NATIONAL UNIVERSITY OF PHARMACY

Drug technology department

Discipline "Pharmacy-based technology of drugs"

Technological peculiarities of suspension preparation

A LECTURE FOR ENGLISH STUDENTS of THE 3-RD COURSE IN THE SPECIALTY "PHARMACY"

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THE PLAN OF THE LECTURE

1. Methods of suspension's preparation.

2. Formulation of suspensions.

3. Quality control and storage of suspensions.

QUESTIONS FOR SELF-CONTROL

1. Factors that influence the biological availability medicinal substances from suspensions.

References:

1. Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Garkavtseva O.A. Chemist's Technology of Drugs: The manual for students of higher schools / Ed. by A.I. Tikhonov and T.G. Yarnykh. – Kharkiv: NUPh; Original, 2011. – 424 p
2. Dry, liquid and soft medicinal forms. A textbook for English students in speciality "Pharmacy" / A.I. Tikhonov, T.G. Yarnykh, A.B. Yuryeva, L.N. Podorozhna, S.S. Zuykina; Ed. by A.I. Tikhonov. – Kharkiv: NUPh; Original, 2011. – 208 p.
3. Tikhonov A.I., Chemist's technology of drugs. Solution of high molecular compounds. Colloidal solution. A lecture for English students of the 3-rd year, speciality "Pharmacy": a handbook for out-of-class work of students / Edited by acad. A.I. Tikhonov. - Kh.: PH of NUofPh, 2009. – 24 p.
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TECHNOLOGY OF SUSPENSIONS

Preparation of suspensions by dispersing method

(with hydrophilic substances)

Dry medicinal substances are grinded in the **mortar**

Grind (according to the **Deryagin's rule**) with half of liquid amount from the mass of dry substance

The resulting mixture (pulp) slowly diluted with water, mixed and transferred to glass bottle for dispensing

(with hydrophobic substances)

Dry medicinal substances are grinded in the **mortar** with alcohol

Add stabilizer and mixed

Grind (according to the **Deryagin's rule**) with half of liquid amount from the mass of dry substance and stabilizer

The resulting mixture (pulp) slowly diluted with water, mixed and transferred to glass bottle for dispensing

TECHNOLOGY OF SUSPENSIONS

Method of "MAKING MUDDY" ("shaking")

For suspensions containing bismuth basic nitrate

I. Weight out a dry medicinal substance in the mortar.

II. Grind (according to the Deryagin rule) with 50% amount of the liquid calculated by the amount of a dry substance (add 0.4-0.6 ml of a liquid (40-60%) per 1.0 g of the powdered substance).

III. Add 5-10 % of the liquid to the mixture obtained, triturate, allow to stand for 1-2 minutes.

IV. When the liquid is settled (the big particles settle at the bottom and the thin particles are on the top of the surface), transfer it into the bottle for dispensing.

V. The stages III-IV are repeated until all precipitate is transferred into a thin dispersed state.

TECHNOLOGY OF SUSPENSIONS

Condensation method of suspension preparation

Rp.:	**Calcii chloridi**	**10,0**
	Natrii hydrocarbonatis	**4,0**
	Aquae purificatae	**200 ml**
	Misce. Da. Signa. 1 table spoon 3 times a day.	

$$CaCl_2 + 2NaHCO_3 \rightarrow CaCO_3\downarrow + H_2O + 2NaCl$$

WCP (reverse side)

Sol. Calcium chloride 50 % (1:2): 10.0 × 2 = 20 ml

Sol. Sodium hydrocarbonate 5 % (1:20): 4.0 × 20 = 80 ml

Purified water: 200 - (20+80) = 100 ml

At first two solutions - calcium chloride solution and sodium hydrocarbonate solution – should be prepared separatelly and then mix these solutions.

Measure 100 ml of the purified water into the bottle for dispensing, add 20ml of 50 % calcium chloride solution and 80 ml of 5 % sodium hydrocarbonate solution.

