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ZAPORIZHZHIA STATE MEDICAL
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DEPARTMENT OF PHARMACEUTICAL, ORGANIC
AND BIOORGANIC CHEMISTRY

PHARMACEUTICAL CHEMISTRY

Section 1.3

ANALYSIS OF MEDICINES OF THE ANTIBIOTIC GROUP

Study and methodical Guide

for 4th year students of the specialty "Pharmacy, Industrial Pharmacy"

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CONTENTS

INTRODUCTION

Pharmaceutical chemistry is studied according to the Model curriculum for training specialists of the second (master's) level of higher education in the field of knowledge 22 "Health Protection" in higher educational institutions of the Ministry of Health of Ukraine in specialty 226 "Pharmacy" educational qualification "Master of Pharmacy" as of 26.07.2016.

Most of the drawings were developed by the authors of this study guide.

According to the order, pharmaceutical chemistry is studied in III, IV and V courses. In the fourth year (VII-VIII semesters) the discipline program is structured into 2 meaningful blocks:

Block 1 - "Pharmaceutical Analysis"

Block 2 - "Special Pharmaceutical Chemistry"

Block 1 consists of three sections:

Section 1 – "Analysis of cardiotonic and antiarrhythmic drugs. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

Section 2 - "Analysis of medicines of the vitamin group. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

Section 3 - "Analysis of medicines of the antibiotic group. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

The present Pharmaceutical chemistry guide for 4th year students of the specialty " Pharmacy, Industrial Pharmacy" complies with curriculum and cover most of topics of 7th semester.

Lecture plan

on pharmaceutical chemistry for 4th year students of the Faculty of Pharmacy (7 semester)

Sl. No.	Lecture topics	Number of hours
1	Cardiotonic and antiarrhythmic drugs. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.	2
2	Vitamins of aliphatic and alicyclic structure. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.	2
3	Vitamins of heterocyclic structure. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.	2
4	Antibiotics of aromatic and alicyclic structure. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.	2
5	Heterocyclic antibiotics: penicillins, cephalosporins. Characteristics, classification, relationship between structure and pharmacological action, mechanism of action, methods of preparation, methods of analysis, application in medicine.	2

PLAN

of laboratory practicals and seminar classes on pharmaceutical chemistry for 4th year students of the Faculty of Pharmacy (7th semester)

No. s/p	Lesson topics	**Class type**	Number hours **Lab., semin.**
1.	Analysis of drugs from the group of monosaccharides.	Labor.	3
2.	Analysis of drugs from the group of oligo-, polysaccharides and antiarrhythmic drugs.	Labor.	3
3.	Analysis of cardiotonic drugs. Cardiac glycosides.	Labor.	3
4.	Control lesson from the section.	Seminar	2
5.	Analysis of drugs from the group of vitamins of the aliphatic series.	Labor.	3
6.	Analysis of drugs from the group of vitamins of the heterocyclic series, derivatives of chroman, pyridine.	Labor.	3
7.	Analysis of drugs from the group of vitamins of the heterocyclic series, derivatives of pyrimidine-thiazole, pterin, isoalloxazine, corin.	Labor.	3
8.	Analysis of drugs from the group of vitamins of the alicyclic and aromatic structure.	Labor.	3
9.	Control lesson from the section.	Seminar	2
10.	Analysis of drugs from the group of antibiotics of the aromatic series.	Labor.	3
11.	Analysis of drugs from the group of alicyclic antibiotics.	Labor.	3
12.	Analysis of drugs from the group of heterocyclic antibiotics.	Labor.	3
13.	Analysis of drugs from the group of glycoside antibiotics.	Labor.	3
14.	Control lesson from the section.	Seminar	3

SPECIFIC GOALS:

"Analysis of medicines of the antibiotic group. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application»

- Learn the properties of drugs from the group of antibiotics.
- Know the main sources and methods of obtaining drugs from the group of antibiotics.
- To propose and carry out the selection of physical, physicochemical and chemical methods of quality analysis of drugs from the group of antibiotics in accordance with the requirements of the SPhU and other regulatory documentation, as well as Quality Control Methods (QCM).
- Explain the peculiarities of the analysis of drugs from the group of antibiotics using physical, physicochemical and chemical methods.
- Interpret the results of studies of the proposed drugs from the group of antibiotics, obtained using physical, physico-chemical and chemical methods.
- Explain the peculiarities of storage of drugs from the group of antibiotics, based on their physical and chemical properties.

Theoretical material

***Anti-infective chemopreparations -** one of the most numerous groups of drugs (drugs). Their division into groups based on predominant activity is based on the classification of pathogens of human infectious diseases. Currently, there are six groups of infectious agents: viruses, bacteria, fungi, prions, parasitic protozoa, parasitic worms and anthropods. Based on this, different groups of chemopreparations are distinguished (anti-viral, antimicrobial, anti-tuberculosis, etc.), and the most common are antibacterial drugs and there are practically no anti-prion agents.

Anti-infective drugs, regardless of their chemical structure and mechanism of action, share a number of unique properties: firstly, unlike most other drugs, the target (receptor) of anti-infective drugs is not in human tissues, but in the cell of a microorganism or parasite; secondly, the activity of anti-infective drugs is not permanent, but decreases over time, which is due to the formation of drug resistance (resistance is an inevitable biological phenomenon and it is practically impossible to prevent it); thirdly, resistant pathogens pose a danger not only to the patient from whom they were isolated, but also to many other people, even separated by time and space.

Antibacterial chemopreparations (preparations) are the largest group among anti-infective drugs - substances that selectively inhibit the vital activity of microorganisms. The selective effect of anti-infective drugs means activity only against the pathogens, while maintaining the viability of the host's cells; and exert an effect not on all, but on certain genera and species of microorganisms and parasites.

There is no generally accepted terminology and classification of anti-infective drugs. Different terms with the same meaning are used. For example, antifungal, antimycotic or antifungal drugs.

