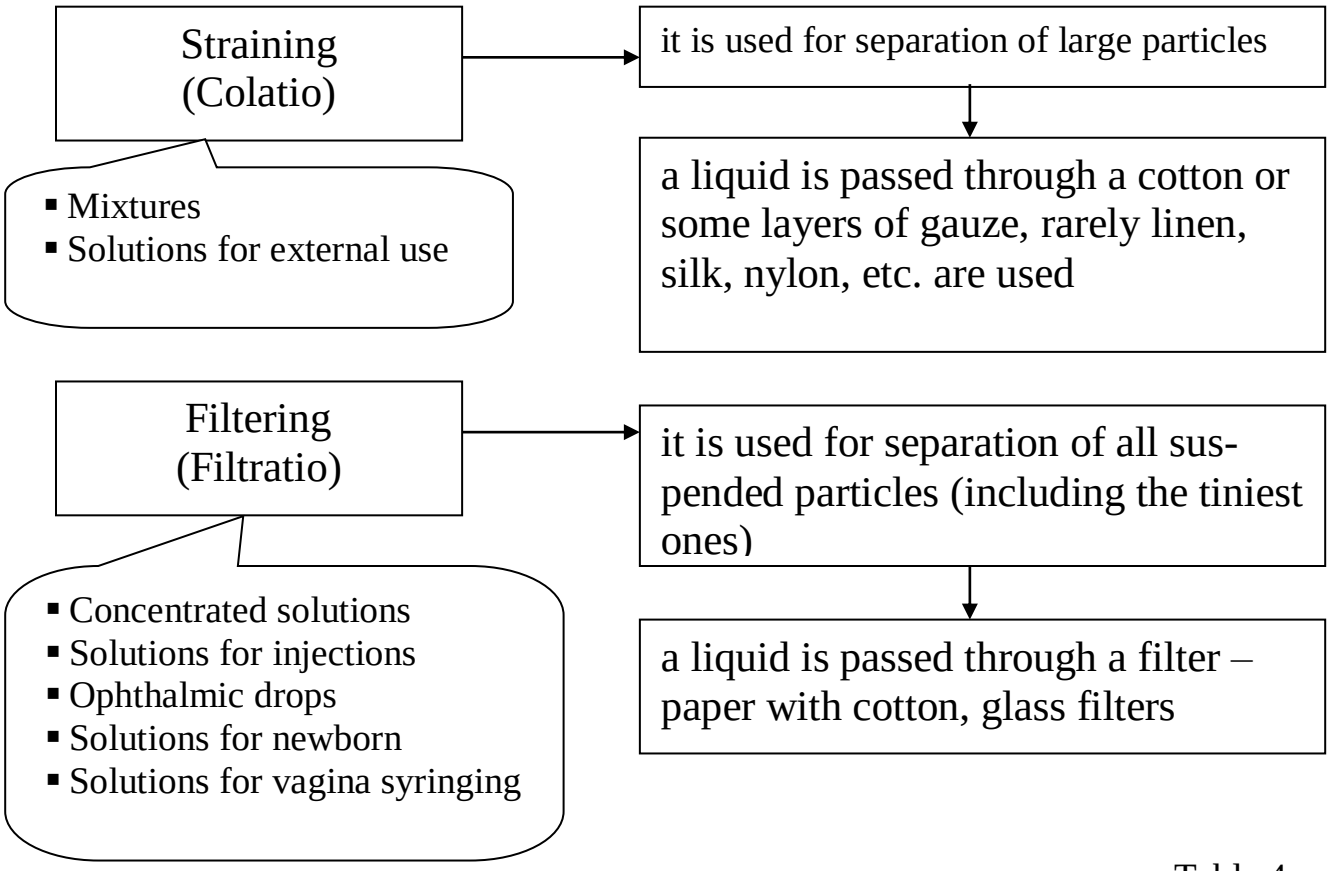


Table 4

PROPERTIES OF GLASS FILTERS

No of filter	**Average number of pores**	**Application in pharmacy practice**	
1	90 – 150 μm	the pores size equals to that of a cotton tampon	For straining of solutions for internal and external use, as the liquid goes spontaneously through them
2	40 – 90 μm	the pore size equals to that of a crumbly filter paper	
3	20 – 40 μm	the pore size equals to that of a thick filter paper	For filtration of ophthalmic drops and solutions for injections; they require vacuum
4	10 – 20 μm	the pore size equals to that of very thick filter paper	

PREPARATION OF CONCENTRATED SOLUTIONS

(Order of MPH of Ukraine № 197 from 07.09.93)

Concentrated solutions are non-dosage type of chemist's intermediate product for preparing medicines with a liquid disperse medium by dissolving or in the mixture with other medicinal substances.

These working solutions are prepared in higher concentrations than they are given in prescriptions.

Preparation of concentrated solutions

Prepare 1 liter of 20 % solution of sodium bromide

By the mass-volumetric method → In the volumetric flask → 1. A medicinal substance 2. Purified water

200.0 g of a dry substance + purified water – up to 1 liter of the solution

By weight taking into account the mass-volumetric concentration → In the auxiliary bottle → 1. Purified water 2. A medicinal substance

Taking into account the density of the solution:

$m = V \times d (\rho)$

where: m – is the weight of the solution, g

V – is the volume of the solution, ml

d (ρ) – is the density of the solution (1.1488 g/m

$m = 1000 \times 1.1488 = 1148.8$ g

The amount of water is:

1148.8 – 200.0 = **949.0 g (ml)**

Taking into account the volume increase coefficient:

VIC_{NaBr} = 0.26 ml/g (the volume, which 1.0 g of a substance takes up when dissolving)

200.0 x 0.26 = 52 ml

The amount of water is: 1000 – 52 = **948 (ml)**

QUALITY CONTROL OF CONCENTRATED SOLUTIONS

These solutions are checked by quality and quantity.

Norms of permitted deviations in concentrated solutions

(Orders of MHP of Ukraine №197 from 07.09.93 and № 276 27.09.91)

Up to **20 %** inclusive	→	**±2 %** from the designated concentration
More than **20 %**	→	**±1 %** from the designated concentration

For 10 % solution:

10.0 - 100 %

x - 2 % x=0.2 10 – 0.2 = 9,8

10 + 0.2 = 10.2 <u>9.8 - 10.2 %</u>

For 50 % solution:

50.0 - 100 %

x - 1 % x=0.5 50 – 0.5 = 49.5

50 + 0.5 = 50.5 <u>49.5 - 50.5 %</u>

The refractometry method is used more frequently for qualitative and quantitative analysis of the concentrated solutions.

DILUTION AND STRENGTHENING OF *CONCENTRATED SOLUTIONS*

*1. If the solution is turned out to be **stronger** than it is required, then it is diluted by water:*

$$X = \frac{A(C - B)}{B}$$, where

X – is the amount of water for dilution, ml;
A – is the volume of the prepared solution, ml;
C – is the actual obtained concentration of the solution, %;
B – is the required concentration of the solution, %.

$$X = \frac{1000(23 - 20)}{20} = 150\,\text{ml}$$ of purified water

Checking of calculation:
(1000 + 150) = 1150 ml –
1150 ml - 230.0 of NaBr
100 ml – x;
x = 20.0 of sodium bromide (20 % solution)

*2. If the solution is turned out to be **weaker** than required, then it is strengthened by adding of a medicinal substance:*

$$X = \frac{A(B - C)}{100 \cdot d - B}$$, where

X – is the amount of a dry substance, g;
A – is the volume of the prepared solution, ml;
C – is the actual obtained concentration of the solution, %;
B – is the required concentration of the solution, %;
D – is density of the solution of the required concentration.