TECHNOLOGY OF SUSPENSIONS

Condensation method of suspension preparation

Opalescence and muddy mixtures are formed after adding tinctures, liquid extracts, aromatic liquids (ammonium anise drops) to aqueous solutions.

Date: №

Rp.: **Kalii bromidi** **3,0**
Tincturae Valerianae **5 ml**
Aq. purificatae ad **200 ml**
Misce. Da. Signa. 1 table spoon 3 times a day.

Sign of the doctor

WCP (reverse side)
V general = 200 ml
Sol. Potassium bromide 20 % (1:5)
3,0 x 5 = 15 ml
Purified water: 200 – (5 + 15) = 180 ml

WCP (front side)

Date: №

Aquae purificatae	180 ml
Solutionis Kalii bromidi 20% (1:5)	15 ml
Tincturae Valerianae	5 ml

V general = 200 ml

Prepared by: (Signature)
Checked by: (Signature)

TECHNOLOGY OF SUSPENSIONS

Dispersion method of suspension preparation

Date: №

Rp.: **Mentholi** **0.5**

Natrii hydrocarbonatis

Natrii bromidi **aa 1.5**

Aquae purificatae **100 ml**

Misce. Da. Signa. Rinsing.

Sign of the doctor

TECHNOLOGY OF SUSPENSIONS

Dispersion method of suspension preparation

Date: №

Rp.: **Mentholi** **0.5**
Natrii hydrocarbonatis
Natrii bromidi **aa 1.5**
Aquae purificatae **100 ml**
Misce. Da. Signa. Rinsing.

Sign of the doctor

Characteristics:
The given medicine is a suspension for external application with a hydrophobic odorous and volatile substance called menthol with distinctly expressed hydrophobic properties; sodium hydrocarbonate and sodium bromide– water soluble substances

WCP (reverse side)

Sol. Sodium hydrocarbonate 5 % (1:20): 1.5 × 20 = 30 ml
Sol. Sodium bromide 10 % (1:10): 1.5 × 10 = 15 ml
Purified water: 100 - (30+15) = 55 ml
Alcohol for menthol
1.0 - 10 drops
0.5 - x x = 5 drops
Tween-80 (stabilizer for menthol) 0.5/5=0.1
1.0 – 16 drops
0.1 – x x= 2 drops

TECHNOLOGY OF SUSPENSIONS

Dispersion method of suspension preparation

Date: №

Rp.: **Mentholi** **0.5**
Natrii hydrocarbonatis
Natrii bromidi **aa 1.5**
Aquae purificatae **100 ml**
Misce. Da. Signa. Rinsing.

Sign of the doctor

WCP (front side)

Date: №

Aquae purificatae 55 ml
Sol. Natrii hydrocarbonatis 5 % (1:20) 30 ml
Sol. Natrii tetraboratis 10 % (1:10) 15 ml
Mentholi 0.5
Tween-80 (1.0 – 16 drops) gtts.II
V general = 100 ml

Prepared by: (Signature)
Checked by: (Signature)

Measure 55 ml of the purified water into the auxiliary bottle add solution sodium hydrocarbonate 5% 30 ml and solution sodium bromide 10% 15 ml.

Weight out 0.5 g of menthol in the mortar, grind it with 5 drops of alcohol (because menthol is a poorly powdered substance).

Add 2 drops of Tween-80 and triturate until a homogeneous mixture is obtained.

Then add 15 drops of the aqueous solution of salts (according to the Deryagin rule), grind and add solutions of salts by small portions.

After mixing transfer the mortar's content in the bottle for dispensing.

TECHNOLOGY OF SUSPENSIONS

Dispersion method of suspension preparation

Date: №

Rp.: **Zinci oxydi** **10.0**
Aquae purificatae **100 ml**
Misce. Da. Signa. For washes.