Traditionally, antimicrobial drugs (AMDs) are divided into natural (antibiotics themselves, for example, penicillin), semi-synthetic (modification products of natural molecules: amoxicillin, cefazolin, etc.) and synthetic (chloramphenicol, sulfonamides, nitrofurans, fluoroquinolones, etc.). Currently, such a division has lost its relevance, since a number of natural AMDs are obtained by synthesis (chloramphenicol), and some drugs, which are usually called antibiotics (fluoroquinolones), are de facto synthetic compounds.

The division of AMD, like other drugs, into groups and classes is well known. Such a division is of great importance from the point of view of understanding the commonality of mechanisms of action, the spectrum of activity, pharmacokinetic features, the nature of undesirable reactions, etc. A number of authors (Kharkevich, Mashkovsky, etc.) include the following groups as antibacterial chemotherapeutic

agents: antibiotics, sulfonamide drugs, antisyphilitic agents, antituberculosis agents, etc.

Antibiotics- substances produced by microorganisms, higher plants, animal tissues in the process of their vital activity and modification products of these substances, which selectively suppress the growth of pathogenic microorganisms, lower fungi, some viruses and cells of malignant formations, while not having a toxic effect on the macroorganism.

Antibiotics used in medical practice are produced by actinomycetes (radiant fungi), molds, as well as some bacteria (synthetic analogues and derivatives of natural antibiotics).

The basis of the therapeutic action of antibiotics is the suppression of the vital activity of the causative agent of an infectious disease as a result of the suppression of a more or less specific metabolic process for microorganisms. Suppression occurs as a result of the binding of the antibiotic to the target, which can be either an enzyme or a structural molecule of the microorganism. It should be noted that antibiotics do not always have satisfactory chemotherapeutic and pharmacological properties, which is mostly due to the resistance of microorganisms to them. Thus, the resistance of microorganisms to antibiotics can be natural or acquired.

- True natural resistance is characterized by the absence in microorganisms of the target of the antibiotic action or the inaccessibility of the target due to initially low permeability or enzymatic inactivation. If bacteria have natural resistance, antibiotics are clinically ineffective. Natural resistance is a permanent characteristic of microorganisms and is easily predicted.
- Acquired resistance is understood as the property of certain strains of bacteria to maintain viability at those concentrations of antibiotics that suppress the main part of the microbial population. Situations are possible when most of the microbial population exhibits acquired resistance. The appearance of acquired resistance in bacteria is not necessarily accompanied by a decrease in the clinical effectiveness of the antibiotic. The formation of resistance in all cases is determined genetically: by the acquisition of new genetic information or a change in the level of expression of one's own genes.

The following biochemical mechanisms of bacterial resistance to antibiotics are known:

1. Modification of the action target.
2. Antibiotic inactivation.
3. Active removal of the antibiotic from the microbial cell.
4. Violation of the permeability of the external structures of the microbial cell.
5. Formation of a metabolic "shunt".

For example, the most common mechanism of resistance of microorganisms to β-lactams is their enzymatic inactivation as a result of the hydrolysis of one of the bondsβ-Lactam ring enzymesβ-Lactamase, to aminoglycosides - their enzymatic inactivation by modification (inactivation of aminoglycosides by binding them to various molecules: AAS - attach a molecule of acetic acid, Arn - attach a molecule of phosphoric acid, nucleotidyl- or ANT - attach a molecule of an adenine nucleotide) etc.

Therefore, today the main direction in the creation of new antibiotics is chemical and microbiological modification of natural antibiotics and obtaining semi-synthetic (ampicillin, amoxicillin, cefotaxime sodium salt, cephalothin, ceftriaxone sodium salt, cephalexin, etc.) and synthetic (chloramphenicol, cycloserine, etc.) antibiotics .

CLASSIFICATION OF ANTIBIOTICS

1. According to the spectrum of action

Closely related to selectivity is the notion of the breadth of the spectrum of activity of antibiotics. Thus, according to the spectrum of antimicrobial activity, antibiotics are classified as:

- affect mainly gram-positive bacteria (biosynthetic penicillins, macrolides);
- affect mainly gram-negative bacteria (polymyxins, etc.);
- have a wide spectrum of action (tetracyclines, cephalosporins, chloramphenicol, aminoglycosides, etc.);
- antituberculosis (streptomycin, rifampicin, cycloserine, kanamycin, etc.);
- antifungal (nystatin, levorin, griseofulvin, etc.);
- active in relation to simpler ones (trichomycin, etc.);
- anticancer (actinomycin, anthracyclines, etc.).

2. According to the nature of antimicrobial action:

Antibiotics act on microorganisms either by suppressing their reproduction (bacteriostatic effect) or by causing their death (bactericidal effect).

3. According to the mechanism of antimicrobial action:

1. violation of the synthesis of the bacterial cell wall (penicillins, cephalosporins);
2. violation of the permeability of the cytoplasmic membrane (polymyxins);
3. violation of intracellular protein and ribosome synthesis (tetracycline, chloramphenicol, aminoglycosides, etc.);
4. violation of the synthesis of RNA (rifampicin) and DNA (bruneomycin, fluoroquinolines, etc.).

