LECTURE COMPLEXE

Discipline	Methods and equipment for pharmaceutical analysis
Discipline code	MOFA 4301
Educational program	6B07201 «Pharmaceutical production technology»
Number of credits (ECTS):	120 hours/4 credits
Course	4
Semester	VII

Shymkent, 2024

The lecture complex was developed in accordance with the working curriculum of the discipline "Methods and equipment for pharmaceutical analysis" (syllabus) and discussed at a meeting of the department

Protocol №21, 10.06.2024 y.

Head of Department, Professor Ordabaeva S.K.

Lecture№1

1. Topic 1. Introduction. State principles and provisions governing the quality of drugs.

2. Objective: To provide students with knowledge about the state system of standardization and certification of drugs and their use in conducting pharmaceutical analysis of drugs at the stages of development, production, storage, and application.

3. Lecture Outline

План:

- Regulatory legal acts in the field of certification and standardization of drugs
- The standardization system in the healthcare of the Republic of Kazakhstan and the standardization of drugs
- Rules for developing regulatory documents for quality control and safety of drugs
- The State Pharmacopoeia of the Republic of Kazakhstan

Among the tasks of pharmaceutical chemistry, a special place is occupied by the analysis of drug quality. Each country has legislation on pharmaceutical preparations, which provides standards and norms for quality indicators for drugs.

Regulatory legal acts in the field of certification and standardization of drugs

The quality of drugs in the Republic of Kazakhstan is regulated by the following regulatory legal acts in the field of certification and standardization of drugs:

- Law of the Republic of Kazakhstan dated January 13, 2004 № 522 "On Drugs";

- Law of the Republic of Kazakhstan dated November 9, 2004 № 603-P "On Technical Regulation";

- Law of the Republic of Kazakhstan dated June 7, 2000 № 53-11 "On Ensuring the Unity of Measurements";

- Standard of the Republic of Kazakhstan ST RK 3.4-2003 "State System of Certification of the Republic of Kazakhstan. Procedure for confirming product conformity. General requirements";

- Standard of the Republic of Kazakhstan ST RK 3.17-2000 "GSS RK. Procedure for certification of drugs".

Law of the Republic of Kazakhstan dated January 13, 2004 № 522 "On Drugs"

The legal and organizational foundations for providing the population of the Republic of Kazakhstan with safe and effective drugs are determined by the Law "On Drugs". The Law regulates relations in the sphere of drug circulation, starting from their creation to consumption, including the stages of search, development, preclinical and clinical trials, production control, quality, efficacy and safety control, standardization, certification, state registration, and marketing. The Law is divided into six chapters.

The Law of the Republic of Kazakhstan dated 09.11.2004 № 603-P "On technical regulation" establishes the legal basis for the state system of technical regulation aimed at ensuring the safety of products and processes in the Republic of Kazakhstan. With the introduction of this law, the laws of the Republic of Kazakhstan dated 16 July 1999 "On standardization" and "On certification" ceased to be in force.

Law of the Republic of Kazakhstan dated June 7, 2000 № 53-II

"On ensuring the unity of measurements"

The Law of the Republic of Kazakhstan dated June 7, 2000, № 53-II "On Ensuring the Unity of Measurements" establishes the legal, economic, and organizational foundations for ensuring the unity of measurements in the Republic of Kazakhstan, regulates relations between government agencies, individuals, and legal entities in the field of metrological activities, and is

aimed at protecting the rights and legitimate interests of citizens and the economy of the Republic of Kazakhstan from the consequences of inaccurate measurement results.

Standardization system in healthcare in the Republic of Kazakhstan

Regulatory documents regulating activities in the field of healthcare are developed in accordance with the Law of the Republic of Kazakhstan dated June 4, 2003 "On the healthcare system." In order to implement this Law, the "Rules for Standardization in the Field of Healthcare" were approved by the Resolution of the Government of the Republic of Kazakhstan dated February 16, 2004.

The purpose of standardization in healthcare is to improve the quality of medical and pharmaceutical services aimed at improving the health of the population.

The main areas of standardization in healthcare: standardization of medical and pharmaceutical services, standardization of technologies used in the process of implementing medical and pharmaceutical activities, standardization of drug provision, standardization of professional activities (qualification of medical and pharmaceutical workers), standardization of organizational (information) technologies.

The most important object of standardization in healthcare are drugs, their production, quality (safety, efficiency), conditions of sale, without which it is impossible to provide high-quality medical services.

A pharmacopoeial monograph (PS) is a regulatory document of a drug that defines a set of quality standards and methods for their determination. Revised every 5 years.

Analytical regulatory document (ARD) - a regulatory and technical document that establishes mandatory requirements for the quality of a medicinal product of a specific manufacturing enterprise, ensuring its equal effectiveness and safety regardless of the series, as well as the consistency and uniformity of its production.

Temporary analytical regulatory document (TARD) - an analytical regulatory document developed for the first industrial (installation) series of new medicinal products.

ARD (TARD) contains a list of quality indicators and testing methods for quality control of a medicinal product and is developed in accordance with the requirements of: the State Pharmacopoeia of the Republic of Kazakhstan; foreign pharmacopeias recognized as valid in the Republic of Kazakhstan; state standards and other regulatory documents governing quality indicators, testing methods, as well as packaging, labeling and transportation of medicinal products.

The quality indicators included in ARD (TARD) must not be lower than the requirements of the State Pharmacopoeia of the Republic of Kazakhstan. ARD (TARD) must ensure the production of a high-quality, effective and safe medicinal product.

The validity period of ARD is established depending on the technological level of a specific production, but not more than 5 years.

The validity period of TARD is established depending on the degree of development of the technological process of production, but not more than 3 years.

Rules for drafting regulatory and technical documents on quality control and safety of medicines

The procedure for compiling, developing and processing an ARD (TARD) per medicinal substance

The AND for a drug substance and new drugs containing it are developed simultaneously.

The quality specification of a drug substance is determined by its physicochemical properties and nature.

The name of the substance is written in Latin, the state and Russian languages, and the international non-proprietary name (if any) in English or Russian.

The chemical name and structural formula are written in accordance with the rules of the International Union of Pure and Applied Chemistry (IUPAC).

The Description section specifies the appearance parameters (physical condition, color, odor), possible changes during storage in air, in the light (indication of hygroscopicity, attitude to the action of light and air), etc.

The Solubility section specifies the solubility parameters of the medicinal substance in solvents of various polarities.

The Identification section specifies the characteristics of the ultraviolet and infrared absorption spectra, if necessary, 2-3 qualitative reactions most specific for the active substance are given.

The boiling point or distillation temperature limit, melting point, solidification, relative density, specific optical rotation, specific absorption index, refractive index and other physical constants are given in separate sections, in which the upper and lower limits of deviation of the parameters in the corresponding units of measurement are specified.

In the Transparency and Color sections, the parameters are specified for a certain concentration of solutions.

In the section "Acidity or alkalinity" the standardization of the indicator is carried out using acid or alkali solutions with a concentration of 0.01 M to 0.1 M in the presence of indicators. In the section pH, the water indicator is determined by the potentiometric method.

The section "Mechanical inclusions" describes the method and permissible standards for mechanical inclusions. The section is introduced for sterile substances used for the preparation of parenteral and ophthalmic drugs.

The section "Related impurities" provides a method for determining and permissible standards for the content of impurities of a technological nature or impurities formed during storage.

The section "Residual organic solvents" is introduced in the case of using toxic solvents at the last stage of production of a medicinal substance.

The sections "Chlorides" and "Sulfates" indicate permissible limits, the content of chlorides and sulfates associated with the production technology, or requirements for their absence.

The section "Sulphate Ash and Heavy Metals" specifies the weight of the medicinal substance and the permissible limits of sulphate ash and heavy metal impurities.

The section "Arsenic" specifies the permissible limits of arsenic impurity content or requirements for its absence.

The sections "Loss on Drying" and "Water" specify the weight of the medicinal substance, a reference to the method for determining the end of the Karl Fischer titration, drying conditions and standards for loss on drying or moisture content.

The section "Microbiological Purity" is introduced for non-sterile medicinal substances. The section specifies the method for determining microorganisms and the permissible limits of their content. If changes have been made to the method, the description is given in full.

The sections "Pyrogens", "Abnormal Toxicity", "Content of Histamine-Like Substances" specify test doses, animal species, route of administration and observation period.

Раздел «Бактериальные эндотоксины» может вводиться вместо или параллельно с разделом «Пирогены».

The section "Sterility" is introduced for substances used in the production of sterile medicinal products that are not subject to sterilization procedures. The section "Quantitative

determination" describes the method for quantitative determination of the active substance contained in the medicinal substance.

In the "Packaging" section indicate:

- packaging methods depending on the quantity of products in a packaging unit (primary, secondary, transport);
- capping methods (types and methods of capping, sealing);
- requirements for primary, secondary and transport packaging and materials used for packaging;
- type of container (glass, cardboard and paper, plastic, metal, etc.);
- brand, grade of packaging material with a reference to the regulatory document of the Republic of Kazakhstan;
- methods of applying inscriptions (self-adhesive labels, paint, etc.);
- a list of documents included in the packaging.

The "Marking" section shall indicate:

- place of marking (on tags, containers, labels, packs, etc.);
- content of marking in accordance with the requirements of the State Pharmacopoeia of the Republic of Kazakhstan and other regulatory documents of the Republic of Kazakhstan;
- special safety requirements (fire and explosion hazard, etc.) and precautions during transportation, storage and use if necessary (warning signs “Poison”, “Flammable”, “Do not throw”, “Freezing is not allowed”, etc.).

The "Transportation" section provides a reference to the current state standard or specifies other transportation conditions and, if necessary, requirements for loading and unloading features, as well as for handling the product after transportation (for example, keeping it at room temperature for a certain time after transportation at subzero temperatures), etc.

The "Storage" section specifies the storage conditions for the product that ensure the preservation of its quality and presentation, if necessary, the storage location, requirements for protection from environmental influences (moisture, sunlight, air, high or low temperatures, etc.).

This section is presented in the following sequence: storage location, storage conditions, special requirements for storing individual groups of drugs, if necessary.

The "Shelf Life/Re-Control Period" section specifies the period of time until the date of the next control, during which the drug substance, under appropriate storage conditions, complies with the requirements of the ARD (TARD). The section “Pharmacological action” provides the main pharmacological action of the medicinal substance, but the title of the section is not given.

4. Illustrative material:

-tables;

- Microsoft Power Point presentations.

5. Literature:

main:

in Russian

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electronic resources:

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2. Харитонов, Ю. Я. Аналитическая химия. Аналитика - 1. Общие теоретические основы. Качественный анализ [Электронный ресурс] : учебник. - Электрон. текстовые дан. (44,3Мб). - М. : ГЭОТАР - Медиа, 2017
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6. Анализ лекарственных веществ. Ч.1. Общие реакции на подлинность: учеб. пособ. / В.А. Смирнов. - Самара. Самар. гос. техн. ун-т, 2008. - 55 с https://aknurpress.kz/reader/web/2637
7. Тюкавкина, Н. А. Биоорганическая химия [Электронный ресурс] : учебник / - Электрон. текстовые дан. (47,4 МБ). - М. : Издательская группа "ГЭОТАР- Медиа", 2011. - 416 с. эл. опт. диск (CD-ROM). - (Электронный учебник).