Checking of calculation:
21.08 × 0.26 (CVI) = 5.5 ml
(1000 + 5.5) = 1005.5 ml
1005.5 ml – 201.08 of NaBr (180.0 + 21.08)
100 ml – x;
x = 20.0 of sodium bromide (20 % solution)

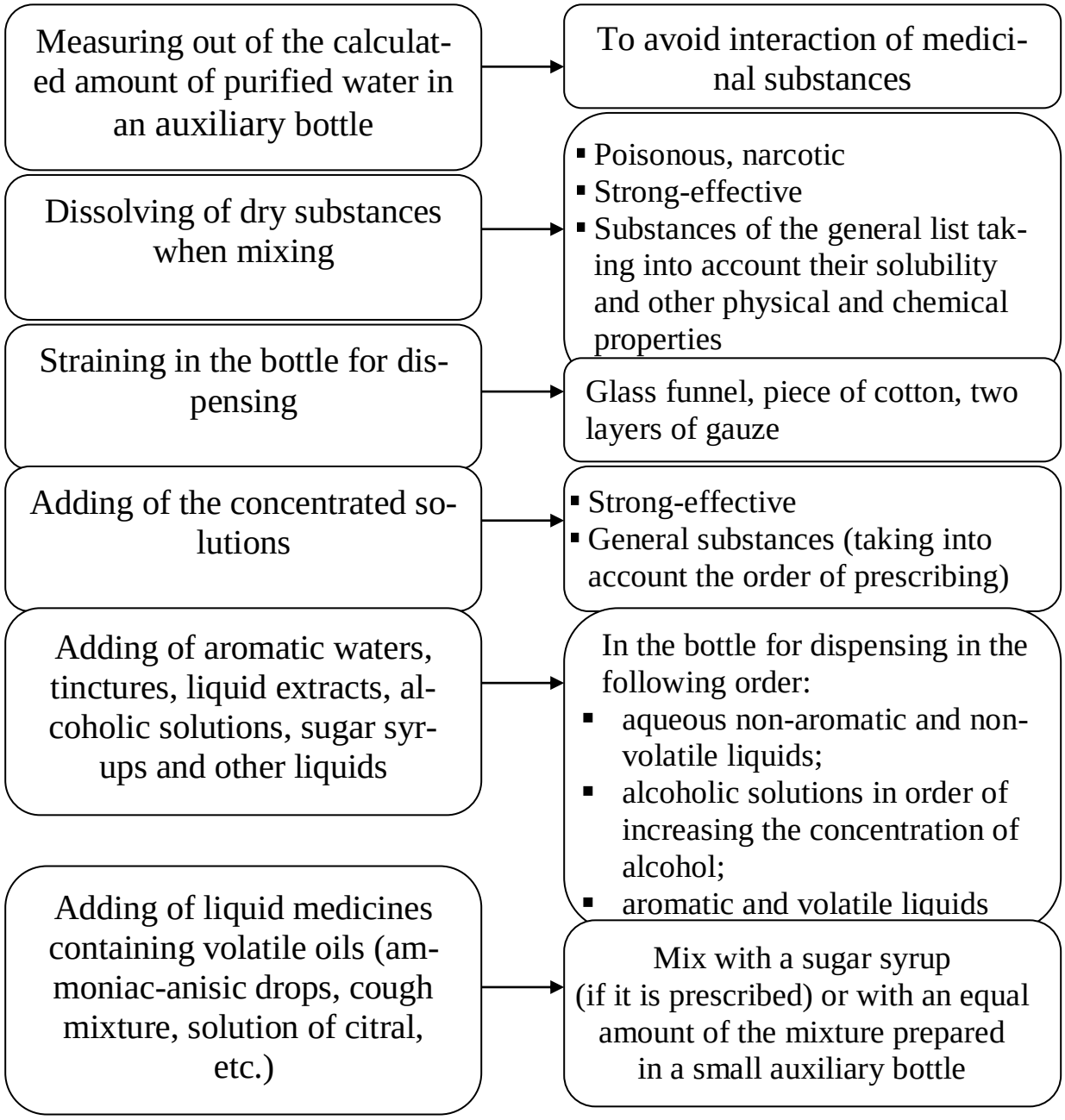
$$X = \frac{1000(20 - 18)}{100 \cdot 1.1418 - 20} = 21.08$$ of sodium bromide

The label should be sticked on the bottle indicating:

- the name of the solution;
- the number of a batch and analysis;
- the concentration of the solution;
- dates of preparation and analysis.

Mixtures are liquid medicinal forms for internal application, which are dosed by spoons (tablespoon, dessert spoon and teaspoon).

PREPARATION OF MIXTURES



PREPARATION OF MIXTURES FROM CONCENTRATED SOLUTIONS

a) Rp.:Natrii hydrocarbonatis 2.0
Sirupi sumplicis 10 ml
Tincturae Valerianae 6 ml
Aquae purificatae 200 ml
M. D. S. Use 1 tablespoon
3 times a day.

b) Rp.: Natrii hydrocarbonatis 2.0
Sirupi sumplicis 10 ml
Tincturae Valerianae 6 ml
Aquae purificatae ad 200 ml
M. D. S. Use 1 tablespoon
3 times a day.

It is necessary to calculate:

- the volume of the mixture
- thy amount of the concentrated solutions
- thy amount of purified water

WCP *(reverse side)*	**WCP** *(front side)*
Solution of sodium hydrocarbonate, 5 % (1:20): 2.0 x 20 = 40 ml Purified water: a) 200 – 40 = 160 ml b) 200 – (40 + 10 + 6) = 144 ml	Data № Pr. Aquae purificatae 160 ml (144 ml) Sol. Natrii hydrocarbonatis 5% (1:20) 40 ml Sirupi simplicis 10 ml Tincturae Valerianae 6 ml a) V_{total} = 216 ml b) V_{total} = 200 ml Prepared by: Checked by:

Registration for dispensing: the number of the prescription, the label "Internal", "Keep out of the reach of children", "Keep in a cool dark place"

PREPARATION OF MIXTURES FROM DRY SUBSTANCES AND CONCENTRATED SOLUTIONS

If the dry substances, in which concentrated solutions are absent, are in total quantity up to 3 % of the volume of the mixture, they are dissolved in the measured quantity of water or another aqueous liquid without VIC, i.e. the volume of the solution is changed insignificantly, it is in the norms of permitted deviations according to the order MPH of Ukraine № 276 from 27.09.91

Rp.: Analgini 3.0
Kalii bromidi 4.0
Aquae purificatae 200 ml
Tincturae Belladonnae 5 ml
Tincturae Valerianae 10 ml
M. D. S. For 1 tablespoon 3 times a day.

Checking of doses of poisonous and strong-effective substances in mixtures.

1. V total = 200 + 5 + 10 = 215 ml Vt/s = 15 ml
2. Number of doses: 215 ml / 15 ml = 14 doses
3. Analgin: M.S.D. = 3.0 / 14 = 0.21 or → 215 ml – 3.0; 15 ml – x; x = 0.21
   M.D.D. = 0.21 x 3 = 0.63

H.S.D. = 1.0; H.D.D. = 3.0

Conclusion: doses are not exceeded

The tincture of belladonna:
M.S.D. = 5 ml / 14 = 0.36 ml or → 215 ml – 5 ml; 15 ml – x; x = 0.36 ml
M.D.D. = 0.36 x 3 = 1.08 ml

H.S.D. = 0.5 ml; H.D.D. = 1.5 ml

C**onclusion: doses are not exceeded**

TECHNOLOGY OF LIQUID MEDICINAL FORMS

The given medicine is an opalescence mixture with strong-effective substances: analgin, the tincture of belladonna; and with an aromatic substance – the tincture of valerian. Doses for strong-effective substances should be checked

WCP *(reverse side)*

Vtotal = 200 + 5 + 10 = 215 ml

% of Analgin:

215 ml – 3.0

100 ml - x

$x = \frac{3{,}0 \cdot 100}{215} = 1.4\ \% < 3\ \%$

$VIC_{Analgini} = 0.68$

0.68 x 3.0 = 2.04 ml

(the volume of water displaced by Analgin)

Norm of the permitted deviation

1 % of the volume more than 200 ml

215 ml – 100 %

2.15 ml – 1 %

2.04 ml < 2.15 ml

VIC should not be taken into account

Sol. of potassium bromide 20 % (1:5): 4.0

x 5 = 20 ml

Purified water:

200 ml - 20 ml = 180 ml

WCP *(front side)*

Date № Pr.

