# METHODOLOGICAL RECOMENDATIONS FOR LABORATORY CLASSES

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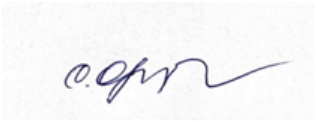
|---|---|
| **Discipline:** | **«Methods and equipment for pharmaceutical analysis»** |
| **Discipline code:** | **MOFA 4301** |
| **Educational program** | **6B07201 «Pharmaceutical manufacturing technology»** |
| **Number of credits (ECTS):** | **120 hours (4 credits)** |
| **Course:** | **4** |
| **Semester:** | **7** |
| **Volume of laboratory classes:** | **30** |

**Shymkent, 2024**

Methodological guidelines for laboratory classes were developed in accordance with the working curriculum of the discipline (syllabus) “Methods and equipment for pharmaceutical analysis” and discussed at a department meeting.

Protocol №21, 10.06.2024 y.

Head of Department, Professor  Ordabaeva S.K.

**Lesson №1**

**1. Topic: Analysis of medicinal products by spectrophotometric method in the UV region.**

**2. Goal:** to master practical skills in carrying out spectrophotometric analysis.

**3. Learning objectives:**

- provide students with knowledge of the basic principles of use, the procedure for organizing and conducting the spectrophotometric method of analysis;
- teach students to conduct the spectrophotometric method of analysis.

**4. Main questions of the topic:**

1. Spectral methods of analysis in the UV, IR and visible regions. The essence of the methods.
2. Classification of optical methods of analysis. Principles of their classification.
3. Application, capabilities and limitations of spectral methods in the analysis of organic compounds.

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
| 2 | Completing laboratory work | 50 |
| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |
| 5 | summing up (giving grades) | 5 |

**Safety rules when working in a chemical laboratory**

Working with small amounts of chemicals reduces the possibility of accidents to a minimum, but does not eliminate them completely. Therefore, everyone working in a chemical laboratory must know and strictly follow all safety regulations.

1. Care should be taken when performing all work, remembering that carelessness, inattention, and insufficient knowledge of the properties of the substances being worked with may result in an accident.

2. If the thermometer breaks during the experiment and mercury spills, it must be collected using a special trap. The smallest particles of mercury are collected with a brush made of white tin. The surface of the table or floor where the mercury was is thoroughly moistened with a 20% solution of iron (III) chloride.

3. Heat the liquid in the test tube gradually, directing the test tube opening away from you and the students working nearby, since partial heating may cause the liquid to be ejected.

4. Do not lean over the test tube in which the liquid is boiling.

5. Determine the smell of any substances in the laboratory, even if their quantity is very small, by directing the vapors or gas towards you with a hand movement.

6. Do not taste any substances in the laboratory.

7. All experiments with odorous, as well as poisonous substances (aniline, bromine, etc.) should be carried out in a fume hood.

8. Dissolve sulfuric acid in water, adding the acid to the water drop by drop, stirring the solution all the time.

9. Cover any spilled acids or alkalis with sand, neutralize them, and only then clean up.

10. Collect shards of broken glass with a brush and dustpan.

11. When working with a gas outlet tube, remove the burner from under the test tube with the reaction mixture only when the end of the gas outlet tube lowered into the liquid has been removed from it. If you remove the burner prematurely, the liquid will be sucked into the reaction tube and the reaction mixture may splash onto your face and hands. 12. Work with ether, benzene, and alcohol away from fire.

**First aid measures in case of accidents**

1. For thermal burns, the affected area should be moistened with a solution of tannin in alcohol or a 2% solution of potassium permanganate.

2. For chemical burns, it is necessary to first remove the substances that caused the burns from the skin, then treat it accordingly:

a) in case of acid or alkali burns, wash the burnt area with a strong stream of water, then neutralize the acid with a 1% solution of sodium bicarbonate, and the alkali with a 1% solution of acetic acid;

b) in case of a bromine burn, treat the affected area with a 10-20% solution of sodium thiosulfate, wash it off with plenty of water, then apply a tampon soaked in a 5% solution of urea; the affected area can be washed with ethyl alcohol;

c) in case of a burn with liquid phenol, rub the whitened area of the skin with glycerin until its normal color is restored, wash with water, apply a gauze tampon soaked in glycerin.

3. In case of chemical burns of the eyes with acid or alkali, it is necessary to rinse the eye with plenty of water, using a special eye bath, then with a 1% solution of sodium bicarbonate if acid got in, or a 2% solution of boric acid if alkali got in.

4. In case of cuts, remove glass fragments from the wound with tweezers, lubricate the edges of the wound with an alcohol solution of iodine, put a sterile dressing on the wound, and bandage it.

5. In case of any minor accident, you should immediately contact the teacher, without limiting yourself to taking measures on your own.

Laboratory work №1 Conduct spectrophotometric determination of 0.25 levomycetin tablets by specific absorption index.

1. Methodology for determination by specific absorption index
1.1 Introduction to the SF-2000 spectrophotometer manual.
1.2 Recording the absorption spectrum of the chloramphenicol solution (SO GF RK). About 0.1 g (accurately weighed) of chloramphenicol is dissolved in water in a 100 ml measuring flask and brought to the mark with water (solution A). 2 ml of solution A are transferred to a 100 ml measuring flask and brought to the mark with water.

The resulting solution is poured into a cuvette with a working thickness of 1 cm. Distilled water is used as a comparison solution. The optical density of the preparation solution is measured relative to the comparison solution in the range of 220-290 nm. The data are presented in the form of Table 1.

Table 1 - Spectrophotometric characteristics

| drug | λ, nm | D |
|---|---|---|
| | | |

Based on the data obtained, a graph of the absorption index versus wavelength (chloramphenicol absorption spectrum) is constructed. The absorption spectrum allows selecting wavelengths for analyzing dosage forms. The maxima and minima of the chloramphenicol solution absorption are found in the resulting UV spectrum.
1.3 Determining the specific absorption index of chloramphenicol at 278 nm. About 0.1 g (accurately weighed) of chloramphenicol is dissolved in water in a 100 ml measuring flask and brought to the mark with water (solution A). 0.5, 1.0, 1.5, 2.0, 2.5, 3.0 ml of solution A are transferred to a 100 ml measuring flask, brought to the mark with water and mixed.

The optical density of the solutions is measured (as specified in 1.2) at 278 nm. The data are presented in the form of a table. 2 and based on the obtained values, the specific absorption rate of the drug is calculated using the formula:

$$E_{1sm}^{1\%} = \frac{D}{C \times b},$$

where $E_{1sm}^{1\%}$ - specific absorption rate;
D - optical density;
b – working length of the cuvette.

Table 2 - Specific absorption rates of chloramphenicol

| Drug concentration, % | λ = 278 nm | |
|---|---|---|
| | D | $E_{1см}^{1\%}$ |
| | | |

The obtained data are used to calculate the content of the drug in the dosage form..

1.3 Spectrophotometric determination of chloramphenicol content in tablets. An exact weighed amount of powder from 1 crushed tablet is placed in a 250 ml measuring flask, shaken for 3-5 minutes with distilled water and brought up to the mark with water. Filter, discarding the first 15 ml of the filtrate. Place 2 ml of the filtrate in a 100 ml measuring flask, bring the solution volume to the mark with water and stir. Measure the optical density at 278 nm.
The chloramphenicol content in the tablets is calculated using the formula:

$$X = \frac{D \times V \times m_a}{E_{1cm}^{1\%} \times m \times V_{al}},$$

where $m_a$ - average weight of dosage form;
m - mass of dosage form taken for analysis;
Val - aliquot volume, ml;
V - volume of dilution of the drug sample, ml.

The obtained data are compared with the permissible deviation standards and a conclusion is made about the compliance of the drug content in the dosage form.

Laboratory work №2 Conduct spectrophotometric determination of 0.25 levomycetin tablets using the calibration graph method.

2. Method of determination using a calibration graph

2.1 Plotting a calibration graph of the dependence of optical density on the concentration of chloramphenicol in solution. A series of 6 chloramphenicol solutions with a content within 0.0005-0.003% is prepared: About 0.1 g of chloramphenicol (accurately weighed) is dissolved in water in a 100 ml measuring flask and brought to the mark with water (solution A). 0.5, 1.0, 1.5, 2.0, 2.5, 3.0 ml of solution A are transferred to a 100 ml measuring flask, brought to the mark with water and mixed.

The resulting solutions are poured into cuvettes with a working thickness of 1 cm. Distilled water serves as a comparison solution. The optical density values of the drug solutions are measured relative to the comparison solution at a wavelength of 278 nm. The data are presented in Table 1.