6. Control questions

1. What regulatory legal acts in the field of certification and standardization of medicines do you know?
2. What is standardization of medicines?
3. What is a quality standard for medicines?

4. Rules for drafting regulatory and technical documents on quality control and safety of medicines
5. What is the State Pharmacopoeia of the Republic of Kazakhstan?
6. What is meant by the certification system of medicines?
7. State regulation in the field of certification, types of certification
8. The procedure for organizing and conducting certification of medicines?
9. How is the quality of medicines ensured?

Lecture №2

1. Topic 2. Pharmacopoeial testing methods for individual quality indicators.

2. Objective: to develop students' knowledge about the state system of standardization and certification of medicines and their use for conducting pharmaceutical analysis of medicines at the stages of development, production, storage and use.

3. Lecture abstract

Plan:

• State Pharmacopoeia of the Republic of Kazakhstan
• Certification system of medicines
• State regulation in the field of certification, types of certification
• Procedure for organizing and conducting certification of medicines
• Ensuring the quality of medicines

Procedure for submitting ARD (TARD) projects for examination and approval

The ARD (TARD) draft signed by the applicant is submitted in the registration dossier in accordance with the rules of state registration and re-registration of medicines in the Republic of Kazakhstan, approved by the Ministry of Health of the Republic of Kazakhstan. The ARD (TARD) draft is accompanied by an explanatory note. The explanatory note must contain:

1) name of the manufacturer and developer (if necessary) of the medicinal product;

2) name and composition of the medicinal product;

3) structural and empirical formula of the active substance(s) and its (their) relative molecular weight;

4) brief description of the synthesis and technology for obtaining the medicinal product, control during the production process;

5) detailed justification of the test methods, quality indicators and standards of their deviation given in the project;

6) information on the number of samples and technological documentation used for the project;

7) justification of deviations from the general requirements of the State Pharmacopoeia of the Republic of Kazakhstan (if any);

8) indication of the novelty or originality of the medicinal product under development; in case of its absence, comparison in quality with analogues based on the relevant monographs of the leading pharmacopoeias;

9) justification of the shelf life and storage conditions of the medicinal product in this packaging, with the submission of a report on stability tests;

10) results of validation of test methods;

11) list of references.

The explanatory note is signed by the applicant of the medicinal product and certified with a seal.

The examination of the ARD (TARD) draft is carried out by an organization determined by the Ministry of Health of the Republic of Kazakhstan. Based on the results of the examination, the ARD (TARD) draft may be returned for revision.

During the examination of the ARD (TARD) draft, an assessment is made of its scientific and technical level and compliance with modern requirements for the quality of the medicinal product.

After the examination, the ARD (TARD) draft is submitted for approval to the Pharmacy Committee of the Ministry of Health of the Republic of Kazakhstan.

The AND (VAND) is approved by the order of the Pharmacy Committee of the Ministry of Health of the Republic of Kazakhstan, registered and entered into the Register of normative and technical documentation in the order of sequential numbering on electronic (paper) media.

State Pharmacopoeia of the Republic of Kazakhstan

The State Pharmacopoeia of the Republic of Kazakhstan is a collection of general and specific pharmacopoeial articles of medicinal products, which has a legislative nature. The stated standards and regulations are applied in the analysis and storage of medicinal products and are mandatory for the pharmacist, physician, as well as all organizations and institutions that study, store, control and use medicinal products.

Structure of a Pharmacopoeial Monograph (SF XI)

1. Latin name.
2. Russian name.
3. Synonyms.
4. Extended structural formula.
5. Gross formula.
6. Molecular weight.
7. Description of appearance.
8. Solubility.
9. Authenticity (requirements – specificity, sensitivity, availability, reproducibility, presence of visible effect).
10. Melting point for solids.
11. Good quality (impurities).
12. Quantitative determination.
13. Storage.
14. Use

Certification system of medicinal products

Certification is a written confirmation by a body independent of the manufacturer (seller, contractor) and the consumer (buyer) of the conformity of a product, process, work, service with the requirements established in regulatory documents.

Certificate of Conformity is a document issued in accordance with the requirements of regulatory documents, indicating that the necessary confidence is provided that the properly identified product, process, work, service meets the requirements of technical regulations, standards or other regulatory documents; Authorized body for standardization, metrology and certification is a government body that manages standardization, metrology, certification and accreditation work;

Certification expert-auditor is a specialist certified in the established manner to carry out certification or accreditation work in a certain field of activity.

Government regulation in the field of certification

The state certification system is a set of government bodies, individuals and legal entities carrying out work in the field of certification within their competence, and regulatory documents establishing the procedure for carrying out work on certification and accreditation in the Republic of Kazakhstan.

The organizational structure of the state certification system is formed by:

- an authorized body for standardization, metrology and certification;
- accredited bodies for certification of products, processes, works, services;
- accredited testing laboratories (centers);
- accredited organizations for the provision of consulting services in the field of accreditation;
- certification experts-auditors.

The state certification system ensures the implementation of a unified policy in the field of certification and establishes the basic rules and procedures for certification, requirements for certification bodies, testing laboratories (centers) and procedures for their accreditation, procedures for the training and certification of certification experts-auditors, etc.

Types of certification

Mandatory certification is the certification of products, works, services included in the list of products, works, services subject to mandatory certification for compliance with the mandatory requirements of a standard or other regulatory document that ensures their safety for life, health of people, property of citizens and the environment.

Voluntary certification is carried out at the initiative of applicants (manufacturers, sellers, performers) in order to confirm the compliance of products, processes, works, services with the requirements of regulatory documents determined by the applicant. Voluntary certification does not replace mandatory certification.

Medicines in accordance with the Law of the Republic of Kazakhstan "On Medicines", "On Certification" are products subject to mandatory certification in the Republic of Kazakhstan. The list of medicines subject to mandatory certification is established by the Resolution of the Government of the Republic of Kazakhstan.

The procedure for organizing and conducting certification of medicinal products is regulated by the State Standard of the Republic of Kazakhstan ST RK 3.17 - 2000 “Procedure for certification of medicinal products”.

The main objectives of certification of medicinal products are: ensuring the safety of medicinal products for human life and health, protection of citizens' property and the environment; protecting the interests of consumers in matters of medicinal product quality; eliminating technical barriers to sales, ensuring the competitiveness of medicinal products in the domestic and foreign markets; creating the necessary conditions for the activities of individuals and legal entities in the single commodity market of Kazakhstan, as well as for participation in international economic, scientific and technical cooperation and international trade.

The State Standard of the Republic of Kazakhstan supervises the work on certification of medicinal products.

Certification of medicinal products is organized and carried out by accredited certification bodies.

The bodies for certification of medicinal products in Kazakhstan are the Testing Center of the RSE "National Center for Expertise of Medicines, Medical Devices and Medical Equipment"

and 13 accredited testing laboratories of the territorial branch of the RSE in the regions of the Republic of Kazakhstan.

Certification of medicinal products is carried out in accordance with the adopted schemes according to ST RK 3.4-94 GSS RK "Procedure for conducting product certification".

The following are subject to mandatory serial control for all indicators: medicinal substances used for the production of medicinal products; narcotic medicinal products, precursors, toxic medicinal products (substances and finished dosage forms); medicinal products for anesthesia, with the exception of oxygen and nitrous oxide; dosage forms for children; barium sulfate and sulfobar. Medicines for injection and eye drops are subject to mandatory serial control for physicochemical parameters.

Certificate issuance procedure.

The decision on the possibility (or impossibility) of issuing a certificate of conformity for certified products and permission to use the conformity mark is made by the certification body based on the analysis of the obtained results and documentation.

The issued certificate is valid without restrictions throughout the territory of the Republic of Kazakhstan.

Certificates receive legal force after they are assigned a registration number of the Register.

4.Illustrative material:

-tables;

-Microsoft Power Point presentation.

5. Literature:

main:

in Russian

1. Анализ лекарственных препаратов, производных ароматических соединений: Ордабаева С.К.-Шымкент: Типография «Әлем».- 2012.-270 с.
2. Асильбекова, А. Д. Промышленные методы получения лекарственных средств: лабораторный практикум / А. Д. Асильбекова, С. К. Ордабаева. - Алматы : New book, 2022.-212 с.
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5. Государственная фармакопея Республики Казахстан.-Алматы: Издательский дом «Жибек жолы».-2014.-Том 3.-864 с.
6. Государственная Фармакопея Республики Казахстан. Т.1. – Алматы: Издательский дом «Жибек жолы», 2015. – 720 с.
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8. Харитонов, Ю. Я. Аналитическая химия. Количественный анализ, физико-химические методы анализа: практикум: учеб. пособие -М.:ГЭОТАР - Медиа, 2012. -368с.
9. Харитонов, Ю. Я. Аналитическая химия. Аналитика 2. Количественный анализ. Физико-химические (инструментальные) методы анализа: учебник - М: ГЭОТАР - Медиа, 2014. - 656 с.
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12. Халиуллин, Ф. А. Инфракрасная спектроскопия в фармацевтическом анализе: учебное пособие / - М.: ГЭОТАР - Медиа, 2017. - 160 с
13. Сейтембетова, А. Ж. Аналитическая химия: учебное пособие / - Алматы : New book, 2022. -124с.
14. Тюкавкина, Н. А. Биоорганикалық химия: оқулық / Қаз. тілінен ауд. жауапты ред. Т. С. Сейтембетов. - М. : ГЭОТАР - Медиа, 2014. - 400 бет. +эл. опт. диск (CD-ROM)
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3. Қазақстан Республикасының Мемлекеттік фармакопеясы.-Алматы: «Жібек жолы» баспа үйі.-2009.-2 Т.-792 б.
4. Қазақстан Республикасының Мемлекеттік фармакопеясы.-Алматы: «Жібек жолы» баспа үйі.-2014.-3 Т.-864 б.
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extra:

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6. Control questions

1. What regulatory legal acts in the field of certification and standardization of medicines do you know?
2. What is standardization of medicines?
3. What is a quality standard for medicines?
4. Rules for drafting regulatory and technical documents on quality control and safety of medicines
5. What is the State Pharmacopoeia of the Republic of Kazakhstan?
6. What is meant by the certification system of medicines?
7. State regulation in the field of certification, types of certification
8. The procedure for organizing and conducting certification of medicines?
9. How is the quality of medicines ensured?

Lecture №3

1. Topic: Methods of photometry in the ultraviolet and visible spectral regions.

2. Objective: developing students' knowledge of photometric methods and the possibilities of using them to solve practical problems related to the analysis of medicinal products.