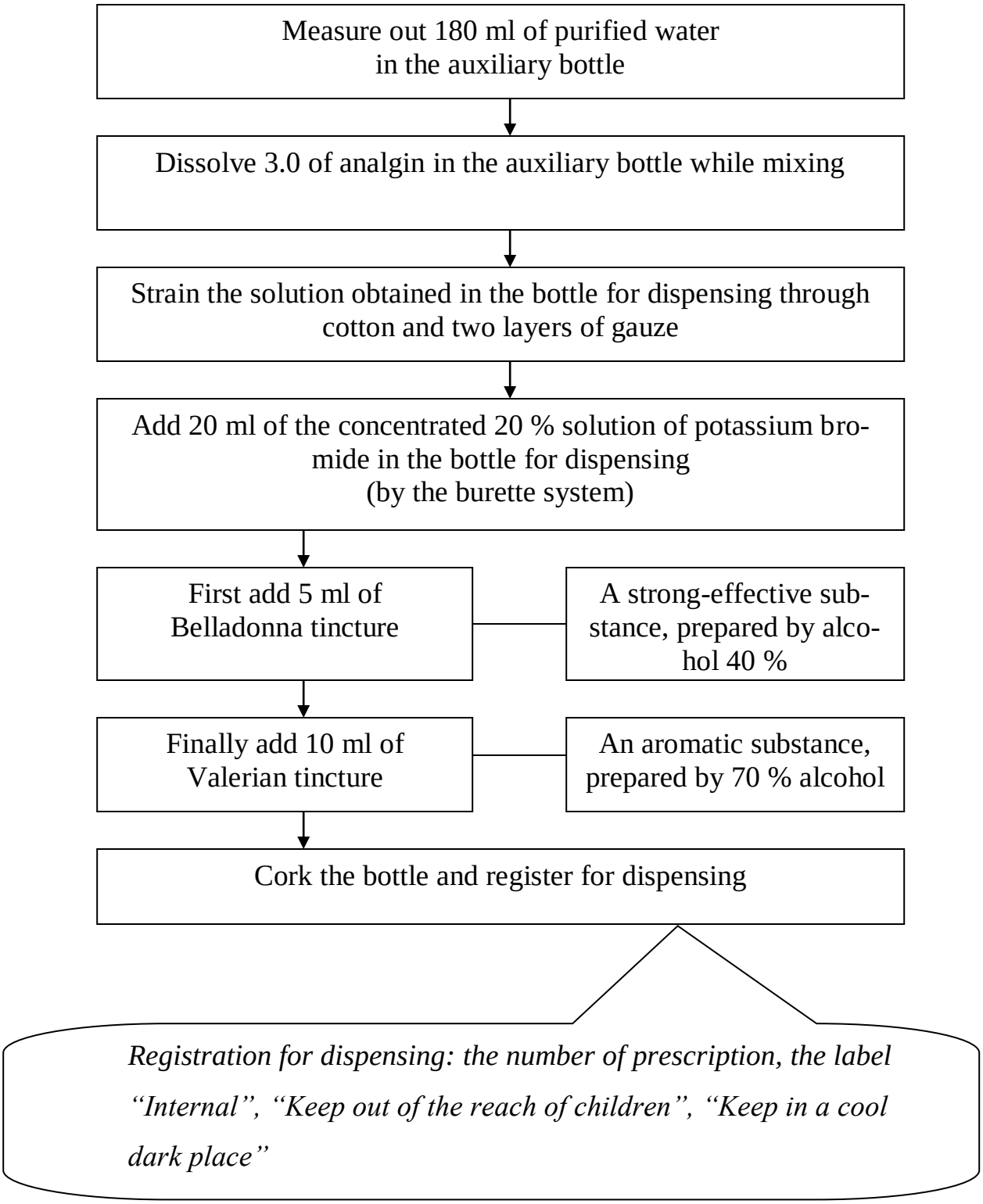
Aquae purificatae	180 ml
Analgini	3.0
Solutionis Kalii bromidi 20 % (1:5)	20 ml
Tincturae Belladonnae	5 ml
Tincturae Valerianae	10 ml

V_{total} = 215 ml

Prepared by:

Checked by:

Technology


Measure out 180 ml of purified water in the auxiliary bottle
Dissolve 3.0 of analgin in the auxiliary bottle while mixing
Strain the solution obtained in the bottle for dispensing through cotton and two layers of gauze
Add 20 ml of the concentrated 20 % solution of potassium bromide in the bottle for dispensing (by the burette system)
First add 5 ml of Belladonna tincture
A strong-effective substance, prepared by alcohol 40 %
Finally add 10 ml of Valerian tincture
An aromatic substance, prepared by 70 % alcohol
Cork the bottle and register for dispensing
Registration for dispensing: the number of prescription, the label "Internal", "Keep out of the reach of children", "Keep in a cool dark place"

PREPARATION OF MIXTURES FROM DRY SUBSTANCES AND CONCENTRATED SOLUTIONS

If dry substances without the concentrated solutions are included in the mixture in the total amount of 3 % and more of the volume of the mixture, then dissolve them in the previously calculated quantity of water or another liquid taking into account VIC as they change the volume of solution by displacing water from the mixture volume that exceeds the norms of the permitted deviation according to the order MPH of Ukraine № 276 from 27.09.91

Rp.: Kalii iodidi
Natrii bromidi ana 5.0
Glucosi 15.0
Aquae purificatae 180 ml
M. D. S. Use 1 tablespoon 3 times a day.

WCP *(reverse side)*

V_{total} = 180 ml
% of glucose 180 ml – 15.0
100 ml – x;
x = 8.3 % > 3 %
VIC of glucose (hum. 10 %) = 0.69
0.69 x 15.0 = 10.35 ml (water displaced by glucose)
The norm of the permitted deviation
2 % of the volume 150-200 ml
180 ml - 100 %
3.6 ml – 2 % 10.35 ml > 3.6 ml
It is necessary to take into account VIC
20 % sol. of potassium iodide (1:5):
5.0 x 5 = 25 ml
20 % sol. of sodium bromide (1:5):
5.0 x 5 = 25 ml
Purified water: 180 ml - (25 + 25 + 10.35) = 119.65 ml ≈120 ml

WCP *(front side)*

Date № Rec.
Aquae purificatae 120 ml
Glucosi 15.0 (hum. 10 %)
Sol. Kalii iodidi 20 % (1:5) 25 ml
Sol. Natrii bromidi 20 % (1:5) 25 ml
V_{total} = 180 ml

Prepared by:
Checked by:

PREPARATION OF MIXTURES FROM DRY SUBSTANCES AND CONCENTRATED SOLUTIONS

If the formulation contains several dry substances without concentrated solutions, then their content is calculated by the total amount

Rp.: Analgini 3.0
Natrii bromidi
Glucosi ana 5.0
Aquae purificatae 180 ml
M. D. S. Use 1 tablespoon 3 times a day.

V total = 180 ml

% of analgin: 180 ml – 3.0
100 ml – x x = 1.7 %

% of glucose: 180 ml – 5.0
100 ml – x x = 2.8 %

} each one is less than 3 %

The sum of dry substances: 3.0 + 5.0 = 8.0

% of dry substances: 180 ml – 8.0
100 ml – x

x = 4.4 % > 3 % it is necessary to take into account CVI

Liquid medicinal forms, in which the solvent is aromatic water or other liquids (water extracts from plant raw material, ethyl alcohol, PEO-400, etc.) are prepared without concentrated solutions and without taking into account VIC when dissolving the substances

Rp.: Kalii bromidi
Natrii bromidi ana 2.0
Aquae Menthae 200 ml
M. D. S. Use 1 tablespoon 3 times a day.

WCP *(front side)*

Date № Pr.

Aquae Menthae 200 ml
Kalii bromidi 2.0
Natrii bromidi 2.0

V_{total} = 200 ml

Prepared by:
Checked by:

5. SPECIAL (DIFFICULT) CASES OF THE SOLUTIONS PREPARATION

Slow and difficult dissolving of medicinal substances in cold water

Large crystal medicinal substances are poorly moistened by water, so they should be grinded in the mortar with a portion of water; then the rest of water is added

- ***copper sulphate (1:3)***
- ***alums* (1:3)**

Substances, which are slowly soluble in cold water, should be dissolved in hot water

- ***boric acid (1:25)***
- ***sodium tetraborate (1:16)***
- ***calcium gluconate (1:30)***
- ***ethacridine lactate (1:50)***

Substances, which are slightly soluble in cold water, should be dissolved in boiling water in the presence of 0.9 % solution of sodium chloride

- ***furacilin(1:*4200)**

Dissolving of medicinal substances, which are easily disintegrated in the presence of organic substances

- ***silver nitrate,***
- ***potassium per-manganate***

Fresh distillated and filtrated purified water is used

Filter through glass filters № 1 and 2, if necessary at least – through a cotton tampon washing with hot water

NB!