Table 1 - Spectrophotometric characteristics

| Drug concentration, % | D |
|---|---|
| | |

Based on the data obtained, a calibration graph is constructed of the absorption index versus the concentration of levomycetin. The calibration graph allows one to determine the quantitative content of levomycetin in the medicinal form.

*2.1* 2.1 Spectrophotometric determination of chloramphenicol content in tablets. An accurately weighed amount of powder from 1 crushed tablet is placed in a 250 ml measuring flask, shaken for 3-5 minutes with distilled water and brought up to the mark with water. Filter, discarding the first 15 ml of the filtrate. Place 2 ml of the filtrate in a 100 ml measuring flask, bring the volume of the solution to the mark with water and stir. Measure the optical density at 278 nm.

The content of chloramphenicol in tablets is found using the calibration graph.

The obtained data are compared with the permissible deviation standards and a conclusion is made about the compliance of the drug content in the dosage form.

**6. Literature:**
**main:**

**in Russian**

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4. Практикум по физико-химическим методам анализа, под ред. О.М. Петрухина.-М., 1987.-248 с.

**7. Methodological provision:**

link to lecture:
https://docs.google.com/document/d/1r1v1cGpnYmc2Jdkkul7Ad904EVBAaIBE/edit?usp=sharing&ouid=103428168790945926723&rtpof=true&sd=true

**8. Control**:

1. The essence of spectral methods in the UV, visible and IR regions. What wavelength ranges are characteristic of each region?
2. Differences in the terms "spectroscopy" and "spectrophotometry".
3. What is the absorption spectrum of a substance? What are absorption spectra in the UV and visible regions?
4. What are IR spectra?
5. What radiation sources are used for spectrophotometry when working in the UV, visible and IR regions of the spectrum?
6. The unit of measurement of wavelength in the UV and IR regions of the spectrum.
7. Definition of the following terms: transmission, transmittance, optical density, molar absorption coefficient.
8. Formulate the laws: Beer's law, Bouguer-Lambert's law and Bouguer-Lambert-Beer's law. Which of them underlies photometric methods of analysis?
9. What is the optical density of the solution if the basic law of light absorption is observed?
10. What causes the selective absorption of light by molecules?
11. What is the role of chromophore and auxochromic groups in a molecule when recording absorption spectra?
12. Definition of the following concepts: chromophore, bathochromic, hypsochromic, hyperchromic, hypochromic effects.
13. What is the basis for the use of spectra in qualitative and quantitative analysis?
14. What is the basis for determining the concentration of solutions using photometric analysis methods?
15. The main stages of determining the concentration of the test solution using the graduated graph method

16. How is the concentration range of standard solutions selected when constructing a calibration curve?
17. In what cases is it unacceptable to use a calibration curve when determining the concentration of the test solution?
18. Advantages of the calibration graph method in comparison with other photometric methods of analysis?
19. What is the basis for determining concentration using the method of comparing the optical densities of the standard and test solutions? The advantages and disadvantages of this method.
20. What requirements are followed when choosing a cuvette for analysis?
21. In what coordinates is the calibration graph plotted? What is its purpose?
22. The structure of the spectrophotometer and its operating principle.
23. List the main characteristics of spectral instruments.
24. How is a monochromatic light flux obtained in a spectrophotometer?
25. What material are cuvettes used from when working in the ultraviolet and visible regions of the spectrum? Why?
26. Basic rules for working with cuvettes.
27. What device in a spectrophotometer converts light energy into electrical energy?
28. The sequence of operations when measuring optical density on a spectrophotometer in the visible and ultraviolet regions of the spectrum.
29. Rules for working on the SF-2000.

**Lesson №2**

**1. Topic: Analysis of medicinal products by spectrophotometric method in the visible region.**

**2. Goal:** to master practical skills in carrying out spectrophotometric analysis.

**3. Learning objectives:**

- provide students with knowledge of the basic principles of use, the procedure for organizing and conducting the spectrophotometric method of analysis;
- teach students to conduct the spectrophotometric method of analysis.

**4. Main questions of the topic:**

1. The essence of the spectral method in the visible region. What wavelength intervals are characteristic of this region?
2. What are absorption spectra in the visible region?
3. The use of photometry in the visible region in the analysis of organic compounds.

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
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| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |
| 5 | summing up (giving grades) | 5 |

Laboratory work №1 Conduct a photometric determination of a 0.01% riboflavin solution.

Method of determination

10 ml of the test solution are transferred to a 25 ml volumetric flask, brought up to the mark with water and mixed. The optical density of the resulting solution (D1) is measured using a photoelectrocolorimeter at a wavelength of 445 nm (blue filter) in a cuvette with a layer thickness of 10 mm. Water is used as a control solution.

In parallel, the optical density of the reference solution (D2) containing 0.004% of a standard riboflavin solution is measured.

The riboflavin content in % (X) is calculated using the formula:

$$X = \frac{D_1 \cdot 0{,}04 \cdot 25 \cdot 10 \cdot 100}{D_2 \cdot 10 \cdot 100 \cdot 100}.$$

where $D_1$ - optical density of the test solution;
$D_2$ - optical density of standard solution.

*Preparation of standard solution*. 0.04 g (exactly weighed) of riboflavin is dissolved in water in a 100 ml measuring flask in a water bath with heating. After cooling, the volume of the solution is brought up to the mark with water and mixed (solution A).

10 ml of solution A are transferred to a 100 ml measuring flask, brought up to the mark with water and mixed.

The content of riboflavin in 1 ml of the dosage form should be no less than 0.009% and no more than 0.011%.

Laboratory work №2 Conduct photometric determination of rifampicin.

Determination method

About 0.1 g (exactly weighed) of rifampicin substance is placed in a 100 ml measuring flask, dissolved in 50 ml of ethyl alcohol, the volume of the solution is brought to the mark with the same solvent and mixed.

2 ml of the resulting solution are placed in a 100 ml measuring flask, the volume of the solution is brought to the mark with a phosphate buffer solution with a pH of 7.4 and mixed (test solution).

The optical density of the test solution is measured on a spectrophotometer at a wavelength of 475 nm in a cuvette with a layer thickness of 10 mm, using a phosphate buffer solution with a pH of 7.4 as a comparison solution.

The content of rifampicin (X) in the substance, in percent, is calculated using the formula:

$$X = \frac{D \cdot 100 \cdot 100}{187 \cdot m \cdot 2}$$

where D - optical density of the test solution;
187 - specific absorption index ($E^{1\%}_{1sm}$) at a wavelength of 475 nm; m is the mass of the substance sample, in grams.

The content of $C_{43}H_{58}N_4O_{12}$ (rifampicin) in the substance must be no less than 97.0% and no more than 102.0%, calculated on a dry matter basis.

**6. Literature:**
**main:**

**in Russian**

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2. Арзамасцев, А. П. Руководство к лабораторным занятиям по фармацевтической химии: учебное пособие / М.: Медицина, 2004. - 384 с. - (Учеб. лит. для студ. фарм. вузов и фак.).
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4. Практикум по физико-химическим методам анализа, под ред. О.М. Петрухина.- М., 1987.-248 с.

## 7. Methodological provision:

link to lecture:
https://docs.google.com/document/d/1r1v1cGpnYmc2Jdkkul7Ad904EVBAaIBE/edit?usp=sharing&ouid=103428168790945926723&rtpof=true&sd=true

## 8. Control:

1. Unit of measurement of wavelength in the visible spectrum.
2. Basic law of light absorption.
3. What is the optical density of a solution if the basic law of light absorption is observed?
4. What causes selective absorption of light by molecules?
5. What is the role of chromophore and auxochromic groups in a molecule when recording absorption spectra?
6. Definition of the following concepts: chromophore, bathochromic, hypsochromic, hyperchromic, hypochromic effects.
7. What is the basis for using spectra in qualitative and quantitative analysis?
8. What is the basis for determining the concentration of solutions using photometric analysis methods?
9. The main stages of determining the concentration of a test solution using the graduated graph method
10. How is the concentration range of standard solutions selected when constructing a calibration curve?
11. In what cases is it unacceptable to use a calibration curve when determining the concentration of a test solution?
12. Advantages of the calibration graph method in comparison with other photometric methods of analysis?
13. What is the basis for determining concentration using the method of comparing the optical densities of the standard and test solutions? Advantages and disadvantages of this method.
14. What requirements are followed when choosing a cuvette for analysis?
15. In what coordinates is the calibration graph plotted? What is its purpose?
16. The structure of a spectrophotometer and its operating principle.
17. List the main characteristics of spectral instruments.
18. How is monochromatic light flux obtained in a spectrophotometer?
19. What material are cuvettes made of when working in the ultraviolet and visible regions of the spectrum? Why?
20. Basic rules for working with cuvettes.
21. What device in a spectrophotometer converts light energy into electrical energy?
22. Sequence of operations when measuring optical density on a spectrophotometer in the visible and ultraviolet spectral range.
23. Rules for working on KFK, SF-2000.