Sign of the doctor

WCP (reverse side)
m total = 100+10=110.0

WCP (front side)

Date: №

Aquae purificatae 55 ml
Sol. Natrii hydrocarbonatis 5 % (1:20) 30 ml
Sol. Natrii tetraboratis 10 % (1:10) 15 ml
Mentholi 0.5
Tween-80 (1.0 – 16 drops) gtts.II
V general = 100 ml

Prepared by: (Signature)
Checked by: (Signature)

Weigh 10.0 g of ZnO in the mortar, triturate it, measure 100 ml of the purified water using a cylinder, add approximately 5 ml of the purified water in the mortar according to the Deryagin rule, triturate and then add gradually the remaining quantity of water. Pour the suspension obtained into the bottle for dispensing.

Stick the labels: № of prescription, «External», «Shake well before use» and «Keep out of the reach of children».

TECHNOLOGY OF SUSPENSIONS

Dispersion method of suspension preparation

Date: №

Rp.: Therpini hydrati 2.0
Natrii hydrocarbonatis 2.0
Aquae purificatae 100 ml
Misce. Da. Signa. 1 tablespoon
3 times a day.

Sign of the doctor

Characteristics:
The given medicine is a suspension for internal application with terpin hydrate, a substance with poor expressed hydrophobic properties and water soluble substance sodium hydrocarbonate.

WCP (reverse side)

Sol. Sodium hydrocarbonate 5 % (1:20):2.0 × 20 = 40 ml
5 % methylcellulose solution 2.0
Purified water: 100 – 40 - 2 = 58 ml

Measure 58 ml of the purified water and 40 ml of the 5 % sodium hydrocarbonate solution into the bottle for dispensing. Triturate 2.0 g of terpin hydrate in the mortar, then add 2.0 methylcellulose solution 5 % and 1.5 ml of the sodium hydrocarbonate solution (according to the Deryagin rule). Mix and triturate all ingredients thoroughly until a homogeneous mixture is obtained. Then add (by small portions) the sodium hydrocarbonate solution, mix and pour the suspension obtained into the bottle for dispensing.

QUALITY CONTROL OF SUSPENSIONS

Quality control of suspensions is carried out according to the :

- *State Pharmacopoeia of Ukraine*;
- instructions and orders of the Ministry of Health of Ukraine

The quality control includes
all types of intra pharmacy control :

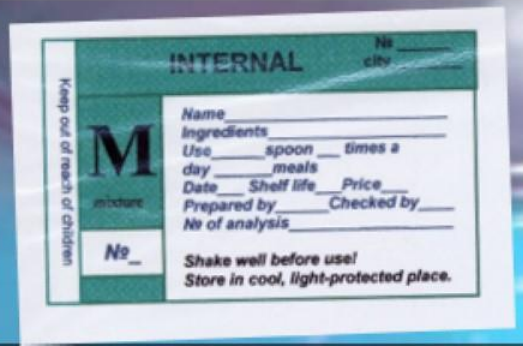
- Writing;
- Questionnaire;
- Organoleptic (color, taste, smell), and checking homogeneity of particles of the disperse phase, dry residue, time of settling;
- Physical (total mass, which, after preparation the drug should not exceed the norms permissible deviations The deviation in the content of the active substances in 1.0 g (ml) of a suspension should not exceed ±10 %)
- Chemical control (optional);
- Control when dispensing.

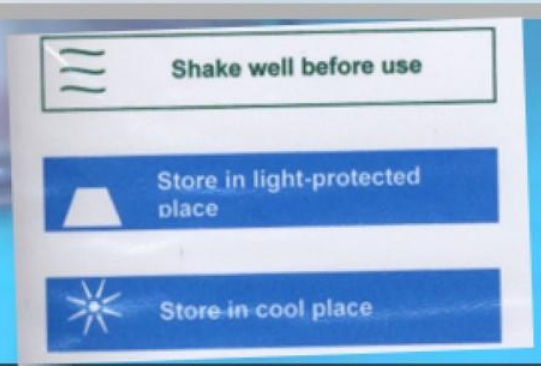
7. QUALITY CONTROL AND STORAGE OF SUSPENSIONS

The terms of storage of suspensions depend on properties of medicinal substances, entering in the prescription.