3. Lecture abstract

Lecture plan:

1. Photometric methods. Classification.
2. The basic law of light absorption.
3. The concepts of "absorption spectrum", "optical density", "specific absorption index", "monochromator", "light filters", etc.
4. Equipment for photometric measurements: SF, KFK. The principle of operation of the devices.

Analysis methods based on the absorption of electromagnetic radiation by the analyzed substances constitute a large group of absorption optical methods. When absorbing light, the atoms and molecules of the analyzed substances pass into a new excited state. Depending on the type of absorbing particles and the method of transforming the absorbed energy, a distinction is made between:

1. Atomic absorption analysis, based on the absorption of light energy by atoms of the analyzed substances.

2. Molecular absorption analysis, i.e. analysis of light absorption by molecules of the analyzed substance in the ultraviolet, visible and infrared regions of the spectrum (spectrophotometry, photocolorimetry, IR spectroscopy).

3. Analysis of the absorption and scattering of light energy by suspended particles of the analyzed substance (turbidimetry, nephelometry).

4. Luminescence (fluorometric) analysis, based on measuring the radiation resulting from the release of energy by excited molecules of the analyzed substance.

All these methods are sometimes combined into one group of spectrochemical or spectroscopic methods of analysis, although they have significant differences.

Photocolorimetry and *spectrophotometry* are based on the interaction of radiation with homogeneous systems, and they are usually combined into one group of ***photometric methods of analysis.***

Photometric methods use selective absorption of light by molecules of the substance being analyzed. According to quantum mechanics, light is a stream of particles called quanta or photons. The energy of each quantum is determined by the wavelength of the radiation. As a result of radiation absorption, the molecule of the absorbing substance passes from the ground state with minimum energy E_1 to a higher energy state E_2. Electronic transitions caused by the absorption of strictly defined quanta of light energy are characterized by the presence of strictly defined absorption bands in the electronic spectra of the absorbing molecules. Moreover, light absorption occurs only when the energy of the absorbed quantum coincides with the energy difference ΔE between the quantum energy levels in the final (E_2) and initial (E_1) states of the absorbing molecule:

$$hv = \Delta E = E_2 - E_1$$

Here h is Planck's constant (h = 6.625.10–34 J•s); v is the frequency of the absorbed radiation, which is determined by the energy of the absorbed quantum and is expressed as the ratio of the radiation propagation velocity *c* (the speed of a light wave in a vacuum c = 3.1010 cm/s) to the wavelength λ; v = *c/λ*. The radiation frequency v is measured in reciprocal seconds (s^{-1}), hertz (Hz).

1 Hz = 1 s–1.

The wavelength λ is measured in angstroms (1 A = 1.10–8 cm), micrometers or microns (1 μm = 1 μm = 1.10–6 m), nanometers or millimicrons (1 nm = 1 mmk = 10 A = 1.10–9 m).

Radiation energy is characterized by an electromagnetic spectrum, which covers the region from kilometer-long radio waves to tenths of an angstrom of γ-radiation and cosmic rays. To characterize a section of the spectrum, the wave number θ is also often used, which shows how many wavelengths fall on 1 cm of the radiation path in a vacuum and is determined by the ratio: θ = 1/λ.

The nature of the absorption bands in the ultraviolet (10–400 nm) and visible (400–760 nm) regions of the spectrum is the same and is associated mainly with the number and arrangement of electrons in the absorbing molecules and ions. In the infrared region (0.8–1000 μm), it is largely associated with the vibrations of atoms in the molecules of the absorbing substance.

Depending on the equipment used in photometric analysis, a distinction is made between the *spectrophotometric method - analysis by absorption of monochromatic light and the photocolorimetric method* - analysis by absorption of polychromatic (non-monochromatic) light in the visible spectrum. Both methods are based on the proportional relationship between light absorption and the concentration of the absorbing substance.

Photometric methods are divided into direct and indirect. In direct methods, the ion being determined M is converted into a light-absorbing compound MR using a reagent R, and then the intensity of light absorption of the solution of this compound is measured. Indirect determinations use auxiliary compounds that, when interacting with the substance being determined, either decompose themselves or form new light-absorbing compounds.

Basic laws of light absorption. When a luminous flux with intensity I0 passes through a layer of a substance (solution), its intensity decreases to the value I as a result of absorption in the

layer, reflection and scattering. The intensities of the incident luminous flux I0 and the luminous flux I that has passed through the solution can be determined experimentally. In relative measurements of light absorption by true solutions, radiation losses due to reflection and scattering are usually neglected.

The relationship between the intensities of luminous fluxes I0 and I is established by the Bouguer-Lambert law, according to which *homogeneous layers of the same substance of the same thickness absorb the same proportion of the incident luminous energy (at a constant concentration of the dissolved substance).*

Mathematically, this law is expressed by the exponential equation:

$$I = I0eal \quad (1),$$

where e – base of natural logarithms;
a – absorption coefficient;
l – thickness of the absorbing layer.

The ratio T = I/I0 is called *transmission*; its values can vary from 0 to 1. This value is often expressed as a percentage. If the value T is related to a layer thickness of 1 cm, it is called the *transmission coefficient*. The absorption of radiation is characterized by *optical density*:

$$A = \lg(I0/I) = -\lg T$$

The relationship between the concentration of the absorbing solution and its optical density lg(I0/I) is expressed by Beer's law, according to which the *optical density of the solution is directly proportional to the concentration of the dissolved substance at a constant layer thickness*:

$$Lg(I0/I) = k1C \quad (2)$$

where k1 – proportionality coefficient;
C – concentration of dissolved substance.

The dependence of the intensity of a monochromatic light flux passed through a layer of a colored solution on the intensity of the incident light flux, the concentration of the colored substance and the thickness of the solution layer is determined by the combined Bouguer-Lambert-Beer law, which is the basic law of light absorption and underlies most photometric methods of analysis

$$I = I0.10–kCl \quad (3)$$

where k is the absorption coefficient, which depends on the nature of the dissolved substance, temperature, solvent and wavelength of light.

If the concentration C is expressed in moles per liter, and l is in centimeters, then k is the molar absorption coefficient at length λ and is denoted by ελ. In this case, the equation takes the form:

$$I = I \times 10 - \varepsilon\lambda Cl \; 0 \quad (4)$$

If the basic law of light absorption is observed, the optical density of the solution is directly proportional to the molar coefficient of light absorption, the concentration of the absorbing substance and the thickness of the solution layer:

$$A = \varepsilon\lambda Cl \quad (5)$$

When plotting the dependence of optical density on concentration (at a constant l value), a straight line is obtained. This straight line passes through the origin of coordinates in the absence of light absorption by the solvent and systematic errors.

Equations 4 and 5 are derived for monochromatic light, i.e. light of a certain wavelength, which can be isolated using a special optical device - a monochromator. In a photocolorimeter, the intensity of light fluxes is measured not in monochromatic light, but in polychromatic light, i.e. on a fairly wide section of the spectrum - in the wavelength range of 20-100 nm.

In this case, in equation 5, instead of the molar coefficient of light absorption ελ, you can use the value of the average molar coefficient of light absorption (εcp), depending on the bandwidth of the light filter (εcp < ελ).

Absorption spectra or, more correctly, the absolute absorption spectrum of a substance is the dependence of the amount of absorbed light on the wavelength. Such spectra for dyes in the visible region (400–700 nm) sometimes have several maxima. Absorption spectra in the ultraviolet (200–400 nm) and visible regions reflect transitions of bound and unbound electrons in a molecule. These are usually delocalized π-electrons of double C=C bonds and unshared pairs of nitrogen and oxygen. Since, as a rule, all electrons in a molecule are at the lower energy level at room temperature, the spectra in this region provide information on the ground and first excited electronic states of the molecule. Due to the fact that the wavelength of the absorbed light corresponds to a certain transition, the peaks in the absorption spectra of a substance are due to the presence of known structures in it. The wavelength at which maximum light absorption is observed is designated as λmax. The position of the absorption spectrum maximum is an important optical characteristic of a substance, and the nature and type of the absorption spectrum characterize its qualitative individuality. A group in a molecule that contributes to its absorption spectrum is called a chromophore. Such a group is, for example, the carbonyl group >C=O, which exists in all amino acids. Another chromophore is the peptide group of polypeptide chains. The main chromophores of proteins include residues of aromatic acids: tryptophan and, to a lesser extent, tyrosine and phenylalanine.

The absorption spectrum of tryptophan, caused by its indole ring with a system of conjugated bonds, has two absorption bands with maxima at 220 and 280 nm. In nucleic acids, the main chromophores are purine and pyrimidine nitrogenous bases of nucleotides. When conjugated bonds are formed in a molecule, the energy of the excited state of electrons decreases, and, consequently, the chromophore begins to absorb light of a longer wavelength.

Such a shift in the absorption spectra is called *bathochromic*. Conversely, a shift in the spectrum to the short-wave region is called *hypsochromic*. *Hyperchromic* and hypochromic effects are, respectively, an increase and decrease in extinction.

It is possible to detect very closely spaced lines of vibrational and rotational transitions in the spectra of molecules only with high *resolution* (resolution is the ability of an instrument to distinguish two closely spaced lines).

Photometric methods for determining the concentration of a substance in a solution. Photometric methods for determining the concentration of solutions are based on comparing the absorption during transmission of light by standard and test solutions. The degree of light absorption by the photometric solution is measured using photocolorimeters and spectrophotometers. The optical density of the standard and test colored solutions is always measured relative to the comparison solution (zero, control solution). An aliquot of the test solution containing all added components except the reagent that forms a colored compound with the substance being determined can be used as a comparison solution. If the added reagent and all other components of the comparison solution are colorless and, therefore, do not absorb rays in the visible region of the spectrum, then distilled water can be used as a comparison solution.

Calibration graph method. To determine the content of a substance using the calibration graph method, a series of 5-8 standard solutions of different concentrations is prepared (at least 3 parallel solutions for each point). When selecting the concentration range of standard solutions, the following provisions are followed:

a) it should cover the range of possible changes in the concentration of the test solution; it is desirable that the optical density of the test solution corresponds approximately to the middle of the calibration curve;

b) it is desirable that in this concentration range with the selected cuvette thickness l and analytical wavelength λ (in most cases λ = λmax of the light-absorbing compound) the basic law of light absorption is observed, i.e. the graph A = f(C) is linear;

c) the range of working values of λ, corresponding to the range of standard solutions, should ensure maximum reproducibility of the measurement results.

Under the above conditions, the optical densities of standard solutions relative to the solvent are measured and a graph of the dependence A = f(C) is plotted. The resulting curve is called a calibration curve and has the form of a straight line emanating from the origin. It is not recommended to extrapolate the calibration line to the optical density values lying above the last experimentally obtained point. Periodically (once a week or less often), the calibration curve is checked using 2-3 freshly prepared standard solutions. Calibration graphs plotted with reagents from different batches, as a rule, do not coincide. Therefore, when changing reagents, the graph must be plotted anew. A graph plotted when working on one device cannot be used to calculate the results obtained on another. Having determined the optical density of the experimental solution Ax, its value is found on the ordinate axis, and then on the abscissa axis - the corresponding concentration value Cx. This method is used when performing serial photometric analyses. It gives good results if the basic law of light absorption is observed.