Solutions of potassium permanganate in concentrations more than 1 % are grinded in the mortar with some portion of warm filtrated purified water, and then the rest of water is added

Dissolving of medicinal substances, which make worse solubility of each other

sodium benzoate and ***calcium chloride*** **–** while dissolving together sedimentation of calcium benzoate is formed – prepare in two auxiliary bottles by mixing of concentrated solutions with water, then pour both solutions into the bottle for dispensing

Dissolving of poorly soluble medicines that make easily soluble com-

osarsol is a poisonous substance (a medicine of arsenic), very slightly soluble in water, easily soluble in solution of sodium hydrocarbonate (if sodium hydrocarbonate is not indicated in the prescription, it is added as 0.61 g per 1.0 g of osarsol). But the order of dissolving changes: at first, the substance of the general list is dissolved and then a poisonous substance is dissolved in the solution obtained

iodine is a poorly soluble in water (1:5000); the ability to dissolve in saturated solutions of potassium or sodium iodides with formation of complex compounds (periodides) is used for obtaining more concentrated solutions – the solution of Lugol. If potassium iodide is not indicated in the prescription, it is added in double quantity in relation to the weight of iodine. The order of dissolving changes: water + potassium (sodium) iodide + a strong-effective substance (iodine)

Solutions of iodine

For external use (1 % aqueous or glycerol solution)

1% solution of Lugol

Rp.: Solutionis Lugoli 1% 100 ml
D.S. To apply for larynx mucous membrane.

: Iodi 1.0
Kalii iodidi 2.0
Aquae purificatae ad 100 ml
D.S.To apply for larynx mucous membrane.

the solution of Lugol on glycerol

Rp.: Iodi 1.0
Kalii iodidi 2.0
Aquae purificatae 3ml
Glycerini 94.0
D.S. For vaginal tampons in vulvovaginitis.

For internal use

5 % solution of Lugol

Rp.: Solutionis Lugoli 5 % 20 ml
D.S. 5-7 drops on milk
3 times a day in
endemic goiter.

: Iodi 1.0
Kalii iodidi 2.0
Aquae purificatae ad 20 ml
D.S. 5-7 drops on milk
3 times a day in endemic goiter.

Peculiarities:

- Iodine is a strong-effective substance – when it is used for internal use, the doses should be checked;
- When dry substances are more than 3 % in the formula, the VIC should be calculated, but for the volume of 20 ml NPD is ± 4 %, as the result the actual volume increase is normal;
- For preparation of the solution of Lugol on glycerol: at first, aqueous solution of Lugol is prepared according to the rules and then glycerol is added by weight.

Checking doses for iodine

Rp.: Solutionis Lugoli 20 ml
D.S. 5-7 drops on milk 3 times a day.

Iodine is a strong-effective substance. The highest doses in the SPU are designated for 5 % alcoholic solution of iodine in drops. In the prescription the aqueous solution is indicated, so the ratio between the quantity of drops in aqueous and alcoholic solutions of iodine should be determined

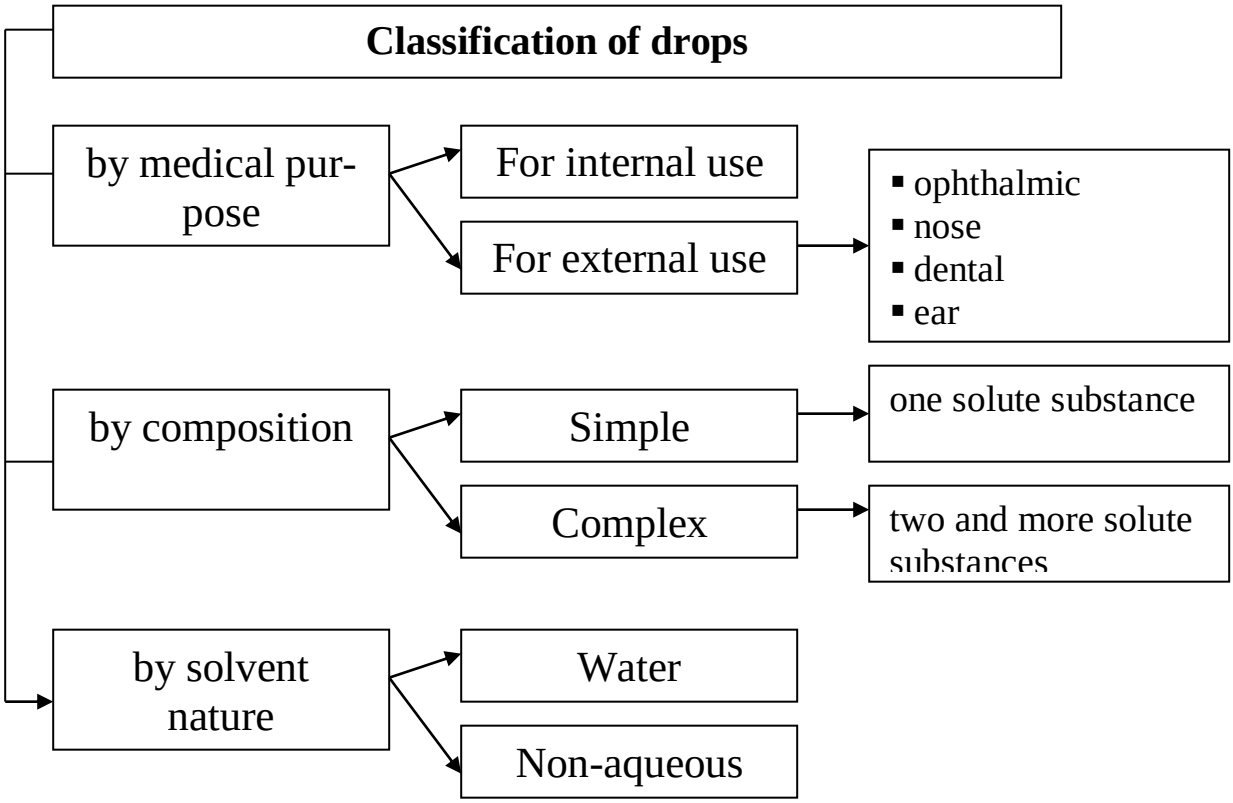
1.0 g of 5 % alcoholic sol. of iodine -----49 drops
1.0 g of aqueous sol. of iodine----------20 drops
20 drops of 5 % water sol. of iodine correspond to 49 drops of 5 % alcoholic sol. of iodine
1 drop of 5 % aqueous sol. of iodine -----x drops of 5 % alcoholic sol. of iodine
1 drop of 5 % aqueous sol. of iodine -----2.45 drops of 5 % alcoholic sol. of iodine
x = 49/20 = 2.45 drops

Using this ratio the doses are checked:
M.S.D. = 7 drops x 2.45 drops = 17.2 drops of 5 % alc. sol. of iodine
M.D.D. = 17.2 drops x 3 = 51.6 drops of 5 % alc. sol. of iodine

H.S.D. of 5 % alc. sol. of iodine = 20 drops
H.D.D. of 5 % alc. sol. of iodine = 60 drops
Doses are not exceeded

6. DROPS

Drops are liquid medicinal forms for internal and external application dosed by drops



Peculiarities of drops formulation

NB! A small volume of drops cause the change in technological stages, mainly in straining of true solutions

- A medicinal substance dissolves in a half amount of solvent
- The solution obtained is strained through a cotton tampon previously washed by purified water
- The rest quantity of the solvent is strained through the same cotton

To use concentrated solutions is rational (ophthalmic drops is an exception)!

CHECKING DOSES FOR POISONOUS AND STRONG-EFFECTIVE SUBSTANCES IN DROPS

Rp.: Solutionis Platyphyllini hydrotartratis 0.2 % 10 ml
D.S. 10 drops 2 times a day.

Plathyphylline hydrotartrate: 0.2 ---- 100 ml
X ----- 10 ml x = 0.02
1 ml of purified water ----- 20 drops
10 ml -------- x x = 200 drops
Number of doses: 200 drops/10 drops = 20 times
M.S.D. = 0.02 / 20 = 0.001 H.S.D. = 0.01
M.D.D. = 0.001 x 2 = 0.002 H.D.D. = 0.03
Doses are not exceeded

Rp.: Papaverini hydrochloride 1.0
Adonisidi 10 ml
Tincturae Convallariae
Tincturae Valerianae ana 15 ml
Mentholi 0.5
D.S. 30 drops 3 times a day.