4. Chemical classification of antibiotics:

1. antibiotics of alicyclic structure (tetracycline group and their semi-synthetic analogues);

2. antibiotics of the aromatic series (levomycetin and its esters);
3. antibiotics of heterocyclic structure (βlactam antibiotics, fig. 1):
   - penams (A, combinedβ-lactamthiazolidine ring system);
   - penems (B, conjugatedβ-lactam dihydrothiazide ring system);
   - clavulanate (Klavamu (oxapenem), C, combinedβ-lactamoxazolidine ring system);
   - carbapenems (D, combinedβ- lactam dihydropyrrole ring system);
   - nocardicins (E, monocyclicβ- Lactams);
   - monobactams (E, monocyclicβ-Sulfamic acid lactams).
   - cephams (F, conjugatedβ-lactamdihydrothiazine ring system containing 7-α-methoxy group);
   - Δ^2-cephems (G, conjugatedβ- lactam dihydrothiazine ring system);
   - Δ^3-cephems (H, conjugatedβ-lactam dihydrothiazine ring system) andΔ^3-oxacephem, (H, conjugatedβ- lactam dihydrooxazine ring system);
4. aminoglycoside antibiotics (streptomycin, kanamycin, neomycin, gentamicin, monomycin and their semisynthetic analogues);
5. macrolide antibiotics (Fig. 2):
   - *12-membered ring* (Methymycin, neomethymycin, YC - 17, litrin - are not used in medical practice);
   - *14-membered ring*(Natural: erythromycin (A), oleandomycin (B), semi-synthetic: roxithromycin, dirithromycin, clarithromycin, flurithromycin, davercin);
   - *15-membered ring (*azithromycin (C));
   - *16-membered ring*(Natural compounds: josamycin, kitazamycin, spiramycin (D), semi-synthetic derivatives: rokitamycin, midekamycin);
   - *17-member ring*(Lancacidin complex - is used in medical practice).
6. anzamycin antibiotics (rifampicin and their semi-synthetic analogues);
7. polyene antibiotics with a glycosidic structure (nystatin, amphotericin, mycoheptin);
8. antibiotics from the group of cyclic polypeptides (gramicidins, polymyxins, etc.);
9. lincosamides (lincomycin, clindamycin, etc.);
10. glycopeptides (vancomycin, etc.);
11. fusidic acid;
12. antitumor antibiotics:
    - derivatives of aureolic acid;
    - quinoline-5,8-dione derivatives;
    - actinomycins;

13. various antibiotics (fuzafungin).

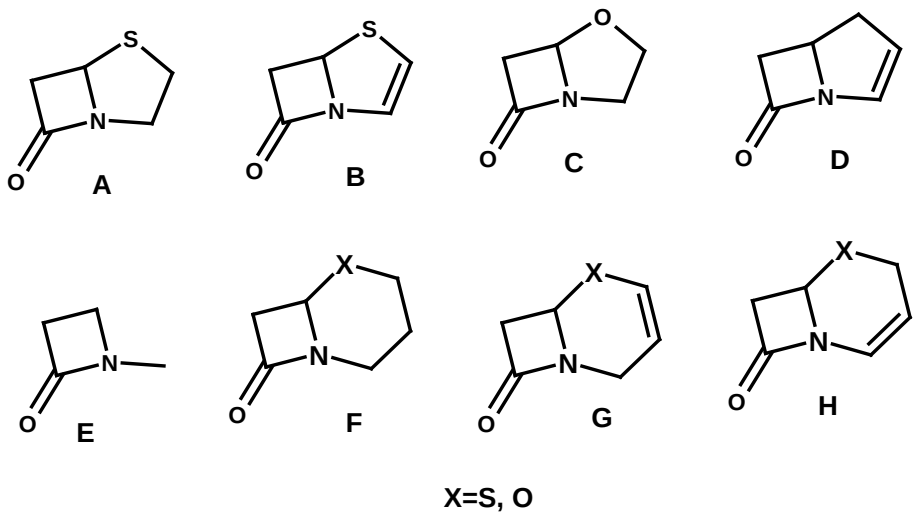


Fig. 1. Heterocyclic systems are included β- Lactam antibiotics.

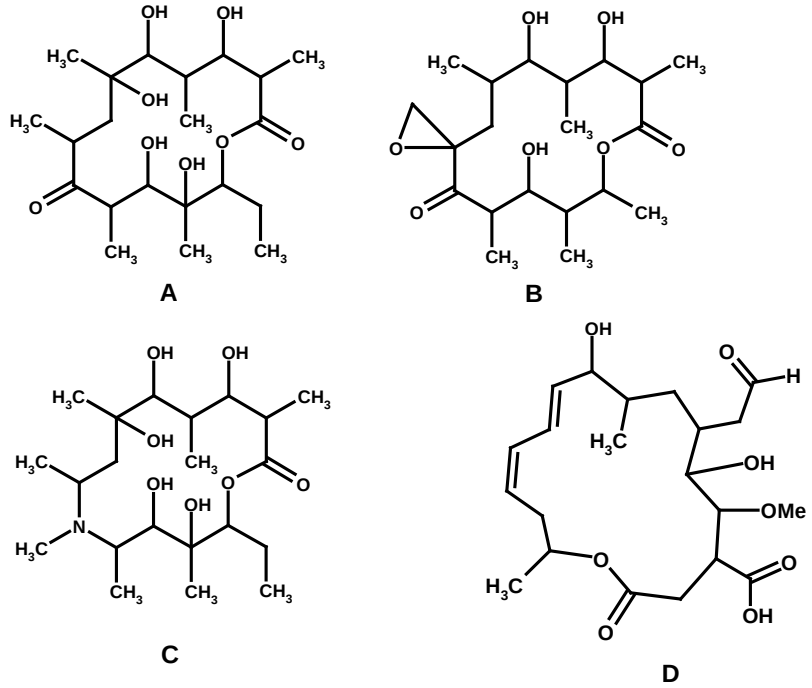


Fig. 2. Principle formulas of the structure of aglycones of macrolide antibiotics.

METHODS OF OBTAINING ANTIBIOTICS

There are three possible ways of obtaining antibiotics:

1). Biosynthesis;

2). Chemical or biotechnological modification of natural antibiotics;

3). Chemical synthesis.

Most antibiotics have a complex chemical structure, so their complete chemical synthesis is very time-consuming and economically unprofitable. The exception is chloramphenicol and some other substances that have a relatively simple chemical structure.

The main way of obtaining most antibiotics is the biotechnological method. Antibiotics are produced by molds, actinomycetes, eubacteria and other microorganisms (Table 1).