**Lesson №3**

**1. Topic: Analysis of medicinal products by photocolorimetric method.**

**2. Goal:** to master practical skills in conducting photocolorimetric analysis.

**3. Learning objectives:**

- ✓ provide students with knowledge of the basic principles of use, the procedure for organizing and conducting the photocolorimetric method of analysis;
- ✓ teach students to conduct the photocolorimetric method of analysis.

**4. Main questions of the topic:**

1. Brief historical overview of spectral methods of analysis.
2. The essence of spectral methods in the UV, visible and IR regions. What wavelength ranges are characteristic of each region?
3. What are absorption spectra in the UV and visible regions?
4. What is the role of chromophore and auxochromic groups in a molecule when recording absorption spectra?
5. Application, capabilities and limitations of spectral methods in the analysis of organic compounds.

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
| 2 | Completing laboratory work | 50 |
| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |
| 5 | summing up (giving grades) | 5 |

Laboratory work №1 Conduct photocolorimetric determination of furacilin.

1. Method of determination

1.1 *Introduction to the KFK photocolorimeter instructions*

1.2 *Quantitative photometric determination of furacilin*.

About 0.02 g (exactly weighed) of the preparation is transferred to a 100 ml measuring flask, 70-80 ml of distilled water is added and heated in a water bath at 70-80$^0$C until the preparation is completely dissolved. The resulting solution is cooled and brought to the mark with water (solution A).

7.5 ml of water, 2 ml of 0.1 M sodium hydroxide solution are added to 0.5 ml of solution A and mixed. After 20 minutes, the optical density of the colored solution

($D_1$) is measured using a photocolorimeter in a cuvette with a working layer length of 3 mm with a blue filter. Water is used as a comparison solution.

In parallel, a reaction is carried out with 0.5 ml of a 0.02% standard solution of furacilin and the optical density of the resulting colored solution ($D_{st}$) is measured.

The furacilin content in % is calculated using the formula

$$X = \frac{D_1 \cdot 0{,}02 \cdot 100 \cdot 0{,}5 \cdot 10 \cdot 100}{D_{ст} \cdot 0{,}02 \cdot 100 \cdot 0{,}5 \cdot 10}$$

*Preparation of standard solution.* About 0.02 g of furacilin (exactly weighed), corresponding to the requirements of the State Pharmacopoeia of the Republic of Kazakhstan, is dissolved in 70-80 ml of water in a 100 ml measuring flask while heating in a water bath at 70-800C. After cooling, the volume of the solution is brought up to the mark with water.

Laboratory work №2 — Conduct photocolorimetric determination of novocaine.

2. Method of determination

*Reagents*. Freshly prepared alkaline hydroxylamine solution: mix 1 volume of 13.9% hydroxylamine hydrochloride solution and 2 volumes of 12% sodium hydroxide solution; 14% hydrochloric acid solution; 10% iron (III) chloride solution in 0.1 M hydrochloric acid solution.

*Standard solution*. 1 ml of standard solution contains 1 mg of novocaine.

*Comparison solution*: 0.4 ml of alkaline hydroxylamine hydrochloride solution, 0.3 ml of hydrochloric acid solution, 0.5 ml of iron (III) chloride solution and 14.8 ml of water.

2.1 *Construction of a calibration graph*. 0.5, 0.6, 0.7, 0.8 and 0.9 ml of a standard solution of novocaine are added to a series of test tubes. Water is added to all test tubes to 1 ml, and then 0.4 ml of an alkaline solution of hydroxylamine. Then the optical density of the obtained solutions is determined using the above method. A calibration graph is constructed of the dependence of optical density on the concentration of novocaine in the solutions.

2.2 *Quantitative photometric determination of novocaine*. Place 1 ml of novocaine solution (0.5 to 0.9 mg of the preparation in the sample) in a test tube, add 0.4 ml of an alkaline solution of hydroxylamine. Shake the liquid and leave for 10-15 minutes. Then add 0.3 ml of hydrochloric acid solution, 0.5 ml of iron (III) chloride solution

and 13.8 ml of water. The optical density of the red-colored solution is measured on a photocolorimeter with a green filter in a cuvette with a layer thickness of 2 cm relative to the comparison solution.

The content of novocaine in the dosage form is found using the calibration graph.

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4. Практикум по физико-химическим методам анализа, под ред. О.М. Петрухина.- М., 1987.-248 с.

## 7. Methodological provision:

link to lecture:
https://docs.google.com/document/d/1r1v1cGpnYmc2Jdkkul7Ad904EVBAaIBE/edit?usp=sharing&ouid=103428168790945926723&rtpof=true&sd=true

## 8. Control:

1. What phenomenon underlies photocolorimetric analysis?
2. What quantities are related by the Bouguer-Lambert-Beer law?
3. What is optical density?
4. List the main units of a photoelectrocolorimeter and indicate their purpose.
5. What are photometric reagents used for? What requirements must they meet?
6. What are light filters? What is their purpose?
7. How is a light filter selected?
8. What requirements are followed when selecting a cuvette for analysis?
9. In what coordinates is a calibration graph plotted? What is its purpose?
10. What is the fundamental difference between spectrophotometers and photoelectrocolorimeters?
11. The structure of a spectrophotometer and its operating principle.
12. How is a monochromatic light flux obtained in a spectrophotometer?
13. What are light filters for?
14. How to choose the right working filter?
15. What material are cuvettes made of when working in the ultraviolet and visible regions of the spectrum? Why?
16. Basic rules for working with cuvettes.
17. What device in a spectrophotometer converts light energy into electrical energy?

18. Sequence of operations when measuring optical density on a spectrophotometer in the visible and ultraviolet regions of the spectrum.
19. Rules for working on the SF-2000.
20. How are working filters and cuvettes selected?
21. What causes selective absorption of light by molecules?
22. Unit of measurement of wavelength in the UV and IR regions of the spectrum.
23. Definition of the following terms: transmission, transmittance, optical density, molar absorption coefficient.
24. Formulate the laws: Beer's law, Bouguer-Lambert's law and Bouguer-Lambert-Beer's law. Which of them is the basis of photometric methods of analysis?
25. What is the optical density of a solution if the basic law of light absorption is observed?
26. What is the absorption spectrum of a substance?
27. Define the following concepts: chromophore, bathochromic, hypsochromic, hyperchromic, hypochromic effects.
28. What is the basis for determining the concentration of solutions using photometric methods of analysis?
29. The main stages of determining the concentration of a test solution using the graduated graph method.
30. How is the concentration range of standard solutions selected when constructing a calibration curve?
31. In what cases is it unacceptable to use a calibration curve when determining the concentration of a test solution?
32. What are the advantages of the calibration graph method in comparison with other photometric methods of analysis?
33. What is the basis for determining concentration using the method of comparing the optical densities of the standard and test solutions? Advantages and disadvantages of this method.
34. What is the fastest way to select a light filter in photocolorimetry for colored liquids?
35. Is it possible to use a yellow light filter in the photometric determination of riboflavin by natural color?
36. For photometric purposes, the following wavelength range is used:

a) corresponding to the absorption maximum;
b) corresponding to the absorption minimum;
c) corresponding to the maximum half-width of the absorption peak;
d) corresponding to the minimum half-width of the absorption peak.

**Lesson №4**

**1. Topic: Analysis of medicinal products by refractometric method.**

**2. Goal:** to master practical skills in carrying out the refractometric method

**3. Learning objectives:**

- provide students with knowledge of the basic principles of use, the procedure for organizing and conducting analysis of a substance using the refractometric method;
- teach students to conduct analysis of a substance using the refractometric method.

**4. Main questions of the topic:**

1. Refractometry. Brief theoretical foundations of the method.
2. General characteristics of the refractometric method of analysis.
3. Refractive index factor, method of its determination, factors influencing its value.
4. Application of refractometry for identification of drugs, for quantitative analysis of concentrated solutions and drugs. Advantages and disadvantages of the method.
5. What values are calculated in refractometry?

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol.

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
| 2 | Completing laboratory work | 50 |
| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |
| 5 | summing up (giving grades) | 5 |

Laboratory work №1 Conduct determination of the content of medicinal substances in medicinal forms using the refractometric method:
5% calcium chloride solution
25% magnesium sulfate solution
5% ascorbic acid solution
0.5% novocaine solution

Method of determination.