Unlike other photometric methods, the calibration graph method allows one to determine the concentration of colored solutions even in cases where the basic law of light absorption is not observed. In order to construct a calibration curve in these cases, a significantly larger number of standard solutions are prepared, differing from each other in concentration by no more than 10%. Such a calibration graph, having an angle of inclination of at least 15° on the flat section, still allows one to carry out photometric measurements, despite the fact that there is no linear relationship between the concentration of the solution and its optical density. The reproducibility of the determinations in this case is lower than in the case of a linear relationship A = f(C).

Method of comparing optical densities of standard and test solutions. To determine the concentration of a substance, an aliquot of the test solution is taken, a colored solution for photometry is prepared from it, and its optical density is measured. Then 2-3 standard colors are prepared in a similar way and their optical densities are measured at the same layer thickness (in the same cuvettes).

The optical density value of the test solution is equal to:

$$Ax = \varepsilon\lambda Cxlx$$

The optical density value of a standard solution is:

$$Aст = \varepsilon\lambda Ccтlcт$$

Dividing one expression by the other we get:

$$Ax/Aст = \varepsilon\lambda Cxlx/(\varepsilon\lambda Ccтlcт)$$

As lx = lст, ελ = const, то Cx = CстAx/Aст.

The comparison method is used for single determinations; it requires mandatory compliance with the basic law of light absorption.

There is another, more accurate method for determining the unknown concentration C_x, called the limiting solution method. Two standard solutions with concentrations C_1 and C_2 are prepared so that the optical density of the first of them A_1 is less than the optical density A_x of the solution being studied, and the optical density A_2 of the second standard solution is, on the contrary, greater than Ax.

The unknown concentration of the substance being studied is calculated using the formula:

$$Cx = C_1 + (C_2 - C_1)(Ax - A_1)/(A_2 - A_1)$$

Equipment for photometric measurements. Two large groups of devices are used for photometric measurements: photocolorimeters and spectrophotometers. In colorimeters, the required spectral ranges are selected using light filters that limit the sections of the spectrum in which measurements can be taken. In spectrophotometers, sections of the spectrum are selected using prisms or diffraction gratings, which allows any wavelength to be set in a given range.

The specific sequence of operations for measuring optical density or transmission depends on the design of the spectrophotometer or colorimeter. However, the basic principles remain the same. First, the required wavelength is set by selecting a light filter on the colorimeter or rotating the corresponding handle on the spectrophotometer. Then, zero is set. To do this, a cuvette with a standard solution is placed in the light stream. By changing the width of the slit, the instrument readings are adjusted to the value specified in the instructions. At the next stage, the standard solution is replaced with the test solution and the optical density or transmission value is read.

Modern **spectrophotometers** allow working with a highly monochromatic radiation flow. They are used for concentration analysis and in studying the absorption spectra of substances.

The structure and operating principle of a spectrophotometer. The structural diagram of a spectrophotometer can be represented as the following main blocks:

1. light source,
2. monochromator,
3. sample compartment,
4. photocell,
5. recording device.

The light beam from the light source enters the monochromator through the entrance slit and is decomposed by a diffraction grating or prism into a spectrum. The control and test samples are introduced into the monochromatic radiation flow from the exit slit into the cuvette compartment one after the other. The radiation that passes through the cuvette hits a photocell, which converts the light energy into electrical energy. The electrical signal is then amplified and recorded..

Monochromators. A monochromator is an optical system that selects radiation of a certain wavelength from the entire spectrum of a light source. These are usually prisms that refract light of different wavelengths differently, or diffraction gratings. Conventional glass prisms are used in the visible region, but they are not suitable for the ultraviolet region, since glass begins to absorb at $\lambda < 400$ nm, so prisms are made of quartz. Diffraction gratings, which are plane-parallel plates with parallel lines - grooves - applied to them, are also used as monochromators. White light is decomposed into a continuous spectrum due to diffraction on parallel grooves. Usually, in monochromators, a beam of light with a certain range of wavelengths is first selected using a prism, and then decomposed again by a grating. This is how strictly monochromatic light is obtained. The main advantage of diffraction gratings is that their resolving power can be increased, since it is directly proportional to the line density. In addition, diffraction gratings have linear resolution over the entire wavelength range, whereas the resolution of a prism monochromator decreases with increasing wavelength.

Cuvettes. The substance being studied is dissolved in the appropriate solution and placed in an optically transparent measurement vessel - a cuvette. The cuvette holder usually has cells for four cuvettes. Since glass absorbs ultraviolet light, quartz cuvettes are used to carry out measurements in the ultraviolet region of the spectrum. Plastic or glass cuvettes can be used for measurements in the visible region. When working with volatile or chemically active substances,

cuvettes are covered with lids. Since the cuvette placed in the spectrophotometer becomes an integral part of its optical system, it must be handled very carefully. Scratches and dirt on the walls of the cuvette strongly scatter and absorb light, distorting the measurement results. This should be especially remembered when working in the ultraviolet region. Cuvettes can be wiped with soft fabrics, such as cotton. It is not recommended to use filter paper for these purposes. Since organic molecules absorb in the ultraviolet region, the optical (transparent) walls of the cuvette must not be touched under any circumstances. It is better to pour the solution into the cuvette by placing it in a cuvette holder previously removed from the device. Cuvettes are quite fragile, especially quartz ones, so they must be handled with care, avoiding mechanical damage. The contents of the cuvette must be homogeneous - this is a necessary condition for obtaining reproducible data. It is necessary to ensure that the solution is not cloudy. Air bubbles, which greatly increase scattering, especially interfere with measurements. Do not pour a very cold solution into the cuvette, since this will cause water vapor from the air to condense on the outer walls of the cuvette, and the walls will become opaque. If the cuvettes are contaminated with foreign impurities, they should be washed with distilled water and (or) a solvent in which the substance being studied is dissolved. Cuvettes can be washed with mild detergents. It is not recommended to wash the cuvettes with concentrated acids or alkalis, or other etching agents. The cuvettes should be filled to such a level that the radiation flow passes entirely through the solution layer. Most often, cuvettes with an optical path of 1 cm are used, into which 2.5–3 ml of solution is usually poured. Such cuvettes hold 4–5 ml, but they are filled completely only when necessary. There are cuvettes with an optical path of 50, 20, 5, 2, and 1 mm.

Photocells. Photocells convert light energy into electrical energy. The electrical signal is then amplified and recorded. Photons, bombarding the surface of the photocell, knock electrons out of it, the number of which is proportional to the intensity of the light. These electrons fly to the positive electrode. As a result, an electric current arises in the closed circuit, which is recorded by the voltage drop across the resistor located in this circuit. The voltage can be amplified, and after compensation of such a signal with a potentiometer calibrated in absorption units, the absorption of the sample is directly recorded on the sensor. Photomultipliers are usually more sensitive than simple photocells. This is due to the fact that the electrons emitted from the photosensitive layer are accelerated by high voltage, and secondary electrons are generated due to collisions in the gas, which leads to an increase in current.

Slit width. The range of wavelengths of light falling on the sample depends on the size of the slit. Therefore, to obtain reliable results, it is necessary to work with the narrowest possible slit for the given experimental conditions. If the slit is chosen correctly, then when its dimensions are doubled, the instrument readings do not change. Usually, the zero absorption value is set by the slit, but in good spectrophotometers this is done by changing the voltage of the photocell. Such adjustment allows working with a constant slit width.

A photoelectric colorimeter is an optical device in which monochromatization of the radiation flux is carried out using light filters.

Photoelectric concentration colorimeter KFK-2

Purpose and technical data. The single-beam photocolorimeter KFK-2 is designed to measure transmission, optical density and concentration of colored solutions, scattering suspensions, emulsions and colloidal solutions in the spectral region of 315-980 nm. The entire spectral range is divided into spectral intervals, isolated using light filters. Transmission measurement limits from 100 to 5% (optical density from 0 to 1.3). The basic absolute error in transmittance measurement is no more than 1%.

Light filters. In order to isolate rays of certain wavelengths from the entire visible spectrum, selective light absorbers - light filters - are installed in the path of light fluxes in photocolorimeters before absorbing solutions. Light filters transmit rays only in a certain range of wavelengths with a transmission half-width of λ1/2max-λ'1/2max and almost completely absorb rays of other wavelengths (see table). The narrower the region of maximum transmission of rays (blurring of the maximum transmission) of a light filter, the higher its selectivity to rays of this wavelength range.

Characteristics of light filters

Marking on the disk	Light filter marking	Wavelength corresponding to maximum transmission, nm	Half-bandwidth, nm
1	315	315±5	35±15
2	364	364±5	25±10
3	400	400±5	45±10
4	440	440±10	40±15
5	490	490±10	35±10
6	540	540±10	25±10
7	590	590±10	25±10
8	670	670±5	20
9	750	750±5	20
10	870	870±5	25
11	980	980±5	25

Determination of the concentration of a substance in a solution using KFK-2.

When determining the concentration of a substance in a solution using a calibration graph, the following sequence should be followed:

- select a light filter;
- select a cuvette;
- plot a calibration curve;
- measure the optical density of the test solution and determine its concentration using the calibration curve.

Selecting a light filter. The presence of a light filter unit and a set of cuvettes in the colorimeter allows you to select a combination of them that will minimize the error in determining the concentration.

If the spectral characteristics of the colored substance are unknown, you can select a light filter for work yourself. In the visible part of the spectrum, the perceived color is the result of selective absorption of a certain section of the white light spectrum. The color of the solution is complementary to the color of the radiation absorption. Therefore, absorption should be measured in the spectrum region complementary to the color reaction. So, if the solution is colored blue-green, then you need to measure the absorption of red by this solution.

Range of wavelengths of absorbed radiation, nm	Color of absorbed radiation	Observed color
400-450	violet	yellow-green

450-480	blue	yellow
400-550	blue-green	orange
500-560	green	red-purple
400-610	blue-green-yellow	red
450-650	green-yellow-red	purple
625-750	red	Blue-green

A more precise selection of a light filter is carried out as follows.

Pour the colored solution into a cuvette and determine the optical density for all light filters. Based on the data obtained, plot a curve, plotting the wavelengths corresponding to the maximum transmittance of the filters along the horizontal axis (see table), and the corresponding values of the optical density of the solution along the vertical axis. Mark the section of the curve for which the following conditions are met:

• the optical density has a maximum value;

• the course of the curve is approximately parallel to the horizontal axis, i.e. the optical density depends little on the wavelength.

The light filter for the work is selected so that the wavelength corresponding to the maximum transmission coefficient of the light filter falls on the above-mentioned section of the spectral curve of the test solution. If these conditions are met for several light filters, then select the one for which the sensitivity of the colorimeter is higher.