Table 1

Producers of some antibiotics

antibiotic	producer
Penicillin	*Penicillium chrysogenum, P. Notatum*
Cephalosporin	*Cephalosporum acremonium*
Streptomycin	*Streptomyces globisporus streptomycini*
Erythromycin	*S. erythreus*
Tetracycline	*S. aureofaciens, S. rimosus*

The same type of microorganisms can synthesize several antibiotics. example, *Streptomyces griseus*synthesizes more than 50 antibiotics.

There are several options for the biotechnological production of natural and semi-synthetic antibiotics.

1. Direct fermentation of the producer microorganism with a substance that is a metabolic precursor of the antibiotic obtained and stimulates the process of its biosynthesis. For example, the biosynthesis of penicillin is carried out in the presence of phenylacetic acid, macrolides - in the presence of propionic acid and propyl alcohol.

2. The use of mutant microorganisms in which certain enzymes involved in the synthesis of the antibiotic are blocked for the biosynthesis of antibiotics. If an analogue of the precursor of the antibiotic is introduced into the medium containing such a microorganism, a modified antibiotic can be obtained. Mutational biosynthesis is used, for example, to obtain semi-synthetic penicillins and cephalosporins.

Most antibiotics are obtained by deep aerobic fermentation of periodic action in aseptic conditions.

The process of antibiotic biosynthesis consists of two stages (Fig. 3):

1. The accumulation of a sufficient amount of biomass, which is grown on a medium for the growth of microorganisms. This stage should proceed quickly, and the nutrient medium should be cheap.

2. Active synthesis of an antibiotic. At this stage, fermentation is carried out in a productive environment. Since antibiotics are secondary metabolites, their biosynthesis occurs not in the phase of cell growth, but in the stationary phase (idiophase). Any mechanisms that inhibit proliferation and active growth activate the process of antibiotic formation.

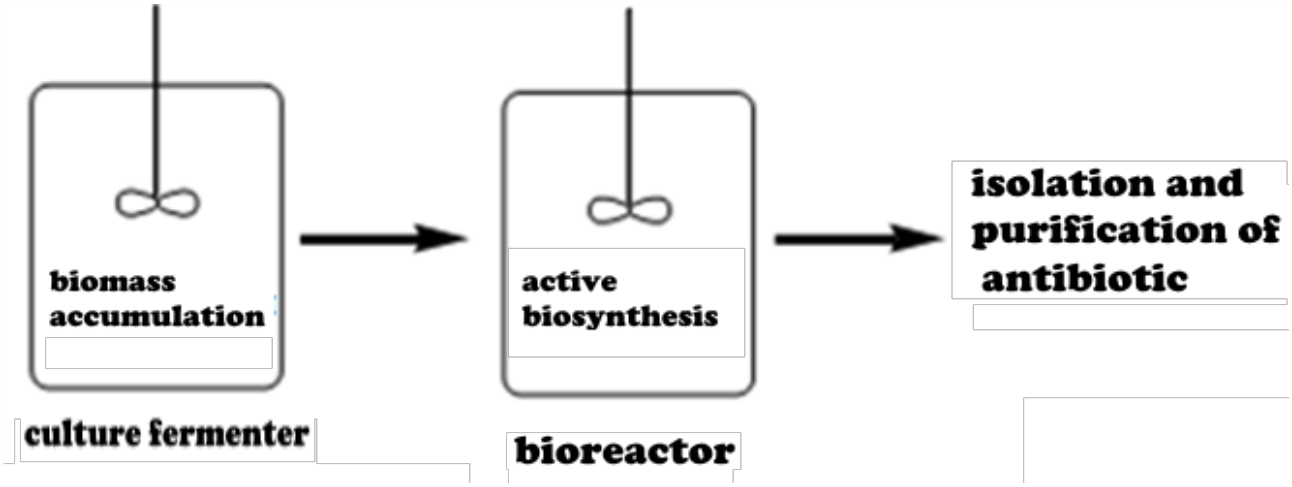


Fig. 3. Schematic diagram of biosynthesis of antibiotics

The final stages of obtaining antibiotics are the stages of isolation and purification. These processes are determined by the nature of the antibiotic, the nature of production and the goals of further use of antibiotics. The following methods are used for isolation and purification of antibiotics:

- ✓ extraction with organic solvents:
- ✓ sorption;
- ✓ precipitation and recrystallization from different environments;
- ✓ ion exchange chromatography, etc.

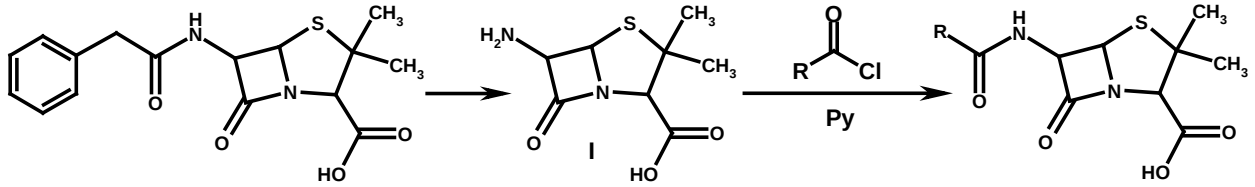
The isolated and purified antibiotics are subjected to lyophilic and spray drying.

Modification of the structure-leader in a rowβ-lactam antibiotics

A) Methods of obtaining semi-synthetic penicillins

Benzylpenicillin and numerous dosage forms created on its basis are distinguished by the highest chemotherapeutic efficiency and lower toxicity. Howeverβ-The lactam cycle of benzylpenicillin is easily destroyed by the action of the penicillinase enzyme (β-lactamases) produced by many microorganisms. These circumstances led to the creation of semi-synthetic penicillins. The solution to such a complex problem became possible after the isolation of 6-aminopenicilanic acid (I, 6-APA), which is the "core" of penicillin. 6-APA is obtained from benzylpenicillin (or other penicillins), acting on the enzyme penicillinase, produced by bacteria (less often chemical methods of cleavage (acid hydrolysis) of penicillins to 6-APA are used, scheme 1). A large number of semi-synthetic penicillins, which are acyl derivatives, have been synthesized on the basis of 6-APA. Carboxylic acid chlorides are used as acylating agents (Scheme 1).