*1.1 Getting to know the instructions for the RL-2 refractometer.*

*1.2 Determination of the refractive index factor F for each of the indicated dosage forms.*

To determine the factor, at least five solutions of exact concentration are prepared with an interval of 1%. The refractive index values are measured and the factor values are calculated using the formula

$$F = \frac{n - n_0}{C},$$

where n - refractive index of the solution;
$n_0$ - refractive index of water (solvent);
C - solution content (for some substances the refractive index factor may change with a change in their content), %.

*1.3 Setting the temperature correction*. The refractometer, distilled water and one of the tested solutions are kept in a room at the same temperature for 30-40 minutes. The water temperature is measured with an accuracy of $0.1^0$C. The refractive index of one of the specified solutions is determined using the refractometer. The temperature correction is calculated using the formula:

$$X = \frac{n - n_{20}}{20 - t},$$

where n – показатель преломления при температуре t;
$n_{20}$ - refractive index at $20^0$C;
t –temperature at which the measurements were taken (if the temperature value differs from $20^0$C by 5-$7^0$C, the correction value should be about 0.0002).

*1.4 Determination of the content of medicinal preparations in the tested dosage forms.* The test solution and distilled water are kept near the device for 30 minutes to equalize the temperature. The refractive indices of water and the dosage form are determined. The content of the medicinal substance solution is calculated using the formula:

$$C = \frac{n - n_0}{F},$$

First, the factor for a 1% solution is used for the calculation and the approximate content of the drug in the solution is found using the given formula. Then the calculations are repeated, using the refractive index factor for the solution with the found drug content. The obtained results are compared with the data found in the reference table of the dependence of the refractive index on the drug content. It should be taken into account that the tabular data are calculated for a temperature of $20^0$C. If measurements are performed at a temperature different from this value, the calculation is carried out taking into account the temperature correction:

$$n_{20} = n - (20 - t)\ 0{,}0002$$

After making adjustments, deviations in the content of medicinal products are calculated and compared with acceptable deviation standards.

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## 7. Methodological provision:

link to lecture:
https://docs.google.com/document/d/1r1v1cGpnYmc2Jdkkul7Ad904EVBAaIBE/edit?usp=sharing&ouid=103428168790945926723&rtpof=true&sd=true

## 8. Control:

1. What phenomenon underlies the refractometric method?
2. The structure and operating principle of a refractometer. Rules for working with refractometers.
3. What is the refractive index, what factors does it depend on, what formula is it calculated by?
4. Specify the formula that takes into account the effect of temperature on the refractive index, explain it?
5. What are the methods for calculating the concentration of a substance in solutions containing one or two components, multicomponent solutions?
6. Give the concept of interpolation and show with a specific example.
7. Methods for calculating the concentration of a solution in the refractometric method of analysis.
8. Possibilities of the method and limitations (advantages and disadvantages) when used in quality control of drugs.
9. Methods for calculating the concentration of a solution in the refractometric method of analysis.
10. At a temperature of 25ºC, the refractive index of the solution is 1.3372, the refractive index factor is 0.0016. Calculate the concentration of the solution.

11. Calculate the concentration of calcium chloride solution using the refractometric table if the refractive index of the solution is 1.3453. Tabular data: n = 1.3445-10%; n = 1.3457-11.0%
12. To determine the refractive index increase factor (F) of anhydrous glucose solution, solutions were prepared with the following concentrations: 1%. 3%. 5%, 10%. The refractive indices of the solutions are respectively 1.3344, 1.3373, 1.3401, 1.3472. Calculate the factor.
13. Provide a general calculation and draw a conclusion about the quality of production of a 5% glucose solution if n of the solution is 1.3403 and n of water is 1.3330. F of anhydrous glucose is 0.00142. The glucose content in 1 ml should be from 0.0485 to 0.0515

**Lesson №5**

**1. Topic: Analysis of medicinal products by thin layer chromatography.**

**2. Goal:** to master practical skills in carrying out the thin layer chromatography method.

**3. Learning objectives:**

- provide students with knowledge of the basic principles of use, the procedure for organizing and conducting the analysis of a substance using thin-layer chromatography;
- teach students how to conduct the analysis of a substance using thin-layer chromatography.

**4. Main questions of the topic:**

1. Thin-layer chromatography (TLC). The essence of the method.
2. Requirements for the sorbent. Selection of the sorbent and mobile phase depending on the chemical structure of the molecules.
3. Qualitative parameters used to identify organic compounds.
4. Possibilities and limitations of using TLC in drug analysis.

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
| 2 | Completing laboratory work | 50 |
| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |

| | | |
|---|---|---|
| 5 | summing up (giving grades) | 5 |

## Technique for conducting the experiment using TLC method

**Basic equipment for TLC.** For analysis, use Sorbfil or Silufol plates with a UV indicator: PTSKh-AF-V-UV (with an aluminum foil backing) or PTSKh-P-V-UV (with a polymer backing) measuring 10×10 cm or 10×15 cm.

A 150×120×80 mm chromatographic chamber is used for 10×10 cm plates, a 190×195×65 mm chamber can be used for both 10×10 cm and 10×15 cm plates.

A microsyringe is used to apply the analyzed solutions to the plate.

For accelerated drying of the plates (both after applying the analyzed solutions and after chromatography), you can use a USP-1 heating device.

To determine the position of the spots of the analyzed substances (detection) after chromatography, the UV irradiator UFS-254/365 (TU 42154-004-16943778-99) is used.

**The principle of TLC.** A *start line and a finish line* are carefully marked on the plate surface so as not to damage the sorbent layer (e.g. with a pencil). A sample of the test drug solution is applied to the start line (with a microsyringe) and a sample of the comparison solution is applied nearby. The comparison solution contains a sample of the active substance being sought. After applying the samples, the solvent is allowed to evaporate from the plate surface, after which the lower edge of the plate (i.e. from the side of the start line) is placed in the PF filling the bottom of the chromatographic chamber. The PF is a solvent or mixture of solvents specially selected for a particular case. Under the action of capillary forces, the PF spontaneously moves along the plate from the start line to the finish line, entraining the medicinal substances contained in the samples. After the PF reaches the finish line, chromatography is interrupted by removing the plate from the chromatographic chamber. The plate is dried and the position of the spots of substances on its surface is determined by irradiating the plate in a UV chamber.

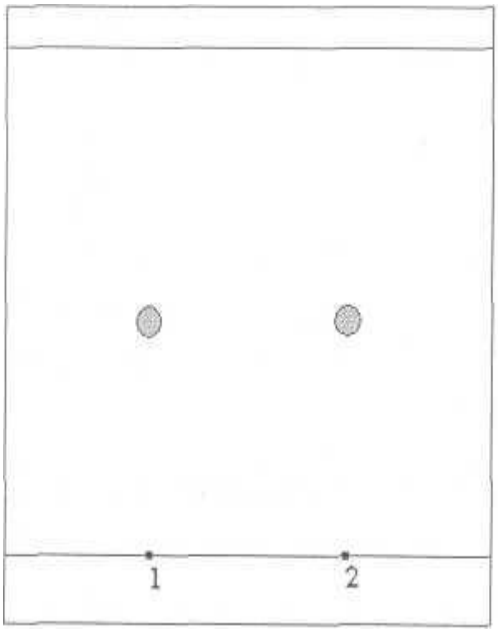


Fig. 1.

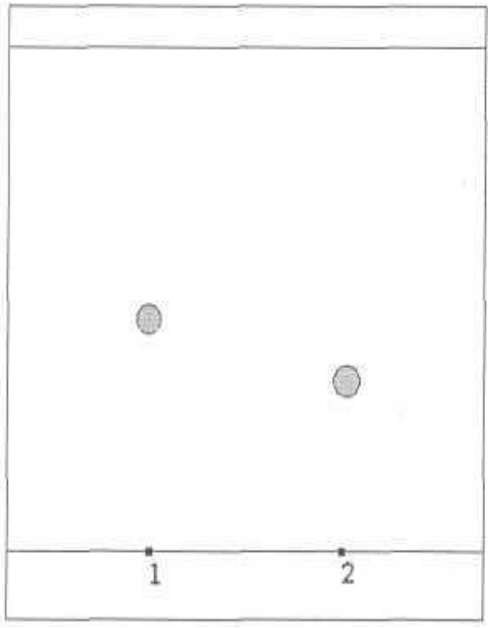


Fig. 2.