1 ml of adoniside ------- 34 drops
10 ml ---------- x; x = 340 drops
1 ml of convallaria tincture ------- 50 drops
15 ml --------- x; x = 750 drops
1 ml of valerian tincture ------- 51 drops
15 ml --------- x; x = 765 drops
The total volume in drops: 340 + 750 + 765 = 1855
The number of doses: 1855 drops / 30 drops ≈ 62
Papaverine hydrochloride:
M.S.D. = 1.0 / 62 = 0.016 H.S.D. = 0.2
M.D.D. = 0.016 x 3 = 0.048 H.D.D. = 0.6
Doses are not exceeded
Adoniside:
M.S.D. = 340 drops / 62 = 5.5 drops H.S.D. = 40 drops
M.D.D. = 5.5 drops x 3 = 16.5 drops H.D.D. = 120 drops
Doses are not exceeded

7. STANDARD PHARMACOPOEIAN LIQUIDS

Standard pharmacopoeian liquids are aqueous solutions of medicinal substances (solid, liquid, gas) in strictly fixed concentrations, indicated in the corresponding articles of the SPU manufactured by pharmaceutical enterprises.

Table 5

The ways of prescribing of Standard Pharmacopoeian Solutions (Liquids)

Chemical name	Conditional name	Average concentration, %
Solution of aluminum acetate, basic	Liquid of Burov	**8**
Solution of potassium acetate	Liquid of Potassium acetate	**34**
Solution of formaldehyde	Formalin	**37**
Solution of hydrogen peroxide, concentrated	Perhydrole	**30**
Solution of hydrogen peroxide, diluted	—	**3**
Solution of ammonia	—	**10**
Acetic acid	—	**3; 30; 98**
Hydrochloric acid	—	**25**
Hydrochloric acid, diluted	—	**8.3**

Calculation of the prescribed liquid amount

<u>If the chemical name of a liquid is specified in the prescription</u>

- **If the concentration of a liquid is specified, the calculations proceed from the actual content of a substance in a standard solution according to the formula:**

$$X = V_x \bullet \frac{B}{A},$$

X – is tne volume of a standard liquid, ml;
V – is the volume of a solution required to prepare, ml;
B –is the concentration given in the prescription, %;
A –is the actual concentration of a standard liquid, %

Rp.: Solutionis Formaldehydi 5 % 100 ml
D.S. For disinfection of premises

X = (5 x 100) / 37 = 13.3 ml of 37 % sol. of formaldehyde
Purified water: 100 ml – 13.3 ml = 86.7 ml
or **X = (5 x 100) / 30 = 16.7 ml** of 30 % sol. of formaldehyde
Purified water: 100 ml – 16.7 ml = 83.3 ml

- **If the concentration of a liquid is not specified in the prescription, the solutions of standard pharmacopoeian liquids are dispensed:**

- 3 % solution of hydrogen peroxide
  (0.05 g of for sodium benzoate is stabilized for intrachemist's stocks)
- 30 % solution of acetic acid

<u>If the conditional name of a liquid is specified in the prescription</u>

When calculating the concentration of a standard solution is taken as a unit (100 %)

Rp.: Solutionis Formalini 5 % 100 ml
D.S. For disinfection of wounds.

or

Rp.: Formalini 5 ml
Aquae purificatae ad 100 ml
D.S. For disinfection of wounds.

37 % solution of formaldehyde 5 ml;
Purified water: 100 ml – 5 ml = 95 ml

If the initial solution is weaker than the standard one in a chemist's (30-35 %), it is necessary to recalculate:

$$\mathbf{CC} = \frac{37,5}{30} = 1,25 \text{ ,}$$

then the solution of formaldehyde 30 % : 5ml x 1.25 = 6.25 ≈ 6.3 ml;
purified water: 100 ml – 6.3 ml = 93.7 ml

WCP *(front side)*

Date №Pr.
Aquae purificatae 93.7 ml
<u>Solutionis Formaldehydi 30 % 6.3 ml (CC = 1.25)</u>

V_{total} = 100 ml

Prepared by:

Calculation of the prescribed liquid amount

The solution of hydrochloric acid is prescribed under the chemical name, but when calculating its concentration is taken as a unit (100 %)

By the SPU:

- **Hydrochloric acid, 25 %**
- **Diluted hydrochloric acid, 8.3 %**
- **Solution of diluted hydrochloric acid, 0.83 % (intrachemist's stock)**

For internal use

If hydrochloric acid is prescribed without indication of the concentration, the diluted hydrochloric acid, 8.3 %, is dispensed in the quantity given in the prescription

Rp.: Acidi hydrochlorici 3 ml
Aquae purificatae 150 ml
D.S. 1 tablespoon 3 times a day before meal

⇒

Diluted hydrochloric acid, 8.3 %, 3 ml
Purified water 150 ml

If hydrochloric acid is prescribed with indication of the concentration, the diluted hydrochloric acid, 8.3 %, is taken as a unit (100 %)

Rp.: Solutionis Acidi hydrochlorici 2 % 200 ml
D.S. 1 tablespoon 3 times a day before meal

⇒

Diluted hydrochloric acid, 8.3 %, 4 ml
Purified water:
200 ml – 4 ml = 196 ml

NB!

Taking into account volatile properties of hydrogen chloride and for increasing the accuracy of small volumes measuring of a strong effective substance, it is recommended to use dilution of this acid (chemist's preparation) - Solutio Acidi hydrochlorici diluti (1:10)
(solution of diluted hydrochloric acid (1:10): 4 ml x 10 = 40 ml
Purified water 200 ml – 40 ml = 160 ml

For external use

25 % hydrochloric acid is used
(the preparation of Demyanovich liquid for treating scabies)

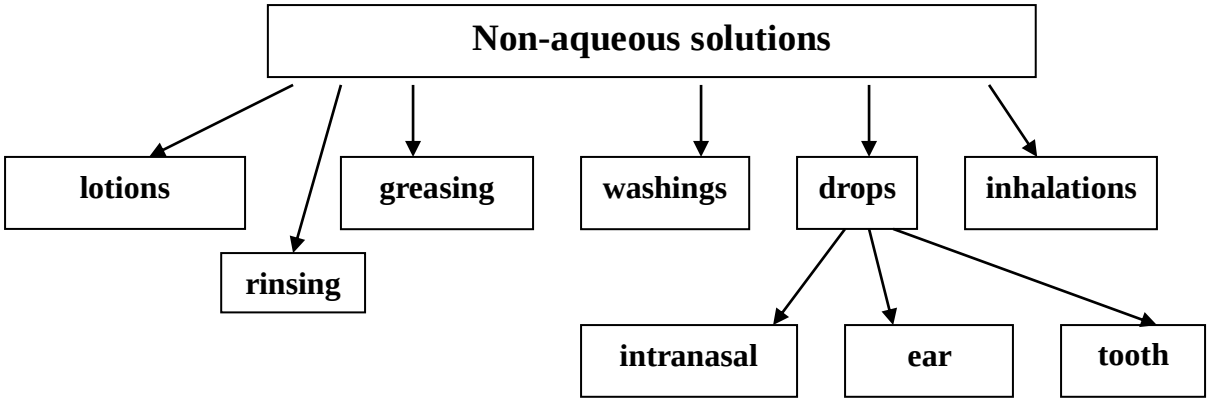
Rp.: Solutionis Natrii thiosulfatis 60 % 100 ml
D.S. External (solution № 1)