Cuvette selection. The preliminary selection of cuvettes is carried out visually, based on the color intensity of the solution. If the solution is intensely colored (dark), cuvettes with a short optical path length (1–5 mm) should be used. In the case of weakly colored solutions, measurements are carried out in cuvettes with a long optical path length (20–50 mm).

4.Illustrative material:

- tables;
- Microsoft Power Point presentations.

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main:

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11. Бошкаева, А. К. Структурные исследования лекарственных веществ методами физико-химического анализа: учеб. пособие/ - Алматы : New book, 2022. - 276 с.
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6.Control questions:

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 spectral regions? Why?
16. Basic rules for working with cuvettes.
17. What device in a spectrophotometer converts light energy into electrical energy?
18. The sequence of operations when measuring optical density on a spectrophotometer in the visible and ultraviolet spectral regions.
19. How to choose a working filter and cuvette?
20. What causes the selective absorption of light by molecules?
21. The unit of measurement of wavelength in the UV and IR spectral regions.
22. Definition of the following terms: transmission, transmittance, optical density, molar absorption coefficient.
23. 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?
24. What is the optical density of the solution if the basic law of light absorption is observed?

25. What is the absorption spectrum of a substance?
26. Definition of the following concepts: chromophore, bathochromic, hypsochromic, hyperchromic, hypochromic effects.
27. What is the basis for determining the concentration of solutions using photometric methods of analysis?
28. The main stages of determining the concentration of a test solution using the graduated graph method.
29. Advantages of the calibration graph method in comparison with other photometric methods of analysis?
30. What is the basis for determining the concentration using the method of comparing the optical densities of a standard and test solution? Advantages and disadvantages of this method.
31. What is the fastest way to select a light filter in photocolorimetry for colored liquids?
32. Is it possible to use a yellow light filter in the photometric determination of riboflavin by natural color?

Lecture №4

1. Topic 4 Spectroscopy methods in drug analysis (IR, Mass, NMR)

1. **Objective:** developing students' knowledge of spectroscopy in the IR region, mass and NMR, and the possibilities of using it to solve practical problems related to the analysis of medicinal products.
2. **Lecture thesis**

Lecture plan:

1. IR, Mass, NMR spectroscopy. Features of the method. Conditions for analyzing IR spectra of organic substances.
2. Possibilities and limitations of using IR, Mass, NMR spectroscopy in pharmacy.

IR spectroscopy is associated with vibrational and rotational motions of molecules and atoms. The energy of quanta, causing a change in the vibrational and rotational energy levels of molecules, is less than the energy of electron transitions, therefore the infrared range corresponds to a longer-wave region of the spectrum than the ultraviolet and visible.

Vibrations of atoms in a molecule are divided into valence (occurring along the axis of the chemical bond and accompanied by a change in its length) and non-valence or deformation, caused by a change in the angles between the bonds.

When recording IR spectra, it is traditional to use not wavelengths, but frequencies of electromagnetic radiation (wave numbers), measured in reciprocal centimeters (cm^{-1}) and corresponding to the number of wavelengths per 1 cm. The frequency of vibrations (ν) and wavelength (λ) are related by the ratio:

$$\nu = \frac{1}{\lambda}$$

The frequency range used in IR spectroscopy is within 700-3700 cm^{-1}. It has been established that certain absorption bands (frequencies), called characteristic (see Table 1), are characteristic for determining groups of atoms in molecules.

Table 1

Characteristic group frequencies of organic compounds in the infrared region

№ п/п	Compound	Oscillation type	Frequency range, sm^{-1}	Intensity

1	2	3	4	5
1	Alkanes, cycloalkanes	Valence C–H asymmetric symmetric deformation C–H asymmetric symmetric	 2962 - 2926 2872 - 2853 1485 - 1430 1380 -1340	 C - ср C - ср ср с
2	Alkenes L-diastereomers L-diastereomers	Valence C=C Valence =C–H Deformation=C–H Deformation=C–H Deformation =C–H	1680 - 1600 3100 - 3000 1000 -800 730 - 650 980 - 900	Пер ср с с с
3	Alkynes	Valence C≡C Valence ≡C–H Deformation ≡C–H	2300 - 2100 3333 - 3267 700 - 610	пер с с
4.	Arenas -monosubstituted o-disubstituted m-disubstituted p-substituted	Valence Sar = Sar Valence Sar –N Deformation Sar –N Deformation Sar –N Deformation Sar –N Deformation Sar –N Deformation Sar –N Overtones of deformation vibrations Sar –N	~1600,~1580 ~1500,~1450 3100 - 3000 900 - 675 710 - 690 770 - 730 770 - 735 710 - 690 810 -750 840 - 810 2000 - 1600	ср, пер пер с, пер с, пер с, пер с, пер с, пер с, пер с, пер сл
5.	Alcohols -primary -secondary - tertiary 	Free valence O–H Bound valence O–H Valence C–O Bending O–H Valence C–O Bending O–H Valence C–O Deformation O–H	 3650 - 3580 3550 - 3200 ~1050 1350 - 1260 ~1100 1350 - 1260 ~1150 1410 - 1310	 пер пер с с с с с
6.	Phenols	Free valence O–H Bound valence O–H Valence C–O Deformation O–H	 3650 - 3580 3550 - 3200 1200 1410 - 1310	 пер пер с с
7.	Ethers - aliphatic - alkylaryl	Valence C–O–C asymmetric asymmetric	 1150 - 1085 1275 - 1200	 с с

	vinyl	symmetric asymmetric symmetric	1075 - 1200 1225 - 1200 1075 - 1020	c c c
8.	Thiols, thiophenols Sulfoxides Sulfones Sulfonic acids	Valence S–H Valence S=O Valence SO2 asymmetric symmetric Valence SO2 asymmetric symmetric	2600 - 2550 1070 - 1030 1350 - 1300 1160 - 1140 1260 - 1150 1080 - 1010	ср c c c c c
9.	Amines - primary - secondary - aliphatic - aromatic	 asymmetric symmetric Free valence N–H Deformation N–H Valence C–N Valence CN	 ~3500 ~3400 3450 - 3300 1650 - 1550 1220 - 1020 1360 - 1280	 ср ср ср c, ср сл c
10.	Azo compounds	Valence N=N	1630 - 1575	пер
11.	Diazo compounds	+ Valence –N≡N	2300 - 2000	Пер
12.	Nitro compounds - aromatic - aliphatic C–nitroso compounds N–nitroso compoundsO–нитрозосоедине-ния транс-форма цис-форма	Valence NO2 asymmetric symmetric asymmetric symmetric Valence NO Valence NO Valence NO Valence NO	 1570 - 1500 1370 - 1300 1570 - 1550 1380 - 1370 1600 - 1500 1500 - 1430 1680 - 1650 1625 - 1610	 c c c c c c c c
13.	Nitriles	Valence C≡N	2260- 2220	ср
14.	Imines, oximes	Valence C=N	1690 - 1630	пер
15.	Aldehydes - aliphatic α, β - unsaturated –aromatic 	Valence C=O Valence C–H 	 1740 - 1720 1705 - 1680 1715 - 1695 2900 - 2820 2775 - 2700	 c c c сл сл
16.	Кетоны - алифатические - алкилариловые - диариловые	Valence C=O	 1725 - 1705 1700 - 1680 1670 - 1660	 c c c

	1,4-хиноны		1690 - 1660	с
17.	Carboxylic acids - aliphatic α, β - unsaturated - aromatic	Valence C=O Valence bound OH	 1725 - 1700 1715 - 1690 1700 - 1680 2700 - 2500	 с с с сл
18.	Esters - aliphatic α, β - unsaturated and aromatic	Valence C=O	 1750 - 1735 1730 - 1717	 с с
19.	Amides	Valence C=O (I amide band) Free valence N–H Bound valence N–H Deformation N–H (II amide band)	1700 - 1630 3500 - 3400 3350 - 3140 1620 - 1590	С ср ср с
20.	Anhydrides	Valence C=O asymmetric symmetric valence C-O	 1870 - 1800 1790 - 1740 11390 - 900	 с с с
21.	Halides	Valence C=O	1810 - 1750	С

IR spectra for some substances are shown in Fig. 1.

Each substance has a set of absorption bands characteristic only for it.

IR spectra are more specific than UV spectra and can be used for precise identification of substances, as well as for determining the structure of an unknown compound (usually in combination with other methods).

IR - spectroscopic determination of substances is performed as follows: the substance is dried, since water also produces a spectrum. Then the substance is mixed with KBr and tableted, then inserted into the device and the absorption spectrum is recorded. Currently, dichloroethane, CCl_4, CS_2, and sometimes chloroform are used instead of KBr.

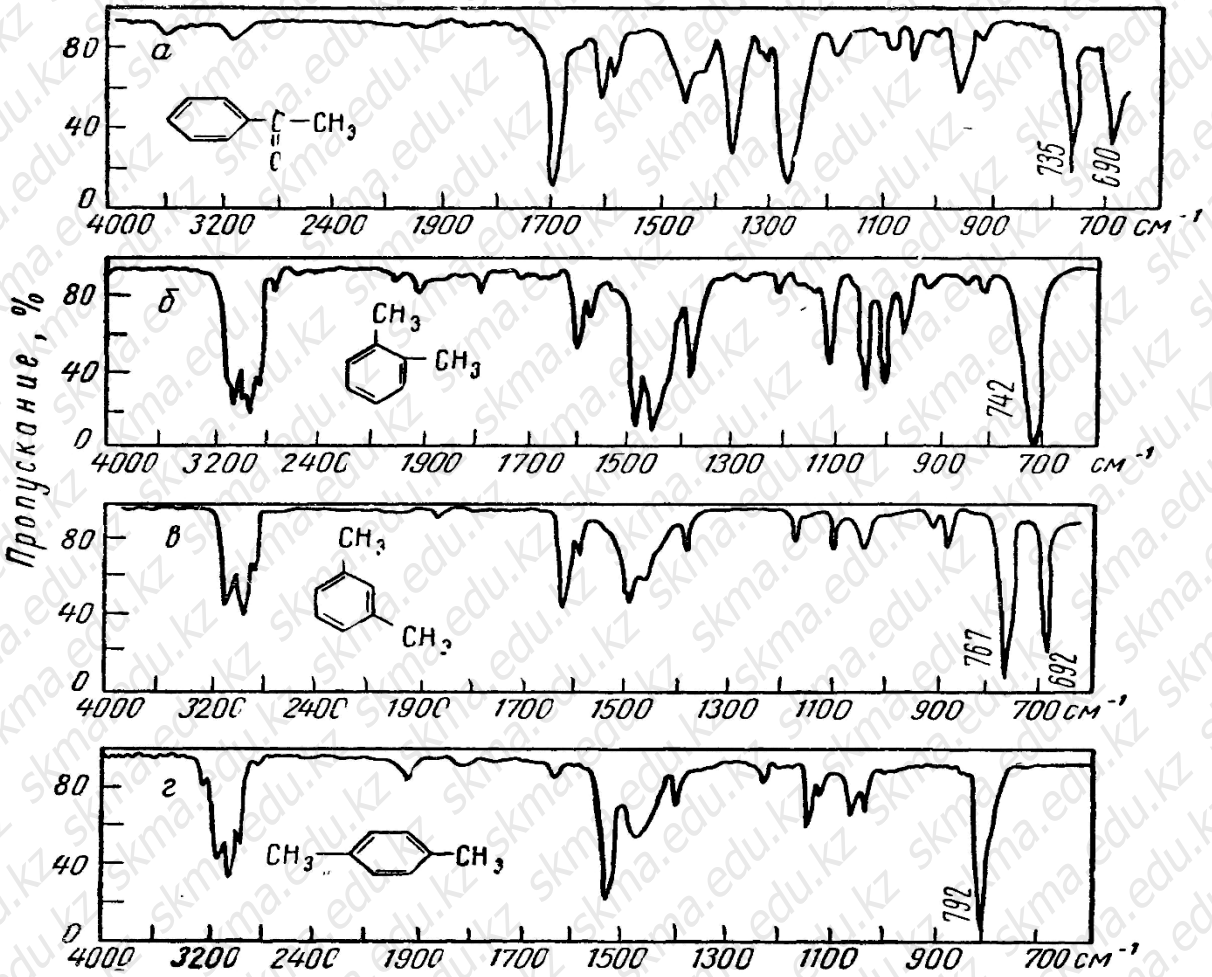

Fig. 1. IR spectra: a) acetophenone; b) o-xylene; c) m-xylene; d) n-xylene

4.Illustrative material:

- tables;
- Microsoft Power Point presentations.