Scheme 1



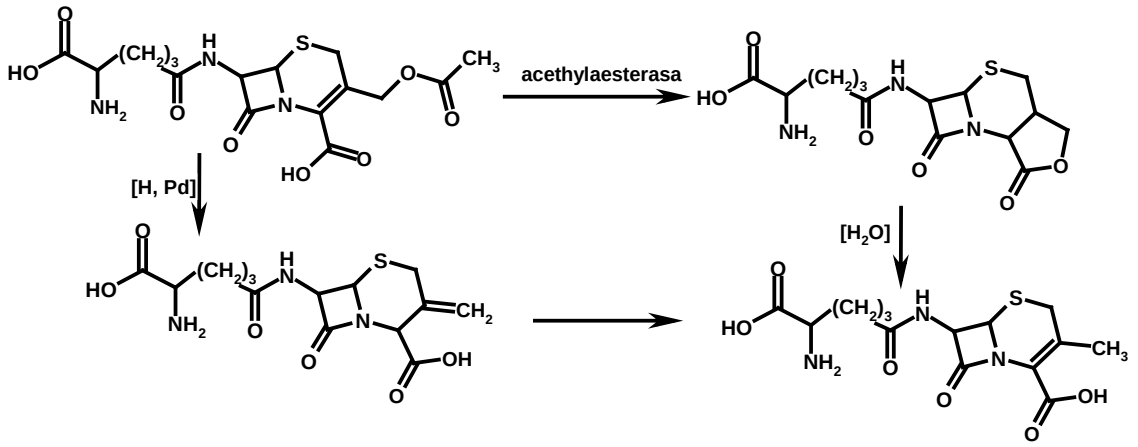
Some of the synthesized semi-synthetic penicillins, while maintaining the high efficiency and low toxicity of benzylpenicillin, have acquired new qualities, such as increased stability and broadening of the spectrum of action.

As a result, semi-synthetic penicillins such as methicillin, oxacillin, ampicillin, carbenicillin, dicloxacillin, carfecillin, andmoxicillinetc.

B) Methods of obtaining semi-synthetic cephalosporins

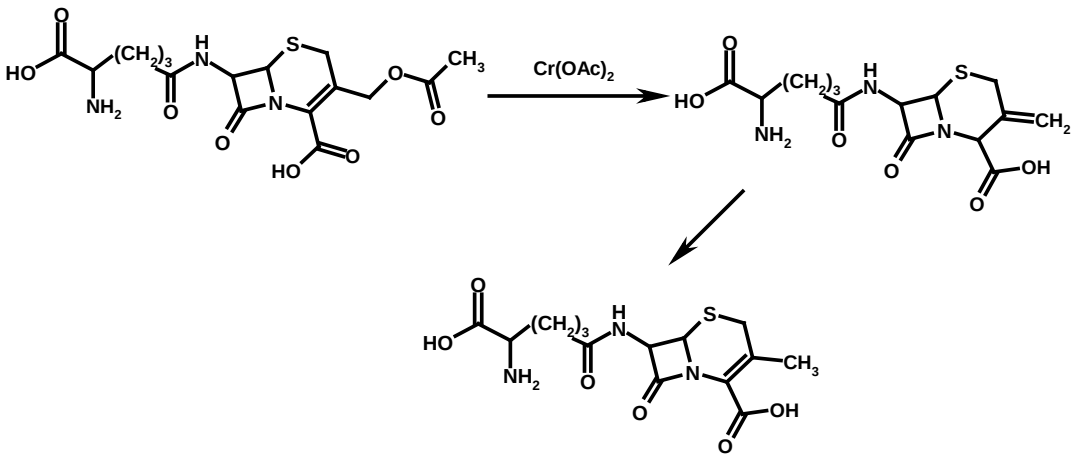
*Modification of cephalosporins in the C-3 position.*The cleavage of the acetoxy group from the natural cephalosporin C was carried out for the first time by hydrogenolysis using significant amounts of a palladium catalyst. These transformations are also produced by hydrolysis in the presence of acetylesterase or intramolecular cyclization with the participation of a carboxy group with the formation of a lactone. At the same time, derivatives of 7-aminodesacetoxycephalosporanic acid (7-ADCA, scheme 2) are formed.

Scheme 2



Today, the conversion of 7-ACA using chromium (II) salts or electrochemically with the formation of 3-methylene cephams is more effective. The latter are quantitatively isomerized in 7-ADCA (Scheme 3). Thanks to nucleophilic substitution at this center, hundreds of modified cephalosporins were obtained.