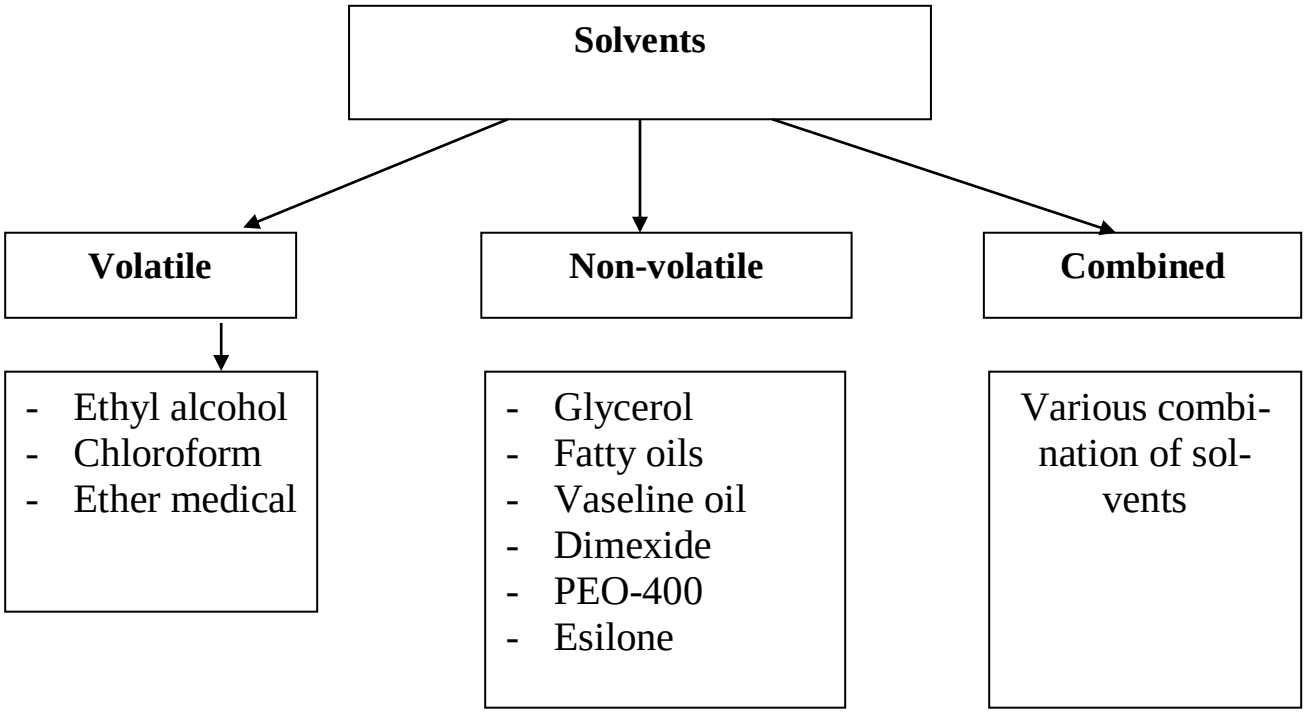
Solution № 1: prepare by weight
If 60.0 g of the substance + 40.0 (ml) of water = 100. 0 of 60 % solution, but V = 73.5 ml
If 60.0 of the substance + water to 100 ml = 100 ml, but 46.37 %.
It should be used:
60.0 ----- 73.5 ml
X -------- 100 ml x = 81.63
Purified water: to 100 ml
or using VIC = 0.51 ml/g
100 – (81.63 x 0.51) = 58.4 ml

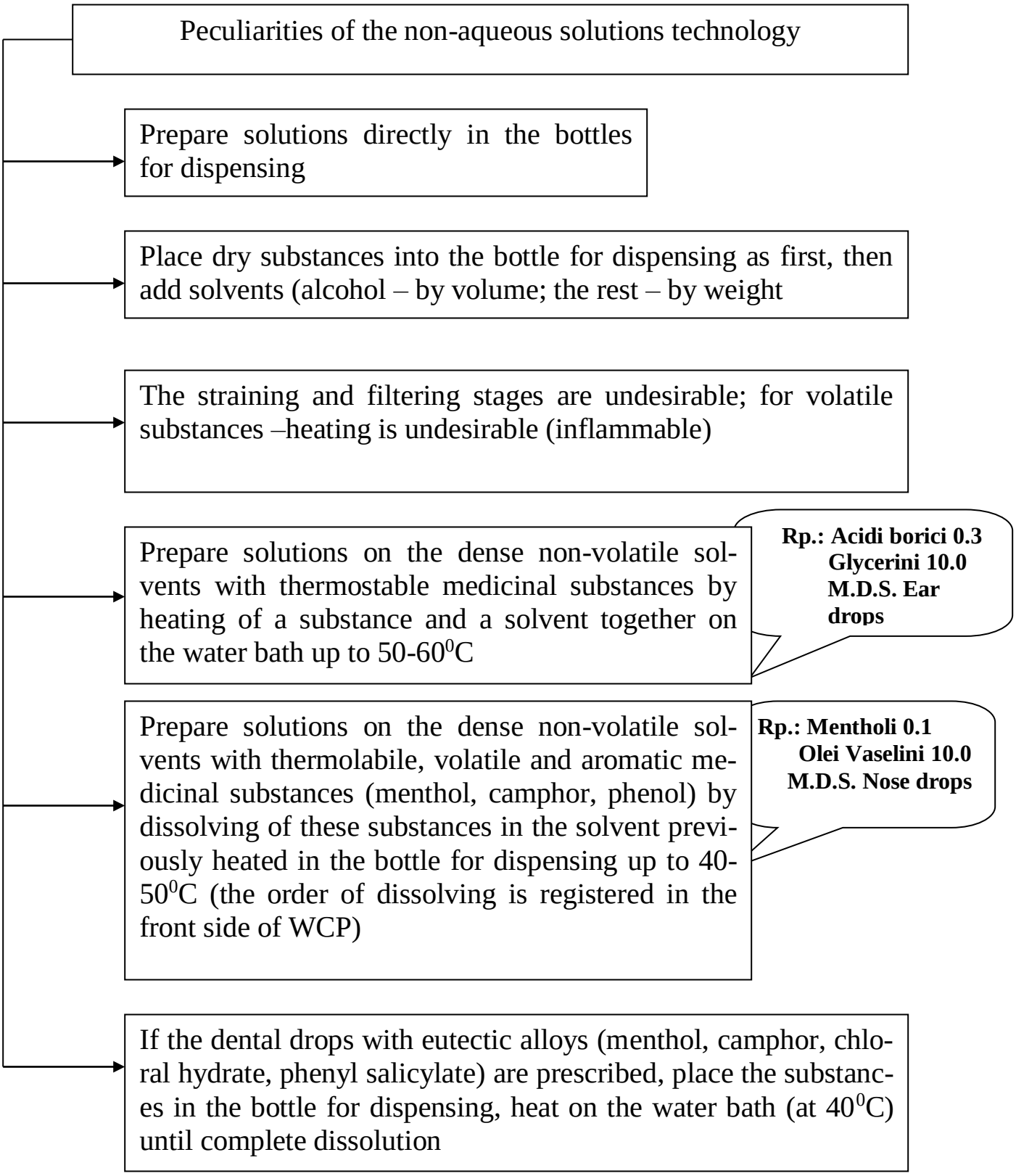
Rp.: Solutionis Acidi Hydrochlorici 6 % 100 ml
D.S. External (solution № 2)

Solution № 2:
Hydrochloric acid, 25%, 6 ml
Purified water: 100 – 6 = 94 ml
or
Diluted hydrochloric acid, 8.3 %, 18 ml
Purified water: 100 – 18 = 82 ml