5.Literature:

main:

in Russian

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6.Control questions:

1. Какое явление лежит в основе фотоколориметрнческого анализа?
2. Какие величины связывает между собой закон Бугера-Ламберта-Бера?
3. Что такое оптическая плотность?
4. Устройство ИК-спектрофотометра и принцип его работы.
5. Основные правила работы при ИК-спектроскопическом анализе.
6. Чем обусловлено избирательное поглощение света молекулами?
7. Единица измерения длины волны в ИК-области спектра.
8. Что такое спектр поглощения вещества?

Lecture №5

1. Theme: Chromatographic methods of drug analysis. Classification.

2.Objective: developing students' knowledge of chromatographic methods and the possibilities of using them to solve practical problems related to the analysis of medicinal products.

3. Lecture thesis

Lecture plan:

1. Chromatographic methods. Classification.
2. The essence of the TLC method. Basic equipment. General principle of TLC.
3. Experimental technique in TLC:

- activation of plates
- preparation of the mobile phase
- saturation of the chromatographic chamber
- application of samples
- development of the chromatogram
- development of the chromatogram

TLC is a type of chromatography in which the separation of substances is ensured by the movement of the mobile phase (solvent) through a thin layer of sorbent applied to the substrate. This is one of the most accessible and inexpensive methods of qualitative, quantitative and semi-quantitative analysis of virtually all classes of low-molecular organic compounds, inorganic substances and polymers, performed using special equipment on plates covered with a layer of sorbent.

The movement of the eluent along the plate is ensured by capillary forces. There are several variants of TLC, differing in the method of solvent supply. The most common is ascending elution (chromatography). To implement this type of TLC, the eluent is poured onto the bottom of the chromatographic chamber, and the lower edge of the plate is placed in the solvent. The front of the eluent in this case moves from the bottom up.

Basic equipment for TLC

For the 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), a USP-1 heating device can be used.

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.

General principle of TLC

On the surface of the plate, carefully, so as not to damage the sorbent layer, mark (e.g. with a pencil) the *start line* and the *finish line*. A sample of the test drug solution is applied to the start line (with a microsyringe) and a sample of the comparison solution nearby. The comparison solution contains a sample of the desired active substance. After applying the samples, the solvent is allowed to evaporate from the surface of the plate, 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 specific 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. 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

about the absence of the test substance (fig. 2).

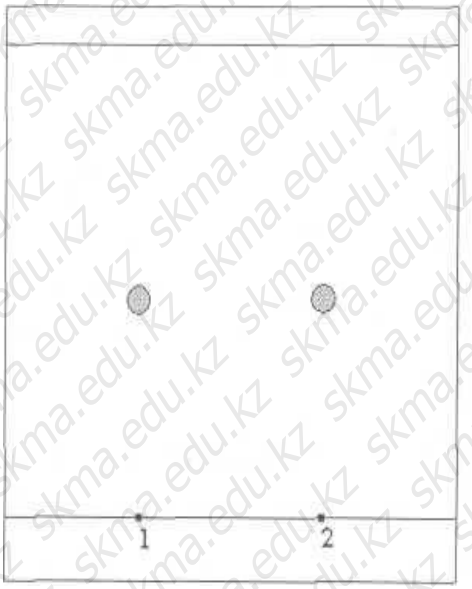

Fig. 1.

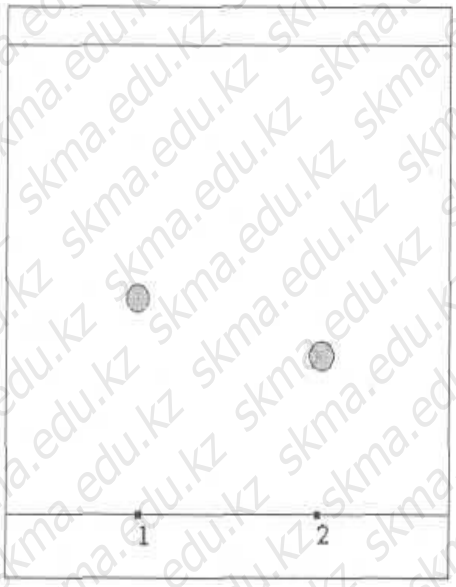

Fig. 2.

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

Experimental technique in TLC

Plate activation. To improve the accuracy of the analysis, it is recommended to activate the plates. To do this, pour acetone or 10% ammonia solution into the chromatographic chamber (30 ml for a 150×120×80 mm chamber or 50 ml for a 190×195×65 mm 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 a temperature of 100°C for 60 minutes (or kept in a drying cabinet at a temperature of 100°C for 60 minutes). 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.

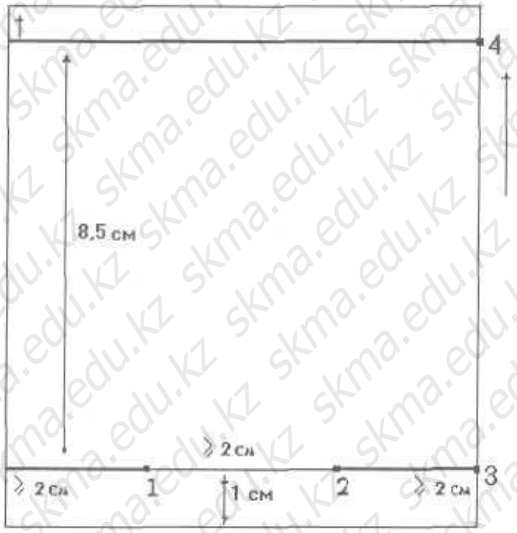

Fig. 3. Plate markings:
1 – comparison solution sample;
2 – test solution sample;
3 – start line;
4 – finish line.

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.

4. Illustrative material:

- tables;
- Microsoft Power Point presentations.

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main:

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6. Control questions (feedback)

1. The main advantage of the UV detector is …
A. selectivity
B. the ability to determine a large number
C. organic compounds
D. low detection limit
E. stability of the baseline
2. 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
e) selectivity of distribution
3. 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 ion exchange between the substance being determined, the stationary and mobile phases
d) chemical interaction of the substance being determined with the mobile phase
e) physical interaction of the substance being determined with the mobile phase
4. 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) carrier gas cylinder, thermostat, evaporator, injector, column, detector, chart recorder
d) stationary phase vessel, thermostat, injector, pump, column
e) stationary phase vessel, thermostat
5. 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
e) width
6. The detector is designed to …
a) uniform movement of the analyzed sample in the column
b) recording the components of the analyzed mixture
c) introducing the sample into the chromatograph
d) complete separation of the components of the analyzed sample
e) uniform movement of the analyzed sample in the injector
7. The basis for qualitative analysis in gas chromatography is the value of …
a) retention time
b) peak height
c) peak area
d) peak width
e) minimum peak
8. The area of the chromatographic peak characterizes …
a) the qualitative composition of the sample
b) the quantitative content of individual components in the sample
c) the content of the liquid phase in the solid carrier;
d) the completeness of separation
e) the quantitative composition of the sample
9. The carrier gas in gas chromatography is …
a) the gas passing through the katharometer cell simultaneously with the analyzed gas
b) the analyzed gas mixture
c) the gas used to move the analyzed mixture along the column and separate it
d) air
e) nitrogen
10. The carrier gas used in GC is …
A. helium
B. air
C. nitrogen
D. argon
E. propane

Lecture №6,7

1. Topic 6,7: Principles of Plane and Column Chromatography. Application Area. Advantages and Disadvantages.
2. Objective: developing students' knowledge of gas and liquid chromatography and the possibilities of using them to solve practical problems related to the analysis of medicinal products.
3. Lecture abstracts
Lecture plan:

1. Gas (gas-liquid and gas-adsorption) chromatography. The essence of the method. The concept of the theory of the method. Retention parameters. The effect of temperature on separation.

Practice of the method, features of chromatography. Methods of quantitative processing of chromatograms (absolute calibration, internal normalization, internal standard).

2. Liquid chromatography: high-performance liquid chromatography. The essence of the method. Application of high-performance liquid chromatography in pharmacy.

3. Application of chromatographic methods in qualitative and quantitative analysis.

Gas and high-performance liquid chromatography are modern physicochemical methods of separation, determination and study of the composition of complex multicomponent mixtures of substances.

Chromatography as an effective method of analysis arose at the beginning of the 20th century and was discovered by the Russian scientist M.S. Tsvet in 1903.

Chromatography is the science of separation methods, as well as qualitative and quantitative determination of components of liquid and gaseous mixtures based on their different sorption (adsorption) under dynamic conditions.

Dynamic conditions in the simplest case are created by the movement of the analyzed mixture of components (mobile phase) through a sorbent layer (stationary phase). The stationary phase (SP) in chromatography can be solid and liquid sorbents. The mobile phase (MP) is a gas or liquid passing through a chromatographic column.

In gas chromatography, the MP is a gas, and in liquid chromatography, it is a liquid. The stationary phase can be solid and liquid sorbents. Gas (GC) and high-performance liquid chromatography (HPLC) are column types of chromatography, where the frontal chromatography method is implemented. HPLC is a variant of liquid chromatography, providing fast and highly sensitive analysis of mixture components with high separation efficiency. The latter is achieved by using small-diameter columns (2-6 mm) with fine-grained sorbent particles (less than 50 μm). A necessary condition for HPLC is the use of high pressure at the column inlet, about 1-40 MPa.