If there is not the special indications, extemporaneous suspensions keep in a cool, protected from light place 3 days, suspensions in which as a liquid an alcohol is used – 10 days.

All suspensions dispense in small bottles from colourless (transparent) glass, that it is possible to see the results of shaking, with additional labels:
«Shake up before application»,
«Keep in the cool place protected from light»,
«Keep out of the reach of children».





Name (English and Latin)	Properties of substances	Peculiarities of introduction into medicinal forms / *Incompatibilities*
Bismuth basic nitrate	Big loses in the pores of the mortar; an amorphous substance. Insoluble in water and in fats	**By the method of "making muddy"**
Calcium chloride	Soluble in water	**Suspensions (the condensation method): As a result of neutralization with the solution of sodium hydrocarbonate insoluble compound - calcium carbonate is formed**
Camphor	An aromatic, volatile, poorly powdered substance. Soluble in fats, ethyl alcohol (not less 70 %). A hydrophobic substance with distinctly expressed properties	**Add stabilizers in the following quantities:** **– gelatose = $m_{camphor}$,** **– 5 % methylcellulose solution = $m_{camphor} \cdot 2$,** **– Tween-80 = $m_{camphor} : 5$**

Name (English and Latin)	Properties of substances	Peculiarities of introduction into medicinal forms / *Incompatibilities*
Hexamethylene tetramine	Soluble in water, a thermolabile substance	**By the general rules.** **Used as 10 % concentrated solution (1:10)** ***Physical and chemical: change of mixture's odour in combination with ammonium chloride, sedimentation of tannins from decoction of Bearberry leaves***
Menthol	An aromatic, volatile, poorly powdered substance. Soluble in fats, ethyl alcohol. Insoluble in water, glycerin. A hydrophobic substance with distinctly expressed properties	**Add stabilizers in the following quantities:** **– gelatose = $m_{menthol}$,** **– 5 % MC solution = $m_{menthol} \cdot 2$,** **– Tween-80 = $m_{menthol} : 5$**
Norsulphazol	Insoluble in water and in fats. A hydrophobic substance with poorly expressed properties	**Add stabilizers in the following quantities:** **– gelatose = $m_{norsulphazol}$,** **– 5 % MC solution = $m_{norsulphazol} \cdot 2$,** **– Tween-80 = $m_{norsulphazol} : 5$**

Name (English and Latin)	Properties of substances	Peculiarities of introduction into medicinal forms / *Incompatibilities*
Phenylsalicylate	A poorly powdered substance. Soluble in fats, Insoluble in water. A hydrophobic substance with poorly expressed properties	**Add stabilizers in the following quantities:** **– gelatose = $m_{phenylsalicylate}$: 2,** **– 5 % MC solution = $m_{phenylsalicylate}$,** **– Tween-80 = $m_{phenylsalicylate}$: 10**
Sodium hydrocarbonate	Soluble in water	**Suspensions (the condensation method): As a result of neutralization with the solution of calcium chloride insoluble compound - calcium carbonate is formed** ***Physical and chemical: precipitation of alkaloids (codeine base) in the presence with codeine phosphate***
Streptocide	A strong effective substance (check of doses), poorly powdered. Insoluble in water and in fats. Soluble in PEO. A hydrophobic substance with poorly expressed properties	**Add stabilizers in the following quantities:** **– gelatose = $m_{streptocide}$: 2,** **– 5 % MC solution = $m_{streptocide}$,** **– Tween-80 = $m_{streptocide}$: 10**