Scheme 3



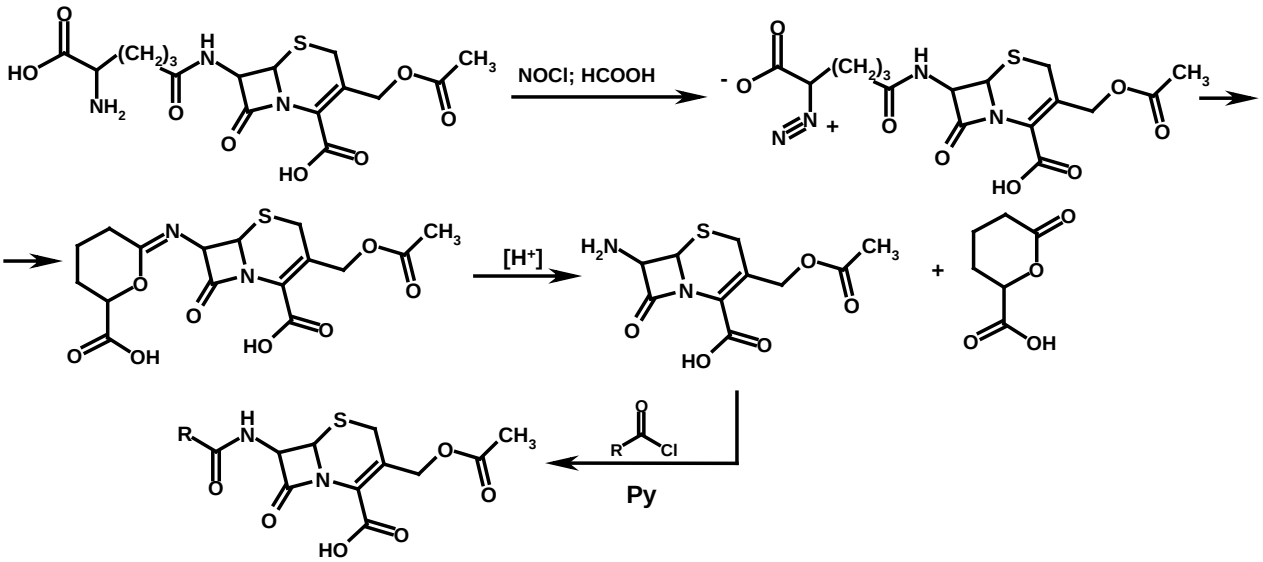
*Modification of cephalosporins according to the C-7 position.*Since benzylpenicillin has greater antibacterial activity than penicillin N, attempts were made to convert cephalosporin C into 7-phenylacetamidocephalosporanic acid. Initially, this was done by mild acid hydrolysis with the formation of 7-aminocephalosporanic acid (7-ACA), but the yields of the final product were negligible. The search for an enzyme that would cleave the side residue of aminoadipic acid in cephalosporin C was extensive, but such an acylase could not be found.

However, the side group can be removed in high yield by chemical methods (Scheme 4). Thus, treatment of cephalosporin with nitrosyl chloride in formic acid led to a diazonium salt, which spontaneously cyclized into an iminoether. After removing the solvent and excess volatile reagent, the side group was cleaved by hydrolysis and 7-aminocephalosporanic acid (7-ACA) was obtained. After small improvements in the technique, the yield was increased to 50%.

Conversion of the 7-amidogroups of cephalosporin C into an iminochloride by the action of phosphorus pentachloride followed by alcohol treatment with the formation of an iminoether and subsequent hydrolytic cleavage became the most simple and effective method. When using dimethyldichlorosilane to protect amino and carboxyl groups, it was possible to obtain 7-aminocephalosporanic acid with a yield of 92.5%.

The availability of 7-ACA led to the production of many semi-synthetic cephalosporins (cephalothin sodium salt, cefuroxime, cefotaxime, cefoxitin, and others), while the development and structure-activity relationship data obtained on the basis of semi-synthetic penicillins were used.

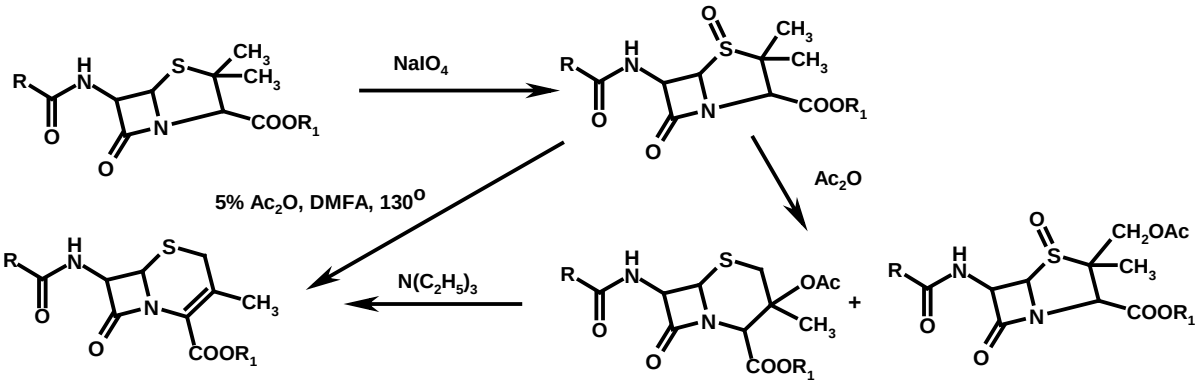
Scheme 4



*Preparation of cephalosporins by modification of penicillins.*Reactions using penicillin sulfoxides became a direct and effective way of converting penicillins into cephalosporins. Since the production of penicillins by fermentation is much cheaper than the production of cephalosporin C, much attention has been paid to this method. It seems quite likely that in the future cephalosporins will be obtained by chemical transformations of penicillins.

Thus, the transformation of a thiazolidine ring into a dihydrothiazine ring involves the oxidation of a sulfur atom in penicillin ether into the corresponding sulfoxide. This transformation is stereospecific, carried out by oxidation of sodium with periodate and gives high yields. Penicillin methyl ether sulfoxide when boiled with acetic anhydride turns with a yield of 60% into a mixture of two isomers (ratio 2: 1) - penicillin and cephalosporin derivatives. The cephalosporin derivative, under the influence of triethylamine, cleaved acetic acid and turned into 7-acylaminodesacetoxycephalosporin.

Scheme 5



The latter was also obtained directly from penicillin sulfoxide with a yield of 10-20% upon rearrangement in xylene at 130 °C in the presence of traces of 4-toluenesulfonic acid. The yield in this reaction can be significantly increased (up to

60%) if it is carried out in a 5% solution of acetic anhydride in dimethylformamide (Scheme 5).

Antibiotic analysis methods.There are no general methods for identifying antibiotics, unlike other groups of drugs. Thus, the basis of qualitative reactions of antibiotics is the individuality of their chemical structure, the nature of functional groups, depending on which they give certain reactions. Today, physicochemical methods based on the absorption of light energy (spectrophotometry in the ultraviolet and infrared part of the spectrum) are widely used for the identification of antibiotics.

Important indicators of the quality of antibiotics are tests for abnormal toxicity, bacterial endotoxins, depressants, pyrogenicity and sterility, which are established by biological means.