In chromatography, separation is achieved due to differences in the distribution of sample components between the mobile and stationary phases. Due to specific differences in sorption or solubility when moving through a layer of the stationary phase, components are grouped into zones separated from each other by the mobile phase. Due to diffusion processes in the mobile and stationary phases, the boundaries of the zones are blurred, so that the maximum concentration of the component is concentrated in the center of the zone. If the change in time of any property of the mobile phase flow is recorded at the exit of the column, the output curve - the chromatogram - will be recorded in the form of peaks (Fig. 1).

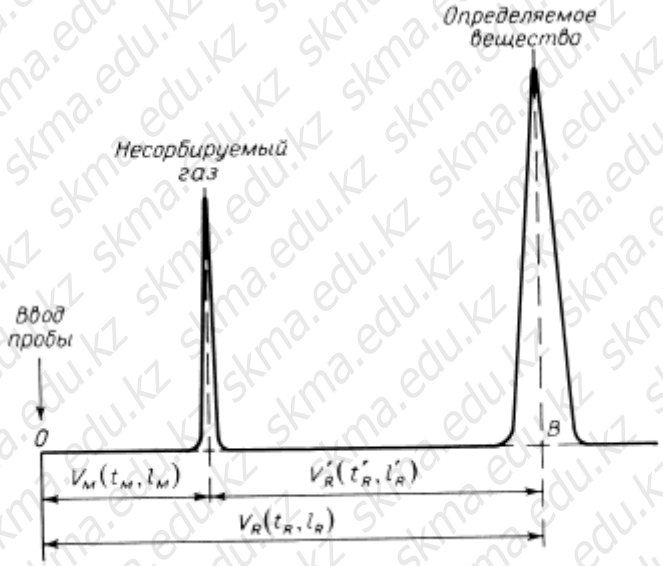


Fig. 1. General view of the chromatogram

The following parameters are measured experimentally:

Total retention time (or retention time) t_R - time from the moment the sample is introduced into the chromatographic column until the moment the maximum concentration of the analyzed substance exits it.

Total retention volume V_R - volume of the mobile phase that has passed

through the chromatographic column from the moment the sample is introduced until the moment the maximum concentration of the analyzed substance exits.

$$V_R = t_R U_c$$

U_c– mobile phase volumetric flow rate

The value of V_R corresponds to the segment OB in Fig. I, if the volume of the mobile phase is plotted on the abscissa axis; if time is plotted on the abscissa axis, then the segment OB corresponds to the total retention time. The segment OB is the total retention distance lg

V_m is the volume of the mobile phase required to elute the unretained substance (or dead retention volume). Corrected retention volume (or reduced retention volume) V'_R

$V'_R = V_R - V_m$

t_m - residence time of unretained substance in a chromatographic system (dead time)

Corrected retention time (or reduced retention time) t'_R

$$t'_R = t_R - t_m$$

Based on the data obtained from the chromatogram, the parameters characterizing the process of retention of the substance in the column are calculated. The retention factor (or capacity coefficient, is the ratio of the amounts of component i in the stationary $m_{i,s.}$ and mobile ($m_{i,m.}$) phases, which is associated with the retention characteristics

$$K_1 = t_R / t_m ,$$

Hence

$$t_{Ri} = (1 + k_i) t_0$$

This is the basic equation characterizing retention in chromatography. As can be seen from equation (1), the retention factor can be determined from the chromatogram data.
In the practice of gas and liquid chromatography, the retention of two compounds (1) and (2), sequentially recorded on the chromatogram, is characterized by the separation factor (α):

$$\alpha = \frac{V'_{R(2)}}{V'_{R(1)}} = \frac{t'_{R(2)}}{t'_{R(1)}} = \frac{l'_{R(2)}}{l'_{R(1)}} = \frac{k_{(2)}}{k_{(1)}}.$$

The separation factor α is sometimes called selectivity. The numerical value of α is always greater than one. However, α does not describe the actual separation of two chromatographic peaks. There are two parameters that determine whether two chromatographic peaks are completely resolved (separated) - the distance between the peaks and their width. The distance between the peaks can be expressed as the difference in retention times (Δt_R), and the width of the peak at its base W is defined as the distance between the tangents to the peak guides (Fig. I). The resolution (R_S) of two peaks is defined as

$$R_S = \frac{2\,(t'_{R(2)} - t'_{R(n)})}{(W_1 + W_2)} = \frac{Дt'_R}{(W_{0.5(1)} + W_{0.5(2)})}$$

$W_{0.5}$ - peak width at half height;
R_S - dimensionless quantity;
Δt_R - and W must be expressed in the same units.

The resolution is equal to one if the distance between two peaks is equal to the average peak width. At $R_S \geq 1$ the peaks should be resolved. However, full resolution may not be achieved if the peak width at the base is large, i.e. the spreading effects are large. The degree of peak spreading determines the column efficiency.

Efficiency in chromatography is the ability of the system to "prevent" (limit) the spreading of the zones of the substances being separated. Efficiency is expressed by the number of theoretical plates N or the height equivalent to a theoretical plate (HETP). A theoretical plate (T.P.) is a section of the sorbent layer on which the distribution of a substance between two phases is completed by establishing equilibrium. The number of theoretical plates can be calculated using the formula:

$$N = 5{,}54\left(\frac{t_R}{W_{0.5}}\right)^2 \text{ или } N \approx 16\left(\frac{t_R}{W}\right)^2,$$

where t_R - total retention time or equivalent to this value total retention distance of a substance - a segment of the time axis of a chromatogram corresponding to the retention time (l_R)
W and $W_{0.5}$ - peak width at the base and at half its height, respectively.
HETT is the height of the sorbent layer (column) required to establish equilibrium:

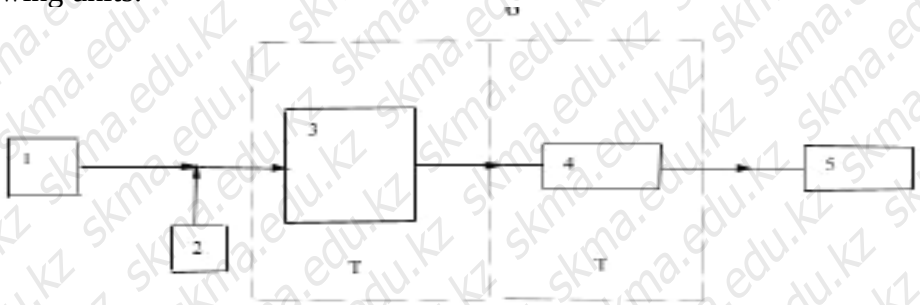
$$H = L/N,$$

where L - length of sorbent layer.

The higher the N and the lower the H, the higher the column efficiency.

HETP depends on the mobile phase flow rate (U). This dependence can be represented as a curve in H-U coordinates, which allows determining the minimum HETP for a given chromatographic system at a certain optimal flow rate.

For all types of column chromatography, the chromatograph block diagram (Fig. 2) includes the following units:



1. Carrier gas supply system 2. Sample injection system. 3. Chromatographic column. 4. Detector. 5. Recorder. In gas chromatography, the mobile phase supply system consists of a gas cylinder, a reducer, and a flow control device; in liquid chromatography, it is a high-pressure pump.

In HPLC, about 70% of all analytical separations are carried out by *reversed-phase chromatography* (RPC). Operation in RPC mode is characterized by the use of a non-polar sorbent and a polar eluent. Sorbents are silica gels with grafted alkylxylyl groups of various lengths (from C_2 to C_{22}) with a direct alkyl group or with phenyl and diphenyl groups. Mobile phases (acetonitrile, water, alcohols and their mixtures) used in RPC allow detection in a wide UV range, easily dissolve almost all the most important compounds included in the composition of biological objects, drugs, etc.

RP HPLC is widely used in determining the purity of drugs

4. Illustrative material:

- tables;
- Microsoft Power Point presentations.

5. Literature:

main:

in Russian

1. Анализ лекарственных препаратов, производных ароматических соединений: Ордабаева С.К.-Шымкент: Типография «Әлем».- 2012.-270 с.
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6. Control questions (обратная связь):

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 adsorption of mixture components on a liquid sorbent
D. different distribution of mixture components between the carrier gas flow and the solid sorbent located in the column.
E. identical adsorption of mixture components on a solid sorbent

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 device for introducing a sample, a column, a detector, a chart recorder;
D. carrier gas cylinder, injector, evaporator, pump, column, detector, chart recorder;
E. carrier gas vessel, injector, evaporator, pump, column, detector, 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
E. introducing the sample in the form of a powder
4. The sorbent used in HPLC is …
A. activated carbon
B. silasorb
C. polysorb
D. separon
E. peat
5. The material from which HPLC columns are made is …
A. glass
B. stainless steel
C. aluminum
D. teflon
E. quartz
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
E. scattering
7. The efficiency of separation of components of a liquid chromatograph is most affected by the block - …
A. dispenser;
B. pump;
C. detector;
D. column.
E. Teflon
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
E. solution concentration
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
E. separation of mixture composition
10. In quantitative analysis, the most frequently used parameter of the chromatographic peak is ...
A. peak height
B. peak width at the baseline
C. peak width at half-height
D. peak area
E. spot area

Lecture №8

1. Topic: Pharmacopoeial methods for testing dosage forms according to the parameters of "dissolution", "disintegration", "wearability", etc.

2. Objective: developing students' knowledge of pharmacopoeial methods for testing dosage forms according to the indicators "dissolution", "disintegration" and "wearability", and the possibilities of using them to solve practical problems related to the analysis of medicinal products.

3. Lecture abstracts

Lecture plan:

1. Pharmacopoeial methods for testing dosage forms. Classification.
2. The "dissolution" indicator.
3. The "disintegration" indicator.
4. The "wearability" indicator.

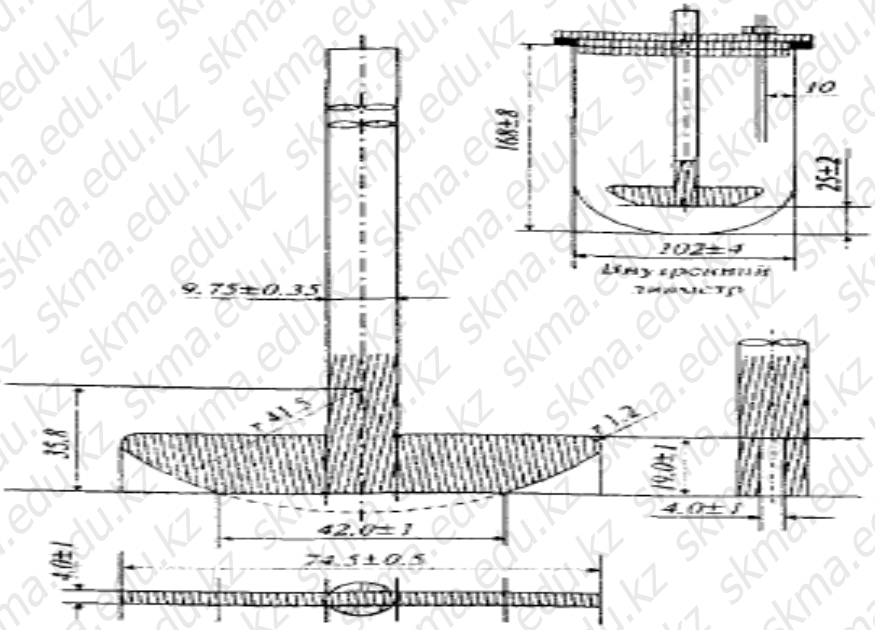
The dissolution test for solid dosage forms is used to determine the rate of dissolution of active ingredients.