1- sample of comparison solution;
22 - sample of test solution

If the spot obtained from the test solution is at the same level as the spot from the comparison solution, this most likely means that these solutions contain the same active substance and this indicates the detection of the test substance (Fig. 1). If the spot from the test solution differs significantly in position from the spot from the comparison solution or is absent altogether, this indicates the absence of the test substance (Fig. 2).

**Activation of plates**. To improve the accuracy of the analysis, it is recommended to activate the plates. To do this, acetone or 10% ammonia solution (30 ml for a 150×120×80 mm chamber or 50 ml for a 190×195×65 mm chamber) is poured into the chromatographic chamber. The plate is placed in the chamber and covered with a lid. The solvent front should reach its upper edge. After this, the plate is removed from the chromatographic chamber using tweezers (avoid touching the sorbent layer with your hands) and dried using the USP-1 device at 100°C for 60 min (or kept in a drying cabinet at 100°C for 60 min). If the plates are not used immediately after activation, they are stored in a desiccator over a layer of desiccant (e.g. calcined calcium chloride or dried silica gel) or in a tightly closed polyethylene bag.

*Note:* Before activation, an arrow is drawn in pencil in the upper left corner of the plate (Fig. 3), showing the direction of movement of the solvent, so that during

chromatography it is the same as during activation of the plates.

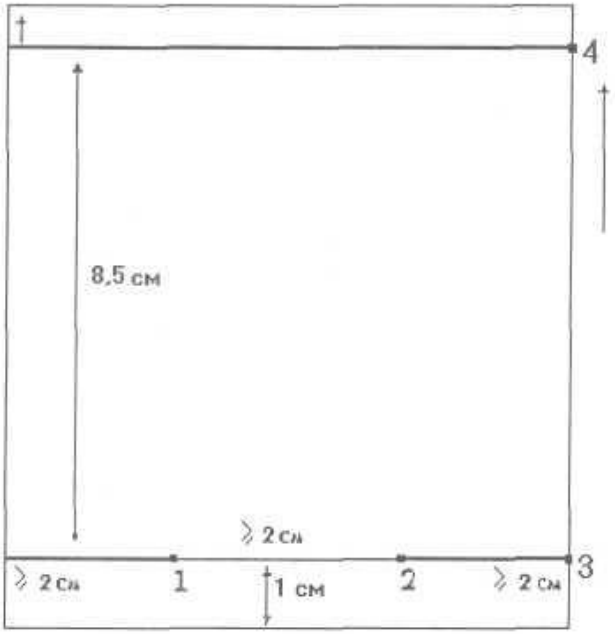


Fig. 3. Plate markings:

1 - comparison solution sample:

2 - test solution sample;

3 – start line;

To speed up the analysis, two chambers can be used: one for activating the plates, the other for subsequent chromatography..

**Preparation of the mobile phase.** The solvents specified in each specific case are added to the conical flask. They are added with constant stirring to obtain a homogeneous transparent solution. The components of the mobile phase should be dosed using a graduated cylinder. The total volume of the mobile phase is about 30 ml for a chromatographic chamber of 150×120×80 mm and about 50 ml for a chromatographic chamber of 190×195×65 mm.

It is necessary to prepare the mobile phase immediately before the analysis. Pre-preparation of the mobile phase (the day before, the night before) is not allowed.

It is impossible to use one portion of the mobile phase for sequentially conducting two or more analyses. In this case, you can prepare a calculated larger volume of the mobile phase (with a small reserve) and take a portion of 30 or 50 ml from it for each analysis.

**Saturation of the chromatographic chamber.** Before chromatography, it is necessary to saturate the chromatographic chamber with PF vapors. To do this, pour the prepared PF into the chamber, cover with a lid and hold for at least 20 minutes. Only after this, place the plate with the applied samples into the chamber.

**Applying the samples.** Using a pencil, carefully, so as not to damage the sorbent layer, mark the start line on the activated plate at a distance of 1 cm from the lower edge of the plate and the finish line at a distance of 8.5 cm from the start line (Fig. 3) so that the direction of movement of the PF is the same as when activating the plate (mark in the upper left corner).

Samples of the test solution and the comparison solution are applied to the start line using a microsyringe, carefully touching the sorbent layer. In this case, the samples are applied in such a way that the distance from the application point to the left (comparison solution) or right (test solution) edge of the plate is at least 2 cm. The distance between two adjacent spots should also be at least 2 cm (Fig. 3). In a similar way, for example, a comparison solution and 3 test solutions prepared from three different preparations containing one active substance (for mass analysis) can be applied to a 10x10 cm or 10x15 cm plate.

When applying samples, one should strive to obtain compact "starting spots" with a diameter of no more than 4-5 mm, which increases the efficiency and clarity of separation. To do this, fractional application (in parts) should be used with drying the plates until the solvent has completely evaporated.

Before starting chromatography, it is recommended to cut the corners at the bottom of the plate at a distance of 6-8 mm from the edge at an angle of 45° to ensure a uniform rise of the solvent front.

*Note*. Before application, between applications, and after application of samples, the microsyringe must be thoroughly washed in methyl or ethyl alcohol at least 5 times to prevent contamination and mixing of samples.

If there are chips in the sorption layer on the edges of the plate, these damages must be trimmed evenly with sharp scissors.

**Development of the chromatogram (chromatography)**. During chromatography, the chamber must be on a stable surface that prevents its vibrations. The plate with the applied samples is placed in the chromatographic chamber using tweezers, slightly moving its lid so that the PF level is below the start line. The plate must be placed in the chamber carefully and quickly, moving the lid as little as possible so as not to disturb the equilibrium established during saturation. The chamber lid is tightly closed and, without moving the chamber any further, chromatography is carried out until the solvent front reaches the finish line. After this, the plate is removed from the chamber using tweezers and placed on a preheated device for drying plates USP-1 (or a drying cabinet), which ensures accelerated removal of the solvent from the plate surface.

**Development of the chromatogram (detection of spots).** Spots of the analyzed substances on the surface of the plate can be seen when it is irradiated with UV light.

The dried plate is placed in a UFS-254/365 chromatographic irradiator and the spots of the substances are examined in the light of a UV lamp at 254 nm.

| | |
|---|---|
| Workplace №1 | Conduct determination of novocaine hydrochloride substance by thin layer chromatography |

Method of determination. 0.2 g of novocaine hydrochloride substance is dissolved in 0.6 ml of water, then diluted with 96% alcohol to 10 ml.

20 μl (400 μg) of the drug under study and 20 μl of the comparison solution (0.2 μg of anesthesin) are applied to the start line of the chromatographic plate coated with silica gel 60 F254. The plate is dried in air, then placed in a chromatographic chamber with benzoyl acetone (4:1) and chromatographed. When the stationary phase reaches the edges of the plate, it is removed from the chamber, dried, and then examined under a UV lamp at a wavelength of 254 nm.

The resulting chromatographic spots of the test solution should not contain any foreign impurities and should not differ in intensity and size from the spots of the comparison solution (no more than 0.005%).

Workplace №2 Conduct determination of methyluracil substance by thin layer chromatography

Method of determination: 0.1 g of the substance is dissolved in 1 ml of 96% alcohol, then diluted with 1 ml of water.

Comparison solution. 0.5 ml of the test solution is brought to 250 ml.

5 μl (250 μg) of the test solution, 5 μl (0.5 μg) and 2.5 (0.25 μg) of the comparison solution are placed on the start line of the chromatographic plate coated with silica gel 60 F254. The plate is dried, then placed in a chamber with a mixture of cold acetic acid - water - butanol (1:1:4) and chromatographed. When the stationary phase reaches the finish line, the plate is removed from the chamber, dried, then examined in UV light at a wavelength of 254 nm.

The resulting chromatographic spots of the test solution should not have foreign impurities, and should not differ in intensity and size from the spots of the comparison solution (0.5)

(no more than 0.2%). If the chromatographic spots of the comparison solution are clearly visible (0.25 μg), then the chromatography has been done correctly.

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## 7. Methodological provision:

link to lecture:
https://docs.google.com/document/d/1r1v1cGpnYmc2Jdkkul7Ad904EVBAaIBE/edit?usp=sharing&ouid=103428168790945926723&rtpof=true&sd=true

**8. Control**:
1. How are components detected and identified on paper and thin-layer chromatograms?
2. What methods allow chromatographing several samples simultaneously?
3. Sorption mechanisms (adsorption, absorption), desorption.
4. Classification of chromatographic methods by the mechanism of separation of the substances under study.
5. Classification of chromatography by technique.
6. Main stages (steps) of chromatography in a thin layer of sorbent.
7. Factors affecting the reproducibility of thin-layer chromatography.
8. Characteristics of sorbents used in TLC.
9. Requirements for TLC plates used for applying sorbent.
10. Selecting a sorbent for TLC.
11. Selecting a mobile phase for TLC.
12. Chromatogram. Methods for detecting substances on a chromatogram during TLC.
13. Qualitative parameters of TLC (Rf, Rs). Factors influencing the values of Rf, Rs.
14. Chromatographic chamber. Techniques for saturating the chromatographic chamber with mobile phase vapors.
15. Using TLC for quantitative measurements.
16. Possibilities and limitations of using the TLC method in pharmacy.