8. NON-AQUEOUS SOLUTIONS



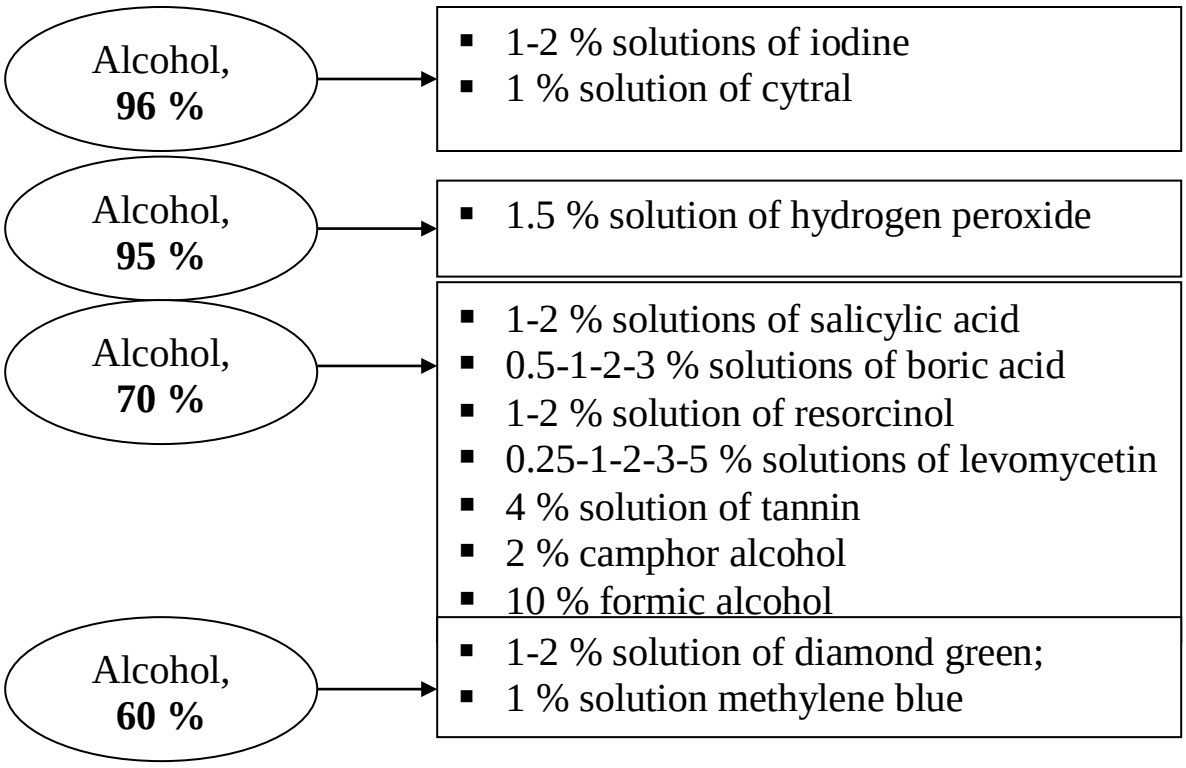



Peculiarities of the non-aqueous solutions technology
Prepare solutions directly in the bottles for dispensing
Place dry substances into the bottle for dispensing as first, then add solvents (alcohol – by volume; the rest – by weight
The straining and filtering stages are undesirable; for volatile substances –heating is undesirable (inflammable)
Prepare solutions on the dense non-volatile solvents with thermostable medicinal substances by heating of a substance and a solvent together on the water bath up to 50-60^{0}C
Rp.: Acidi borici 0.3
Glycerini 10.0
M.D.S. Ear drops
Prepare solutions on the dense non-volatile solvents with thermolabile, volatile and aromatic medicinal substances (menthol, camphor, phenol) by dissolving of these substances in the solvent previously heated in the bottle for dispensing up to 40-50^{0}C (the order of dissolving is registered in the front side of WCP)
Rp.: Mentholi 0.1
Olei Vaselini 10.0
M.D.S. Nose drops
If the dental drops with eutectic alloys (menthol, camphor, chloral hydrate, phenyl salicylate) are prescribed, place the substances in the bottle for dispensing, heat on the water bath (at 40^{0}C) until complete dissolution

TECHNOLOGY OF ALCOHOL SOLUTIONS

(Order MPHS №197 from 07.09.93)

- If the concentration of alcohol is not specified in the prescription, 90 % ethyl alcohol is used, except the cases when concentration is specified by NTD:



- The index of VIC when dissolving dry substances prescribed in the quantity more than 3 % is not taken into account in alcoholic solutions;
- When the concentration of alcohol required is absent in the chemist's, it is prepared from the alcohol with a higher concentration using alcoholic tables № 3, 4, 5 SPh, or calculating the amount of alcohol according to the formula:

$$X = V \cdot \frac{B}{A},$$

where: X – is the quantity of a stronger alcohol, ml;
V –is the quantity of ethyl alcohol of the required concentration, ml;
B – is the required concentration of alcohol, %;
A – is the concentration of a stronger alcohol has to be diluted, %.

DILUTION OF ETHYL ALCOHOL

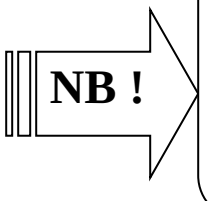
Alcoholic tables are used for calculation of the quantity of alcohol and water:

The table 3 (Appendix 6) – for obtaining alcohol of different strength at 20°C (calculation of the quantity of water);

The table 4 (Appendix 7) – the quantity of alcohol of different strength and water (in ml at 20°C), which are necessary to mix for obtaining 1 liter of alcohol with the required concentration;

The table № 5 - for dilution of alcohol in a higher concentration (95.1 – 96.7%).

- **Ethyl alcohol is in chemist's shop on the qualitative-quantitative account; the prescription is made out in addition by seal "Medical establishment". It also remains in a chemist's for 1 year, the drug is made out by "Signature"; on the back side of the prescription recalculation of volumetric units into the weight ones should be performed (as the account is made by weight)**



The quantity of purified water by difference of volumes of alcohol of the required concentration and a strong alcohol is not permitted to calculate, because the reduction of the volume of the water-alcoholic solution (the phenomenon of contraction) is not taken into account

Rp.: Acidi salicylici 0.3
Spiritus aetylici 30 ml
M.D.S. Wipe skin of the face.

Doctor's seal Doctor's signature
Seal "Medical establishment"

The given medicine is an alcoholic solution for external use. According to the Order of Ministry PHU №197 from 07.09.93 the solution is prepared on 70 % alcohol.

***WCP** (reverse side)*

ethyl alcohol 70 %:

x = 30x70 / 90 = **23.3 ml**

purified water – up to 30 ml

or

by table № 3:

for 1000 ml $_{(90\ \%\ alcohol)}$ – 310 ml of water

for 23.3 ml ($_{90\ \%\ alcohol)}$ – x

x = **7.22 ml**

by table № 4:

ethyl alcohol:

for 1000 ml $_{(70\ \%\ alcohol)}$ – 778 ml $_{(90\ \%\ alcohol)}$

for 30 ml $_{(70\ \%\ alcohol)}$ – x

x = **23.4 ml**

purified water:

for 1000 ml $_{(70\ \%\ alcohol)}$ – 240 ml $_{(water)}$

for 30 ml $_{(70\ \%\ alcohol)}$ – x

x = **7.2 ml**

a)*WCP (front side)*

Data №Pr.

Acidi salicylici 0.3

Spiritus aethylici 70 % 30 ml

V_{total} = 30 ml

Prepared by:

Checked by:

b)*WCP (front side)*

Data №Pr.

Acidi salicylici 0.3

Spiritus aethylici 90 % 23.3 ml

Aquae purificatae ad 30 ml

V_{total}=30 ml

Prepared by:

Checked by:

c)*WCP (front side)*

Data №Pr.

Acidi salicylici 0.3

Spiritus aethylici 90 % 23.3 ml

Aquae purificatae 7.2 ml

V_{total}=30 ml

Prepared by:

Checked by:

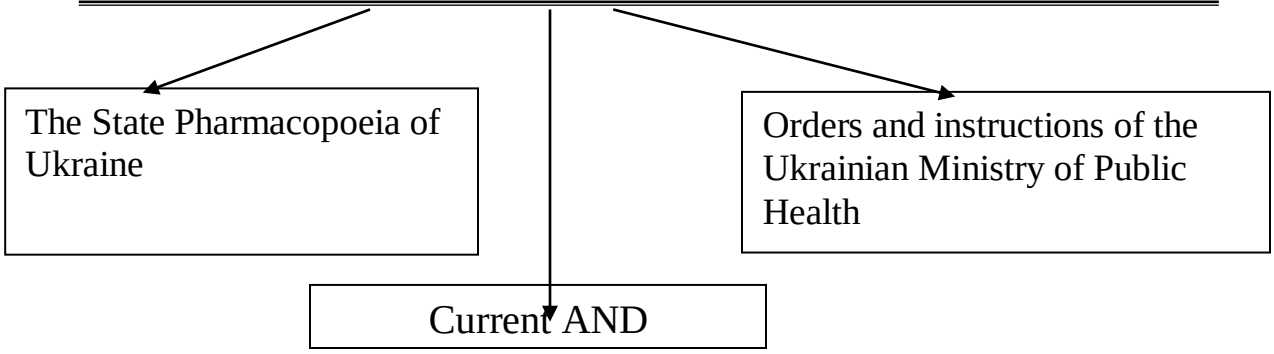
Technology:

1. Place 0.3 g of salicylic acid directly into the dry bottle for dispensing.
2. Add 30 ml of 70 % alcohol or the calculated amount of 90 % alcohol and purified water.
3. Dissolve while mixing.
4. Close the bottle by a cork and a cover, register for dispensing:

- the prescription number;
- “Signature”;
- the additional labels (“Keep in a cool dark place”, “Keep out of the reach of children”, “Keep out of fire”.

9. QUALITY CONTROL AND REGISTRATION FOR DISPENSING OF LIQUID MEDICINAL FORMS

The quality control of liquid medicinal forms is carried out according to:



The quality control includes ***all kinds of the intra-chemist's control***:

- written;
- questionnaire;
- organoleptic (color, smell, taste), homogeneity and the absence of particulate matters;
- physical (the total weight that should not exceed the permissible deviation limits after preparing a medicine);
- chemical (selectively);
- control at dispensing.