The methods of quantitative determination of antibiotics, which are used today in pharmaceutical analysis, are divided into biological, physico-chemical (chromatographic, spectrometry in the UV and IR region of the spectrum) and chemical (titrimetric).

The most important analytical method used for both identification and purity control and quantification of antibiotics is HPLC. A surface-phase variant of HPLC with spectrophotometric detection is usually used. TLC and spectroscopic methods (IR and UV spectroscopy) are also used to identify antibiotics, and UV spectroscopy is used for quantitative determination.

The quantitative determination of some antibiotics, for which HPLC determination is difficult, is carried out by the microbiological method. Examples of such antibiotics are aminoglycosides (kanamycin, gentamicin, etc.). These substances do not absorb electromagnetic radiation of the near UV range and therefore cannot be directly (that is, without additional transformation into other compounds) determined by the HPLC method with spectrophotometric detection.

Determination of biological activity of antibiotics. The activity of antibiotics is determined by comparing the degree of inhibition of the growth of sensitive microorganisms as a result of exposure to the tested antibiotic and a standard sample in known concentrations. Quantification is carried out using:

- method A (diffusion method);
- method B (turbidimetric method).

The diffusion method is carried out on solid media. The environments are inoculated with a certain number of test microorganisms specified in the regulatory documentation. Next, a solution of the studied antibiotic and a standard sample is applied to the surface of the medium. After incubation for a certain time, the diameter of the zones of inhibition of the growth of the test microorganisms, caused by the antibiotic under study and the standard sample, is measured.

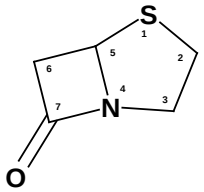
Determination of the activity of antibiotics by the turbidimetric method is carried out similarly, but in a liquid medium located in a test tube. The degree of inhibition of microorganism growth is judged by the degree of turbidity of the medium.

Many antibiotics are mixtures of substances, therefore, in addition to the usual parameters (mass, mass fraction), action units (UA) are used to characterize the quantitative content of the active substance in the antibiotic sample. This approach was especially relevant in the period before the widespread use of HPLC for the quantitative determination of antibiotics.

*For UA of antibiotic activity, the minimum amount of antibiotic is taken,*capable of inhibiting the development or retarding the growth of a standard strain of the test organism (various strains of Staphylococcus aureus) in a certain amount of nutrient medium. Conventional units of action are expressed in UA/ml or UA/mg, that is, the amount of UA is contained in 1 ml of solution or in 1 mg of the drug.Usually 1 unit corresponds to 1 μg of a pure antibiotic (streptomycin, tetracycline), although there are exceptions, for example, 1 unit of the sodium salt of benzylpenicillin corresponds to 0.5958 μg of this substance.

Structure-activity relationship among some antibiotics

*1. Penicillins (penam):*only penicillins possess biological activity, in which the C (5) atom in the foam has an R-configuration.



Let's consider the influence of different types of foam modification on the biological activity of the obtained derivatives. Oxidation of sulfur in position S (1) to foams with the formation of 1-S-oxides and 1-S-sulfones weakens the antibacterial properties of the compounds. However, the introduction of a second oxygen atom leads to obtaining compounds - irreversible inhibitors β- Lactamase.

Modification of the substituents in the C (2) position of foams with the formation of 2α- and 2β-acetoxymethyl derivatives leads to a significant drop in antibacterial activity. Removal of methyl groups in the C (2) position does not affect the activity of the compounds against gram-negative, but reduces the activity against gram-positive microorganisms.

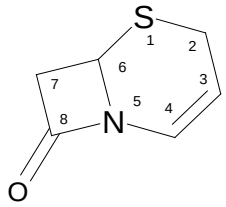
Modification of the carboxyl group in the C (3) position of foams, which leads to its removal or the formation of amides, nitriles, isocyanates, aldehydes, alcohols, and other derivatives, is accompanied by a sharp decrease in the antibacterial activity of the compounds. All these C (3) derivatives have no practical significance. The exception is esters, which by themselves also have very low antibacterial activity,

however, due to the presence of an ester bond, they can easily be absorbed into the blood from the gastrointestinal tract and hydrolyzed in vivo under the action of esterases to form acids with high activity . In this regard, they are used as so-called proantibiotics, which are easily absorbed when administered orally.

Modification in position C (5) of foam leads to a complete loss of antibacterial properties of the compound, firstly, due to an increase in the strength of the acylamide bond inβ- to the lactam ring and, secondly, due to steric difficulties during the interaction of the antibiotic with PSB.

The introduction of substitutes in C (6) of the foam position is of key importance from the point of view of creating new medicinal products. In the early 1960s, intensive modification of the N-acyl fragment in the 6-position of penam led to the production of more than 20,000 semi-synthetic penicillins, of which 37 were widely used as medical drugs. The aminopenicillins obtained in this way are superior to natural antibiotics in activity and acid resistance, and acid penicillins (oxacillin, carbenicillin, methicillin, and others) in resistance toβ-lactamase, as they are competitive inhibitors of these enzymes. The replacement of the amide group in the 6th position with an amidine group led to the creation of amidinopenicillins, among which compounds with pronounced activity against gram-negative microorganisms were found.

*2. Cephalosporins.*Unlike natural penicillins, natural cephalosporin has no biological activity. However, the structural modification of cephalosporin, primarily itsΔ^3- cephem core, radically improves the pharmacological properties of the compound. Virtually all analogues of cephalosporin that show biological activity have 6R and 7R configuration of the corresponding carbon atoms.



Consider the impact of different types of modificationΔ^3-cephem on the biological activity of the obtained derivatives. modificationΔ^3-cephem in S (1) position with formationα- andβ-sulfoxides of cephalosporin leads to a decrease in biological activity, andα-isomer is more activeβ-isomer.