**Lesson №6**
**1. Topic: Analysis of medicinal products by high performance liquid chromatography.**
**2. Goal:** to master practical skills in carrying out the method of high-performance liquid chromatography
**3. Learning objectives:**
- provide students with knowledge of the basic principles of use, the procedure for organizing and conducting the analysis of a substance using high-performance liquid chromatography;
- teach students to conduct the analysis of a substance using high-performance liquid chromatography.

**4. Main questions of the topic:**

1. 1. High-performance liquid chromatography (HPLC). The essence of the method.
2. 2. Classification of methods depending on: the scale of the columns used; the separation mechanism; the nature of the stationary and mobile phases; the state of aggregation of the stationary phase.
3. 3. Selection of sorbent and mobile phase for HPLC.
4. 4. Detectors used in HPLC.
5. 5. Possibilities and limitations of HPLC application in pharmacy.

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
| 2 | Completing laboratory work | 50 |
| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |
| 5 | summing up (giving grades) | 5 |

Workplace №1 Conduct qualitative and quantitative determination of salicylic acid impurities in acetylsalicylic acid using reversed-phase HPLC

Stages of work:

1. Carrying out chromatography of solutions of acetylsalicylic acid (aspirin) and salicylic acid.
2. Qualitative analysis of the chromatogram of aspirin and determination of the amount of salicylic acid impurity.

Equipment, conditions and objects of chromatography

1. Liquid chromatograph "Milichrom".
2. Chromatographic steel column (62x2 mm) filled with reversed-phase sorbent (C18 with a grain size of 5 μm).
3. Eluent - 40% ethanol solution in 1% acetic acid solution.
4. Eluent flow rate - 50 μl/min.
5. Detector - spectrophotometric.
6. Wavelength when recording a chromatogram - 280 nm.
7. Sensitivity range - 0.8.

8. Chart tape speed - 180 mm/h.
9. Acetylsalicylic acid (aspirin).
10. Salicylic acid of "reagent grade".
11. Acetic acid solutions of 1% and 5%.

Carrying out the work.

Before starting the work, the prepared mobile phase must be degassed - freed from dissolved air, which disrupts the normal operation of the chromatograph, causing a drift of the zero line, reducing the adsorption level. Degassing is carried out with a helium flow through the eluent for 3-5 minutes

Preparation of solutions for chromatography. For the work, solutions of salicylic acid with a concentration of 1 mg / ml and aspirin with a concentration of 4 mg / ml are required, which are prepared according to an accurate weight taken on an analytical balance (the required volume of the solution is determined by the teacher).

The solvent is the eluent - 40% ethanol solution in 1% acetic acid solution. To prepare the mobile phase, mix 40 ml of ethyl alcohol and 60 ml of 1% acetic acid solution, which is prepared by dilution from glacial acetic acid. To carry out chromatography, prepare a 5% acetic acid solution.

Carrying out chromatography. Switch on the chromatograph according to the instructions. Set the chromatography conditions - wavelength, sensitivity, measurement time, chart tape speed. Fill the pump and column with eluent, set the eluent feed rate. Then chromatograph a solution of aspirin and salicylic acid. To do this, 10 μl of 5% acetic acid solution (to create the optimal pH value for sorption), 5 μl of salicylic acid solution and 10 μl of 5% acetic acid solution are collected in the sample inlet device. Carry out chromatography. The salicylic acid peak should occupy no more than 30% of the chart tape width. If the peak on the chromatogram is significantly larger or smaller than this value, change the sample volume or sensitivity range. Under specified conditions, take two or three chromatograms of salicylic acid and acetylsalicylic acid. The aspirin solution sample is collected in the same way as salicylic acid. (On the chromatogram of aspirin, the peak of acetylsalicylic acid is “off the charts”).

Processing of results

1. Identification of the salicylic acid peak on the aspirin chromatogram is carried out based on the equality of the retention time on the chromatogram of the individual component and in the analyzed sample. The retention time $t_R$ is calculated from the chromatogram

$$t_{R'} = l_R / V,$$

where $l_R$ is the distance on the chromatogram from the moment of sample injection to the top of the peak, cm
V - chart tape speed, cm/min.

2. Calculate the salicylic acid content in aspirin. The calculation of the impurity content is based on measuring the heights of the salicylic acid peaks on the chromatogram of an individual salicylic acid solution (hc, cm) and the analyzed solution (ha, cm). Since the concentration of the salicylic acid solution in the standard solution is known, the salicylic acid content in aspirin as a percentage will be

$$C_{ca}\% = \frac{h_a \; C_c V_c}{h_c C_a^{исх} V_a} \times 100$$

where $h_a$ - height of the peak of salicylic acid in the analyzed solution of acetylsalicylic acid, cm;
$h_c$,- height of the peak of salicylic acid in a standard solution, cm;
*Cc* - concentration of standard salicylic acid solution mg/ml;
$C_a^{исх}$ - concentration of the analyzed solution of acetylsalicylic acid, ml/ml;
$V_c$ - sample volume of standard salicylic acid solution, µl;
$V_a$ - volume of the sample of the analyzed solution of acetylsalicylic acid taken for analysis, µl;

The obtained data are entered into a table and a conclusion is made about the quality of the drug - acetylsalicylic acid.

Table 1 - Results of determination of the content of salicylic acid in acetylsalicylic acid

| *N* Chr-gram | Salicylic acid | C ml/ml | V, об.пр., см3 | h, sm | h, a.sm | Ci, % | Ci a, % |
|---|---|---|---|---|---|---|---|
| 1<br>2<br>3 | Standard solution | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1<br>2<br>3 | Analyzed solution | | | | | | |

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**main:**

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Практикум по физико-химическим методам анализа, под ред. О.М. Петрухина.-М., 1987.-248 с.

**7. Control**:

1. The HPLC method is based on …

a) different adsorption of mixture components on a solid sorbent;

b) different distribution of components between two liquid phases when one of them passes through a column under pressure;

c) different distribution of mixture components between the carrier gas flow and the solid sorbent located in the column.

2. The block diagram of a chromatograph in the HPLC method includes …

a) a vessel for the mobile phase, a pump, a filter, a thermostat, an injector, a column, a detector, a chart recorder;

b) a cylinder with a carrier gas, an evaporator, a thermostat, an injector, a column, a detector, a chart recorder;

c) a vessel for the stationary phase, a thermostat, a sample injection device, a column, a detector, a chart recorder;

d) a cylinder with a carrier gas, an injector, an evaporator, a pump, a column, a detector, a chart recorder.

3. The sample is dosed by …

a) syringe;

b) automatic dispenser;

c) micropipette;

d) introducing the sample in the form of a tablet.

4. The sorbent used in HPLC is …

a) activated carbon;

b) silasorb;

c) polysorb;

d) separon.

5. The material from which HPLC columns are made is …

a) glass;

b) stainless steel;

c) aluminum;
d) teflon.
6. The principle on which the operation of a refractometric detector is based is …
a) light emission;
b) luminescence of the substances being determined;
c) light absorption;
d) light refraction.
7. The efficiency of separation of components of a liquid chromatograph is most influenced by the unit - …
a) dispenser;
b) pump;
c) detector;
d) column.
8. Identification of substances in GLC, HPLC is carried out ...
a) by boiling point and dielectric constant;
b) by the area of the chromatographic peak;
c) by retention time, study of zones in the column by spectral or chemical analysis methods;
d) connecting a spectral analyzer to the column.
9. Quantitative analysis includes ...
a) sample injection, calculation of retention time;
b) separation, calculation of mixture composition;
c) instrument calibration, separation, measurement of peak area;
d) sample injection, separation, calculation of retention index.
10. The most frequently used parameter of the chromatographic peak in quantitative analysis is ...
a) peak height;
b) peak width at baseline;
c) peak width at half-height;
d) peak area.
11. The main advantage of the UV detector is …
a) selectivity;
b) the ability to determine a large number of organic compounds;
c) low detection limit;
d) baseline stability.
12. The most frequently used retention parameter is …
a. absolute time;
b. relative time;