For the test, an apparatus with a stirrer paddle, a basket or, in special cases, a flow-through cuvette can be used, unless otherwise specified in the monograph.

Preparation of 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.

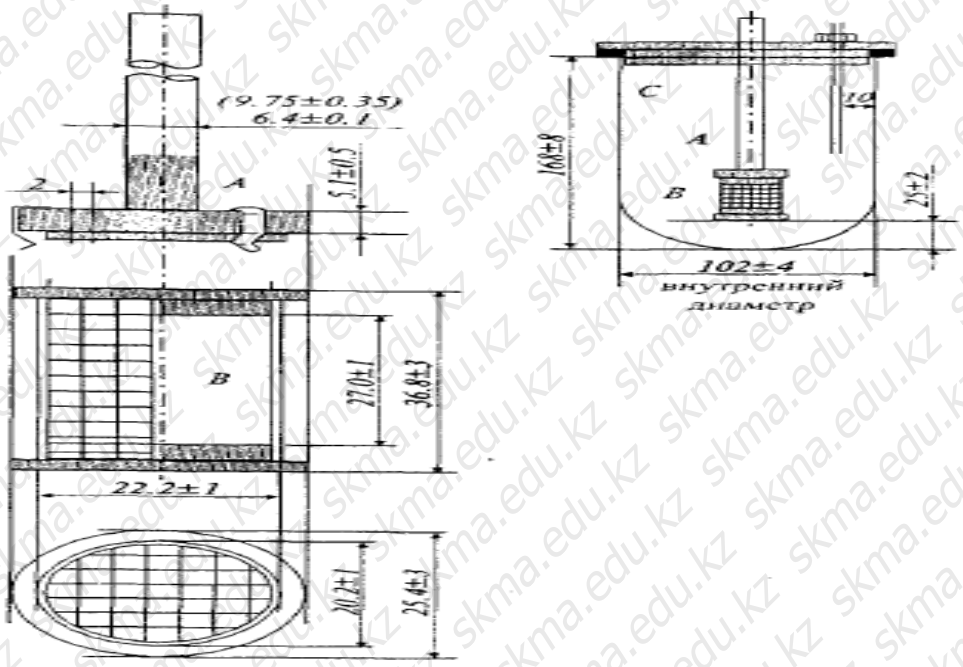
For an apparatus with a basket: place the preparation in a dry basket, which is lowered into the appropriate position before starting to rotate.

Conducting the dissolution test. Turn on the apparatus according to the instructions. The dissolution conditions are set - pH of the dissolution medium, temperature (37.0±0.5)0C, 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.



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

Dissolution test for solid dosage forms: Basket device



In cases where the degree of dissolution is specified for only one period of time, the test may be carried out in a shorter time. If the degree of dissolution is specified for two or more periods

of time, sampling must be carried out without stopping the instrument at a strictly specified time with an accuracy of (±2%).

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

Place one tablet or capsule in each of the six tubes and, if specified, place a disk; suspend the basket in a vessel containing the liquid specified in the general and monographs.

The disintegration test determines whether tablets or capsules disintegrate within the specified time when they are placed in a liquid medium under the experimental conditions specified below.

The samples are considered to have disintegrated when the grid shows:

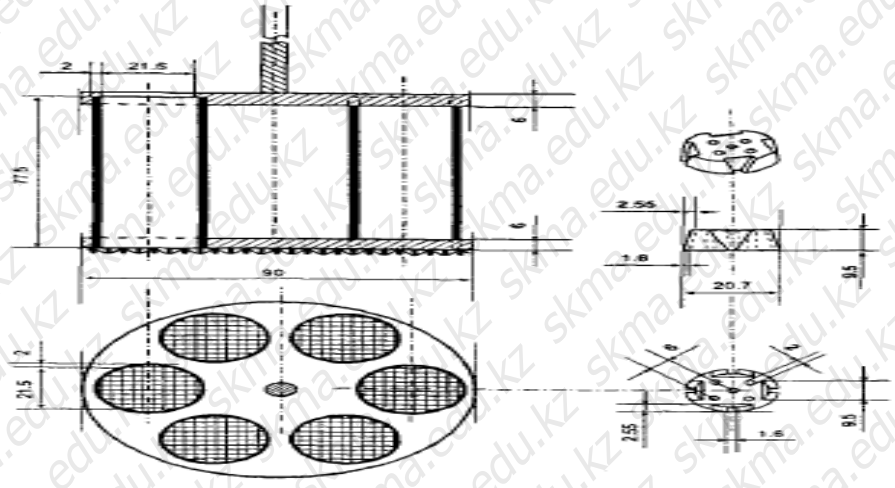
a) no residue;

b) a residue consisting of a soft mass without a noticeably hard, non-wettable core;

c) 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).

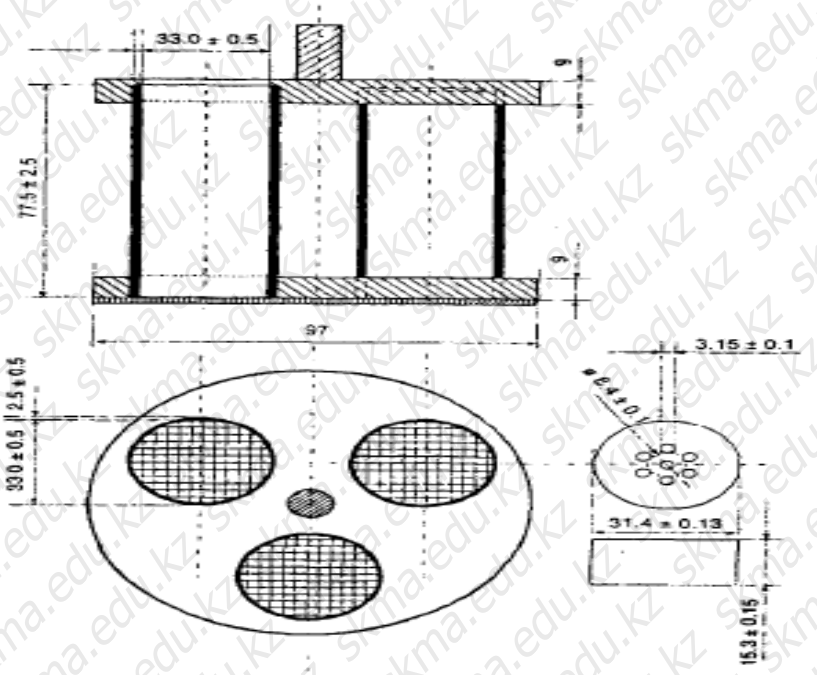
The device is switched on after the specified time, the basket is removed and the condition of the tablets or capsules is examined. The preparation passes the test if the tablets or capsules have disintegrated.

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



Disintegration of tablets and capsules

The design of the basket may vary.



The test is usually carried out once. If the results obtained are questionable or the loss in mass exceeds 1%, the test is repeated twice more and the average of the 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 able to fall freely. It is usually sufficient to set the axis at an angle of 100 to the base.

The test allows one to determine the abrasion of uncoated tablets under certain conditions, i.e. damage to the tablet surface due to mechanical impact or abrasion.

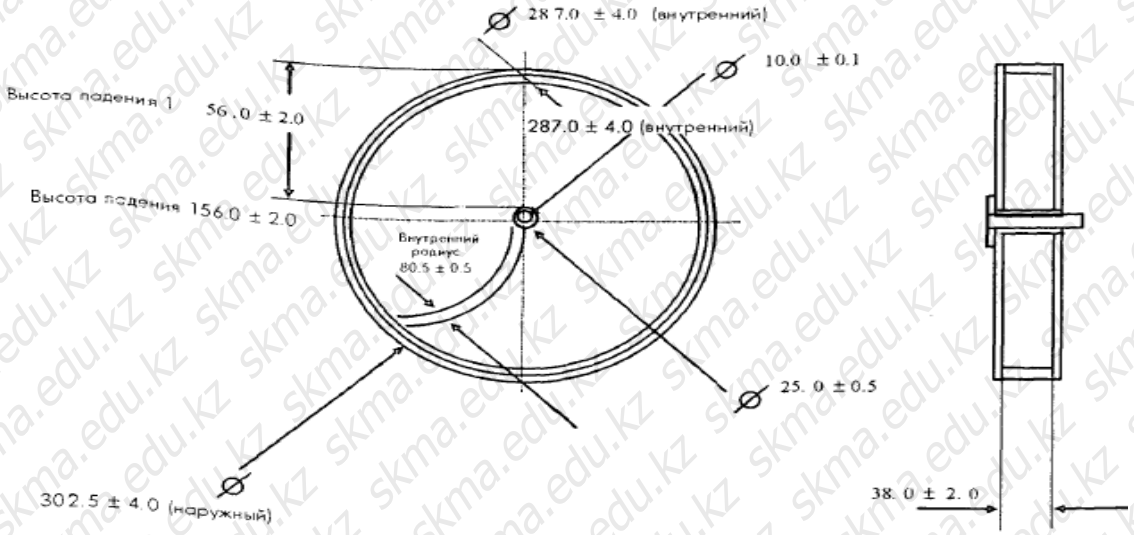


Рисунок 2.9.7.-1. *Прибор для определения истираемости таблеток*

Размеры указаны в миллиметрах

Friability is expressed as a loss in mass, calculated as a percentage of the initial mass of the tablets being tested. The number of tablets taken for testing must be indicated.

4. Illustrative material:

- tables;
- Microsoft Power Point presentations.

5. Literature:

main:

in Russian

1. Анализ лекарственных препаратов, производных ароматических соединений: Ордабаева С.К.-Шымкент: Типография «Әлем».- 2012.-270 с.
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6. Control questions:

1. General requirements for tablets according to the State Pharmacopoeia of the Republic of Kazakhstan.
2. Regulatory materials on quality control of industrially produced dosage forms.
3. Requirements for tablet dosage forms, tablet quality specifications.
4. General requirements for the quality of dragees. Dragee quality specifications.
5. General requirements for the quality of capsules. Dragee quality specifications.
6. Features of the analysis of tablet dosage forms.
7. Definition of the "dissolution" test, according to the requirements of the State Pharmacopoeia of the Republic of Kazakhstan?
8. Definition of the "disintegration" test, according to the requirements of the State Pharmacopoeia of the Republic of Kazakhstan?
9. Definition of the "friability" test, according to the requirements of the State Pharmacopoeia of the Republic of Kazakhstan?