Registration for dispensing:

- label "Internal" or "External"
- solutions with poisonous substances are sealed up, registered by "Signature" and "To be handled with caution"
- special conditions for storage – "Keep in a cool place", "Shake well before use".

10. EQUIPMENT IN TECHNOLOGY OF LIQUID MEDICINAL FORMS

Mixers

- *Magnetic mixer MMZM* — used for mixing of the liquids in containers from non-magnetic materials with a plane bottom
- *Mixer for concentrated solutions* — used for mixing of solutions in 10 liters glass containers
- *Mixer for solutions preparation MI-02* — used for mechanical mixing of solutions and other liquids in the technological process

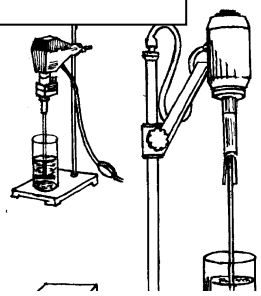
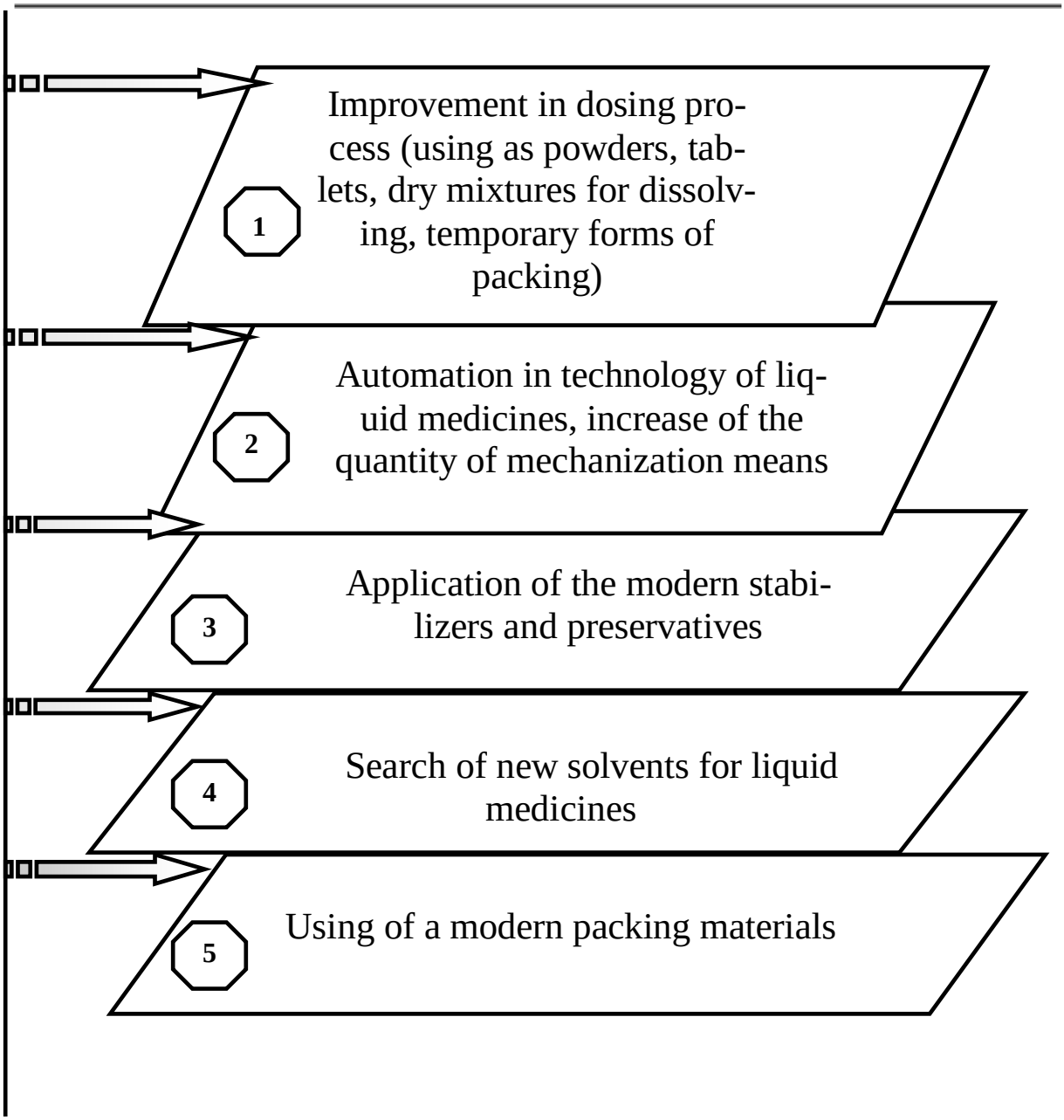


Fig. 9. A mixer for concentrated solutions

Dosing facilities for liquids

- *Pharmacy doser for liquids DPM-250* — for intrachemist's stock of liquid medicinal forms by 20 - 250 ml doses
- *Glass pharmacy pipettes APK-2* — - for dosing of liquids by a small batch; - for measuring in technology of liquid medicines for individual prescriptions
- *Device for dosing and measuring of liquids by drops UPD-1* — for measuring of microdoses in technology of medicines according to individual prescriptions and for analysis

11. WAYS OF IMPROVING LIQUID MEDICINAL FORMS



QUESTIONS FOR SELF-CONTROL

1. Characteristics of solutions as a disperse system, their classification.
2. Requirements to solvents. Ways of obtaining purified water in pharmacy conditions. Requirements to purified water.
3. Rules of the preparation of concentrated solutions for burette system. The quality control of the concentrated solutions, storage conditions.
4. Checking of doses for poisonous and strong-effective substances in mixtures.
5. Preparation of solutions using dry substances in quantity up to 3 % and more than 3 % if their concentrated solutions are absent. Introduction of aromatic water, syrups, Galen's medicines into mixtures.
6. Rules for calculation of water amount and standard pharmacopoeian liquid depending on the way of prescribing.
7. Characteristic of non-aqueous solvents (alcohol, vegetable oils, vaseline oil, glycerol, chloroform, etc.).
8. Calculation for alcohol dilution using the formula and alcoholometry tables.
9. Characteristics of highly-molecular compounds and their classification.
10. Characteristics and properties of colloidal solutions. Formulation of protected colloids solutions: collargol, protargol, ichthyol.
11. Characteristics of suspensions as a medicinal form and dispersive system. Requirements for suspensions.
12. Characteristics of stabilizers and the mechanism of their activity. The dispersive method of preparing suspensions with different hydrophobic (of different levels of hydrophobia) and hydrophilic (swelling and unswelling) medicines.
13. Characteristics of emulsions as a medicinal form and dispersive system. Classification of emulsions. Types of oil emulsions and methods of their determination
14. Characteristics of infusions and decoctions as medicinal forms and dispersive systems. Factors affecting the process of extraction of the active substances from the raw material.

15. Peculiarities of preparing water extractions from the plant medicinal raw material containing alkaloids, cardiac glycosides, volatile oils, tannins, antraglycosides, saponins.
16. Rules of preparing water extractions by using concentrated extracts and adding some different medicinal substances.

TESTS

1. At the chemist's shop a prescription should be prepared according to the formula:

Rp.: Extracti Belladonnae 0.2
Solutionis Calcii chloridi 2% 200 ml
Misce. Da. Signa. 1 tablespoon 3 times a day.

What amount of the concentrated solution of calcium chloride (20 %) is it necessary to use?

A 20 ml
B 4 ml
C 5 ml
D 10 ml
E 40 ml

2. Liquid medicinal forms are prepared using a concentrated solution of medicinal substances or using VIC during dissolution of the substances if the prescribed solvent is:

A Polyethylenglycol-400
B Aromatic water
C Glycerol
D Alcohol
E Purified water

3. What amount of Formalin (37%) should be used for preparation of a medicine:

Rp.: Solutionis Formalini 3 % 100 ml
Da. Signa. For disinfection of footwear.

A 3 ml
B 8.1 ml
C 12.3 ml
D 30 ml
E 37 ml

4. What liquid is it necessary to add in the auxiliary bottle at first according to the Order of the Ukrainian MPH № 197?

A Syrup of sugar
B Convallaria tincture
C Belladonna tincture
D Adoniside
E Purified water

5. What is the concentration of Lugol's solution for internal use?

A 1%
B 5%
C 10%
D 0.5%
E 3%