c. relative volume;
d. absolute volume.
13. For automatic calculation of the peak area, a liquid chromatograph unit is used - …
a. electronic amplifier;
b. chart recorder;
c. integrator;
d. electrometer.
14. The advantage of HPLC over gas-liquid chromatography is …
a. low detection limit;
b. the ability to determine non-volatile and low-boiling compounds;
c. selectivity of determination;
d. reliability of the device in operation.
15. The mechanism of separation of substances in the gas-liquid chromatography method is …
a. adsorption on the surface of the stationary phase;
b. distribution between two immiscible phases;
c. reversible exchange of ions between the substance being determined, the stationary and mobile phases;
d) chemical interaction of the substance being determined with the mobile phase.
16. The block diagram of a gas-liquid chromatograph is …
a. vessel for the mobile phase, pump, column, detector;
b) cylinder with carrier gas, injector, column, detector, chart recorder;
c) cylinder with carrier gas, thermostat, evaporator, injector, column, detector, chart recorder;
d) vessel for the stationary phase, thermostat, injector, pump, column.
17. The parameter characterizing a chromatographic column is …
a. length;
b. column material;
c. chemical composition of the solid carrier;
d. nature of the stationary phase.
18. Retention time is the time elapsed from the start of sample injection until …
a. the appearance of the zone of the corresponding component with maximum concentration at the column outlet;
b. the start of the detector signal;
c. the end of the detector signal;
d. the last maximum detector signal.
19. The detector is designed to …
a) uniformly move the analyzed sample in the column;

b) record the components of the analyzed mixture;
c) introduce the sample into the chromatograph;
d) completely separate the components of the analyzed sample.
20. The basis of qualitative analysis in gas chromatography is the value of …
a. retention time;
b. peak height;
c. peak area;
d. peak width.
21. The area of the chromatographic peak characterizes …
a. qualitative composition of the sample;
b. quantitative content of individual components in the sample;
c. content of the liquid phase in the solid carrier;
d. completeness of separation.
22. The carrier gas in gas chromatography is…
a. the gas passing through the katharometer cell simultaneously with the gas being analyzed;
b. the gas mixture being analyzed;
c. the gas used to move the analyzed mixture along the column and separate it;
d. air.
23. Gas adsorption chromatography differs from gas-liquid chromatography in …
a. instrumentation;
b. separation mechanism;
c. objects of analysis;
d. detectors.
24. The carrier gas used in GC is …
a. helium;
b. air;
c. nitrogen;
d. argon;
e) propane.
25. In pharmaceutical analysis, HPLC, GLC and GC are used in …
a. establishing the authenticity of medicinal substances;
b. purity testing;
c. studying complex mixtures;
d. quantitative determination of components of complex mixtures;
e. study of the stability of medicinal substances during storage.
a. What is the dead volume of the column? What volumes does it include?

2. Why are small amounts of the compounds to be determined usually injected into the chromatographic column?
3. What is the relative retention volume and relative retention time?
4. What is the standard deviation of the chromatographic peak? What units is this value measured in?
5. What is the most important reason for the broadening of the chromatographic peak?
6. Why can the peak of the unretained component be asymmetric?
7. How can the height equivalent to the theoretical plate be determined experimentally?
8. Which theory of chromatography provides the basis for optimizing the chromatographic process?
9. Name three methods of detection in gas and liquid chromatography.
10. Which detectors are preferable in chromatographic analysis - universal or selective?
11. The signal magnitude of which detectors in gas chromatography depends on the nature of the carrier gas?
12. Why should the thermal conductivity of the carrier gas be as high as possible when using a katharometer as a detector?
13. What parameters of the chromatographic peak are used for quantitative analysis?
14. List the main methods of quantitative chromatographic analysis. In what cases is one method or another used?
15. In what cases is the peak height and peak area measured in quantitative chromatographic analysis?
16. List the methods for measuring the area of the chromatographic peak.
17. In what coordinates is the calibration graph plotted so that some change in the experimental conditions (temperature, flow rate, etc.) does not affect the quantitative chromatographic determination of the component?
18. What experimental data confirm that the researcher is conducting quantitative chromatographic analysis in the region of linearity of the sorption isotherm?
19. What is the role of the mobile phase in gas and liquid chromatography?
20. Give examples of stationary phases in gas-solid-phase and gas-liquid chromatography.
21. Which stationary phase in gas-liquid chromatography is called selective?
22. Give examples of stationary phases in adsorption high-performance liquid chromatography.
23. Compare the sizes of chromatographic columns in gas and high-performance liquid chromatography.
24. Compare the flow rate of the mobile phase in gas and liquid chromatography.
25. Why are low-viscosity mobile phases preferred in liquid chromatography?

26. Compare the efficiency of different types of gas and liquid chromatography. How can it be increased?
27. How to calculate the efficiency of a capillary column in chromatography?
28. How does the diameter of a capillary column affect its efficiency?
29. What is gradient elution in gas and liquid chromatography?
30. What are the advantages of temperature programming in gas chromatography?

**Lesson №7**

**1. Topic: Analysis of dosage forms for the dissolution test.**

**2. Goal:** master practical skills in conducting the "dissolution" test

**3. Learning objectives:**

- provide students with knowledge of the basic principles of use, the procedure for organizing and conducting the analysis of dosage forms for the dissolution test;
- teach students to conduct the analysis of dosage forms for the dissolution test.

**4. Main questions of the topic:**

General requirements for tablets according to the State Pharmacopoeia of the Republic of Kazakhstan:

- dissolution (2.9.3. Dissolution test for solid dosage forms);

1. Regulatory materials on quality control of industrially produced dosage forms.

2. Requirements for tablet dosage forms, tablet quality specifications.

3. General requirements for the quality of dragees. Dragee quality specifications.

4. General requirements for the quality of capsules. Dragee quality specifications.

5. Features of analysis of tablet dosage forms.

6. Definition of the Dissolution test, according to the requirements of the State Pharmacopoeia of the Republic of Kazakhstan?

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol.

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
| 2 | Completing laboratory work | 50 |
| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |

| | | |
|---|---|---|
| 5 | summing up (giving grades) | 5 |

Workplace No. 1 Test 50 mg furagin tablets according to the section:
- dissolution.

Workplace No. 2 Test 500 mg phthalazole tablets according to the section:
- dissolution;

Workplace No. 3 Test 0.5 g chloramphenicol tablets according to the section:
- dissolution.

Workplace No. 4 Test nitroxaline tablets according to the section:
- dissolution.

Stages of work:

Conducting a dissolution test for tablets of furagin, phthalazole, chloramphenicol and nitroxalin.

Equipment, conditions and objects for the dissolution test

1. Paddle device or basket device.
2. Water P, 0.1 M hydrochloric acid, phosphate buffer solutions with pH from 6.8 to 7.6.
3. Thermometer.
4. Water bath (37±0.5)0 C.
5. Furagin, phthalazole, chloramphenicol and nitroxaline tablets.

Carrying out the work.

Before starting the work, remove dissolved gases from the prepared dissolution medium, as they can cause the formation of bubbles, which significantly affect the results.

Preparing the preparation for the "dissolution" test. Place one unit of the preparation to be tested in the apparatus. For an apparatus with a paddle: before starting to rotate the paddle, place the preparation on the bottom of the vessel; solid dosage forms that may float are placed horizontally on the bottom of the vessel using a suitable device.

For an apparatus with a basket: place the preparation in a dry basket, which is lowered into the appropriate position before starting to rotate.

Carrying out the "dissolution" test. Turn on the apparatus according to the instructions. The dissolution conditions are set - pH of the dissolution medium, temperature $(37.0\pm0.5)^0$ C, rotation speed (usually 50 rpm for the paddle and 100 rpm for the basket), time, method and volume of the sampled test solution (at least 500 ml) or conditions for continuous monitoring, analysis method, quantity or amount of the required active ingredients that must dissolve within the specified time.

Processing of results

When using a device with a paddle or basket, the specified volume or volumes of samples are collected at the specified time or at the specified intervals, or continuously from the area midway between the surface of the dissolution medium and the upper part of the basket or paddle at a distance of at least 10 mm from the vessel wall.

In cases where the degree of dissolution is regulated for only one time interval, the test may be carried out in a shorter time. If the degree of dissolution is regulated for two or more time intervals, samples must be collected without stopping the operation of the device at a strictly specified time with an accuracy of (±2%).

The test is carried out in parallel for six units of the test preparation. Unless otherwise specified in the monograph, for each unit of the test preparation, not less than 75% and not more than 115% of the active substance from its content specified in the "Composition" section must pass into the solution within 45 minutes.