Name (English and Latin)	Properties of substances	Peculiarities of introduction into medicinal forms / *Incompatibilities*
Sulphur	A coloured substance. Insoluble in water, moderately in fats. A hydrophobic substance with distinctly expressed properties	**Add a stabilizer *(potassium or green soap)* in the amount 0.2 g per 1.0 g of sulphur**
Terpinhydrate	Insoluble in water and in fats. A hydrophobic substance with poorly expressed properties	**Add stabilizers in the following quantities:** **– gelatose = $m_{terpinhydrate}$: 2,** **– 5 % MC solution = $m_{terpinhydrate}$,** **– Tween-80 = $m_{terpinhydrate}$: 10**
Zinc oxide	An amorphous substance. Insoluble in water and in fats. A hydrophilic substance	**Suspensions (the dispersion method): Without stabilizing**
Magnesium oxide	An amorphous substance. Insoluble in water and in fats. A hydrophilic substance	**Suspensions (the dispersion method): Without stabilizing**

Test	Explanation
Suspensions as heterogeneous systems can be characterized by kinetic and sedimentary instability. What substance is used for increasing suspension's stability with hydrophobic substances? **A** Glucose **B** Sodium chloride **C** Boric acid **D** Sodium sulphate **E** Gelatose	

Test	Explanation
Suspensions as heterogeneous systems can be characterized by kinetic and sedimentary instability. What substance is used for increasing suspension's stability with hydrophobic substances? **A** Glucose **B** Sodium chloride **C** Boric acid **D** Sodium sulphate **E** Gelatose	For increasing stability with hydrophobic MS are used stabilizers. The most often used stabilizers are gelatose, tween-80

Test	Explanation
A pharmaceutist prepared a suspension. It must contain the following amount of the liquid in order to comply with the Deriagin's rule: **A** 1-0.8 ml of 1.0 substance **B** 0.4-0.6 ml for 1.0 substance **C** 1.5-0.7 ml for 1.0 substance **D** 0.9-2 ml for 1.0 substance **E** 0.1-1.0 ml for 1.0 substance	

Test	Explanation
A pharmaceutist prepared a suspension. It must contain the following amount of the liquid in order to comply with the Deriagin's rule: **A** 1-0.8 ml of 1.0 substance **B** 0.4-0.6 ml for 1.0 substance **C** 1.5-0.7 ml for 1.0 substance **D** 0.9-2 ml for 1.0 substance **E** 0.1-1.0 ml for 1.0 substance	Deriagin's rule: The maximum effect of dispersion in the liquid medium is obtained when adding 0.4-0.6 (0.5) ml of a liquid per 1.0 g of a dry substance (50 %)

Test	Explanation
A pharmacist should prepare a suspension from phenylsalicylate of prescribed in the amount 2.0. How many gelatose should the pharmacist add? **A** 2.5 **B** 2.0 **C** 1.0 **D** 0.5 **E** 0.2	

Test	Explanation
A pharmacist should prepare a suspension from phenylsalicylate of prescribed in the amount 2.0. How many gelatose should the pharmacist add? **A** 2.5 **B** 2.0 **C** 1.0 **D** 0.5 **E** 0.2	As phinilsalycilate is hydrophobic substance with poorly expressed properties, gelatose should be obtained in the amount 2.0 / 2 = 1.0 of gelatose 1.0 – 0.5 of Gelatose 2.0 – x x = 1.0

Test	Explanation
What stabilizer should be used for preparation of suspensions with sulphur? **A** Starch **B** 5% solution of methylcellulose **C** Gelatose **D** Potassium or green soap **E** Lanolin	

Test	Explanation
What stabilizer should be used for preparation of suspensions with sulphur? **A** Starch **B** 5% solution of methylcellulose **C** Gelatose **D** Potassium or green soap **E** Lanolin	For preparation of suspensions with sulphur potasium or green soap use (as stabilizer)

Conclusions

1. Methods of suspension's preparation were explained.

2. Formulation of suspensions were studied.

3. Quality control and storage of suspensions were considered.

THANK YOU FOR YOUR ATTENTION