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link to lecture:
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## 8. Control:

1. Features of the analysis of tablet dosage forms.
2. How to determine the average weight of tablets?
3. Disintegration of tablets, what are the requirements for tablets, according to the State Pharmacopoeia of the XI for this indicator?
4. Determination of the strength of tablets for abrasion according to the requirements of the State Pharmacopoeia of the XI ?
5. Definitions of the "Dissolution" test, according to the requirements of the State Pharmacopoeia of the XI ?
6. Definitions of talc according to the State Pharmacopoeia of the XI ?
7. Determinations of the content of medicinal substances in tablets?
8. How is the dosage uniformity test in tablets carried out?
9. Features of the analysis of capsule dosage forms?
10. Determinations of the average weight and deviation from the average weight of capsules?

11. Determinations of the dosage uniformity of capsule dosage forms?
12. Determinations of capsule disintegration?
13. Definitions of the "Dissolution" test of capsules?
14. Features of the analysis of a solid dosage form - dragees.
15. Quality requirements – dragees.

**Lesson №8**

**1. Topic: Analysis of dosage forms for the tests “disintegration”, “wearability”.**

**2. Goal:** to master practical skills in conducting tests "disintegration", "abrasion".

**3. Learning objectives:**

- ✓ provide students with knowledge of the basic principles of use, the procedure for organizing and conducting the analysis of dosage forms for the tests "disintegration", "wearability".
- ✓ teach students to conduct the analysis of dosage forms for the tests "disintegration", "wearability".

**4. Main questions of the topic:**

General requirements for tablets according to the State Pharmacopoeia of the Republic of Kazakhstan (2.9.1. Disintegration of tablets and capsules. 2.9.7. Friability of uncoated tablets.):

- friability;
- disintegration;

1. Regulatory materials on quality control of industrially produced dosage forms.
2. Requirements for tablet dosage forms, tablet quality specifications.
3. General requirements for the quality of dragees. Dragee quality specifications.
4. General requirements for the quality of capsules. Dragee quality specifications.
5. Features of analysis of tablet dosage forms.
6. Definition of the "Dissolution" test, according to the requirements of the State Pharmacopoeia of the Republic of Kazakhstan?
7. Disintegration of tablets, what are the requirements for tablets, according to the State Pharmacopoeia of the Republic of Kazakhstan for this indicator?
8. Determination of the abrasion resistance of tablets according to the requirements of the Republic of Kazakhstan?

**5. Methods of learning and teaching:** knowledge control, laboratory work in pairs, writing and defending the analysis protocol

The laboratory session is allocated 150 minutes, which are distributed as follows:

| № п/п | Stages of the lesson | Time, min |
|---|---|---|

| | | |
|---|---|---|
| 1 | initial control of knowledge on the topic of the laboratory lesson | 15 |
| 2 | Completing laboratory work | 50 |
| 3 | writing and defending the protocol | 15 |
| 4 | knowledge control on the topic of the laboratory lesson | 15 |
| 5 | summing up (giving grades) | 5 |

Workplace №1 Phthalazole tablets 0.5g section:
- disintegration;
- abrasion.

Workplace №2 Ampicillin trihydrate tablets 0.25g
Section:
- disintegration;
- abrasion.

Workplace №3 Furazolidone tablets 0.02g Section:
- disintegration;
- abrasion.

Workplace №4 Ascorbic acid tablets 0.5g Section:
- disintegration;
- abrasion.

Workplace №5 Acetylsalicylic acid tablets 0.5g Section:
- disintegration;
- abrasion.

Stages of work:

1. Conducting a "disintegration" test for tablets of phthalazole, ampicillin trihydrate, furazolidone, ascorbic acid and acetylsalicylic acid.
2. Conducting a "friability" test for tablets of phthalazole, ampicillin trihydrate, furazolidone, ascorbic acid and acetylsalicylic acid.

Equipment, conditions and objects for carrying out the disintegration test

1. PHARMA TEST tablet disintegration tester.
2. Rigid basket with a mesh bottom-stand (basket).
3. Six cylindrical transparent tubes (77.5±2.5) mm long, with an internal diameter of 21.5 mm and a wall thickness of about 2 mm.
4. Basket raising and lowering frequency within 28-32 cycles per minute over a distance of 50 mm to 60 mm.
5. Liquid temperature from 35 0C to 39 0C.
6. The basket is suspended in the liquid specified in the relevant general and specific articles, in a suitable vessel, preferably in a 1 liter beaker.
7. Tablet flow tester EF-1W

8. Drum with an internal diameter of 283 to 291 mm and a depth of 36 to 40 mm.
9. Rotation speed 25±1 rpm
10. Phthalazole.
11. Ampicillin trihydrate.
12. Furazolidone.
13. Ascorbic acid.
14. Acetylsalicylic acid (aspirin).

Carrying out work on the tablet disintegration test.

Place one tablet or capsule in each of the six tubes and, if specified, place a disk; hang the basket in a vessel with the liquid specified in the general and specific articles.

Turn on the device; after the specified time, remove the basket and examine the condition of the tablets or capsules. The preparation passes the test if the tablets or capsules have disintegrated.

Processing of results.
Samples are considered to be disintegrated when on the grid:

a) there is no residue;
b) there is a residue consisting of a soft mass without a perceptibly hard non-wettable core;
c) there are only fragments of the coating (tablets), or only fragments of the shell on the grid, or, if discs were used, fragments of the shell adhering to the lower surface of the disc (capsule).

Carrying out the work on the "abrasion" test of tablets.

If the mass of one tablet is less than 0.65 g, 20 tablets are taken for the test; if the mass of one tablet is more than 0.65 g - 10 tablets. The tablets are placed on a number 1000 sieve and dust is carefully removed using compressed air or a soft brush. The tablets are weighed (accurately weighed) and placed in the drum. After 100 revolutions of the drum, the tablets are removed and dust is again carefully removed. If none of the tablets are chipped or cracked, the tablets are weighed with an accuracy of milligram.

Usually the test is carried out once. If the obtained results are in doubt or the loss in mass exceeds 1%, the test is repeated twice more and the average of three measurements is calculated. Unless otherwise specified in the monograph, the loss in mass should not exceed 1% of the total mass of the tablets tested. When testing tablets with a diameter of 13 mm or more, in order to obtain reproducible results it may be necessary to adjust the drum so that adjacent tablets do not rest against each other and are allowed to fall freely. Usually it is sufficient to set the axis at an angle of $10^0$ to the base.

Processing of results

Abrasion is expressed as a loss in mass, calculated as a percentage of the initial mass of the tablets being tested.

It is necessary to indicate the number of tablets taken for testing.

**6. Literature:**

**main:**

**in Russian**

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## 7. Methodological provision:

link to lecture:
https://docs.google.com/document/d/1r1v1cGpnYmc2Jdkkul7Ad904EVBAaIBE/edit?usp=sharing&ouid=103428168790945926723&rtpof=true&sd=true

## 8. Control:

1.What are the acceptable tolerances for tablets weighing 80 mg or less??
А) 10%
Б) 20%
В) 5%
Г) 4%
Д) 2%

2. What are the acceptable tolerances for tablets weighing more than 80 mg but less than 250 mg?
А) 7,5%
Б) 20%
В) 5%
Г) 4%
Д) 2%

3. What are the acceptable tolerances for tablets weighing 250 mg or more?
А) 5%
Б) 20%
В) 7,5%
Г) 4%
Д) 2%

4. For what purpose are sliding and lubricating agents used in the preparation of tablets?
A) improving flowability and reducing sticking
B) improving flowability
C) reducing sticking

D) improving disintegration
E) improving flowability
5. In the absence of other indications in the individual article, what deviation standards are allowed for determining the average tablet weight?
А) 5%
Б) 7%
В) 10%
Г) 3%
Д) 15%
6. How long (min) should it take for dispersible tablets to disintegrate?
А) 3
Б) 5
В) 1
Г) 4
Д) 10
7. How many tablets are taken to determine the friability of uncoated tablets weighing less than 0.65 g?
А) 20
Б) 5
В) 10
Г) 4
Д) 10
8. At what temperature is the disintegration of tablets determined?
А) 15ºС to 25ºС
Б) 5ºС to 15ºС
В) 1ºС to 10ºС
Г) 5ºС to 14ºС
Д) 9ºС to 13ºС
9. What percentage of the active substance should pass into solution in 45 minutes when determining the "Dissolution" test for tablets?
A) at least 75%
B) at least 85%
C) at least 95%
D) at least 65%
E) at least 90%
10. What weight of powder should be taken from ground tablets (pieces) for quantitative determination?
A) at least 20
B) at least 30
C) at least 10

D) at least 5
E) at least 25