ModificationΔ^3-cephem in the C (2) position with the formation of an alkoxy group is accompanied by a decrease in antibacterial properties as the alkyl substituent increases. Structural modification of the substituent in the C (3) positionΔ^3- cephem is one of the main ways of influencing the antibacterial properties of the antibiotic. The substituent in the C (3) position also has a significant effect on the pharmacokinetic properties of the compound. These substituents are characterized by

a great structural diversity, primarily due to the use of various nitrogen and sulfur-containing heterocyclic systems. The creation of cephalosporins of the IV generation is associated with the introduction of heterocyclic substituents with quaternary ammonium nitrogen into the C (3) position of iminocephalosporins, which led to an increase in the activity of the compounds, especially against gram-negative bacteria (for example, the first cephalosporins of the IV generation cefepime and cefpyr).

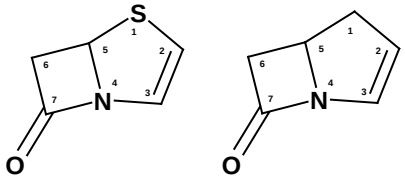
Introduction of ester protection of the carboxyl group in the C (4) positionΔ^3-cephem, cleaved by non-specific esterases of blood serum, allows to obtain procephalosporins. This, as well as in the case of propenicillins, significantly improves the pharmacokinetic characteristics of the drugs.

Introduction of deputies in C (6) of the provisionΔ^3- cephem leads to a complete loss of the antibacterial properties of cephalosporins.

Provision C (7)Δ^3-cephem is key from the point of view of creating new medicines. Also, as in the case of penicillins, the structural modification of the N-acyl fragment in 7βthe position of cephem is the most radical way of influencing the antibacterial properties of the antibiotic. For example, the introduction of clause C (7).Δ^3-cephem of the substitute based on 2-(N-protected-2-aminothiazol-4-yl)-2(Z)-(methoxyimino)acetic acid led to the creation of third-generation cefasporins (iminocephalosporins) with an extended spectrum of antibacterial activity and showing a higher activity against gram-negative bacteria (for example, cefotaxine, ceftazidime) is comparable to second-generation cefasporins. Introduction of methoxy and N-formylamino group in 7α- the position of cephem gives compounds resistance to beta-lactamases.

*Nuclear analogues of cephalosporins.*Replacement of the sulfur atom in position S (1) by cephem with oxygen, as well as the displacement of the substituent inΔ^3-cepheme from position C (3) to position C (2) lead to a significant increase in the antibacterial activity of cephalosporins.

*3. Penems and carbapenems.*Penems and carbapenems are two structurally close types of beta-lactam antibiotics, the heterocyclic skeleton of which is formed by a penem and a carbapenem, respectively. As in the case of penicillin, derivatives that have the R-configuration of the C (5) atom have antibacterial activity.



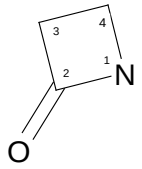
Let's consider the influence of some types of modification of penems and carbapenems on the biological activity of derivatives. The inclusion of oxygen in the S (1) position of penem leads to the production of 1-oxa-2-penems - chemically unstable substances that are effective inhibitorsβ- Lactamase. Introduction of a

methyl group into C (1)β- the position of carbapenems leads to the stabilization of the antibiotic in relation to the action of dehydropeptidase of the kidneys. Variation of the structure of the substituent in the C (2) position of penem has little effect on the biological properties of the antibiotic. Penems containing thioethyl or carbamoyloxymethyl groups in the C (2) position show the greatest activity.

Modification of the carbapenem in the C (2) position can lead to an increase in the acid resistance of the derivatives, as well as an increase in their resistance to the action of beta-lactamases. The introduction of an amidine group into the 2-thioethyl fragment of a carbapenem increases the activity of the antibiotic against gram-negative bacteria.

*With (6) position in penem and carbapenem.*A characteristic feature of both of these β-lactams, which distinguishes them from penicillins, is their presence of a broad spectrum of antibacterial activity even in the absence of a substituent in the C (6) position. Moreover, 6β-acylamide derivatives of penem and carbapenem are chemically unstable and biologically inactive. The best antibacterial properties are penem and carbapenem derivatives containing a 1R-hydroxyethyl group in 6β-antibiotic provisions. It protects the beta-lactam ring and ensures the stability of antibiotics in terms of action β- Lactamase.

4. monobactams. Monobactam is the most promising representative of monocyclic beta-lactam antibiotics of natural origin. Its heterocyclic skeleton is monobactam, or azetidinone-2. The discovery of monobactam disproved the idea that it is impossible to show antibacterial properties in isolationβ-lactam ring without the "support" of a heterocyclic or carbacyclic system condensed with it.

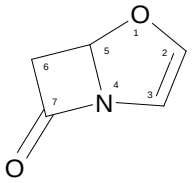


Consider the role of substituents in various positions of monobactam in the biological activity of derivatives. Provision N (1). The main role of the acid substituent (most often - SO_3H) at the amide nitrogen of monobactam is reduced to the weakening of the acylamide bond in the β-lactam ring, which is extremely stable in the inactive N-unsubstituted azetidinone-2. Replacing the sulfonyl group with other electron-withdrawing substituents does not lead to a significant change in the antibacterial activity of the derivatives. Provision C (3). Modification of the N-acyl fragment in 3β-positions of monobactam (3S-configuration), as in the case of penicillins and cephalosporins, is the most effective way of influencing the antibacterial properties of derivatives. The most active were monobactams, the N-acyl fragment of which is borrowed from cephalosporins of the third and fourth generations. Stereoisomeric derivatives that have the 3R configuration are inactive.

Introduction of methoxy and N-formylamino groups in 3α-position leads to increased antibiotic resistance toβ-lactamase, as well as in the case of penicillins and cephalosporins.

The introduction of methyl or carbamoyloxymethyl groups in the C (4) position of monobactam helps to increase the resistance of derivatives toβ-lactamase However, increasing the size of the substituent in parallel with increasing resistance to beta-lactamases reduces the antibacterial activity of antibiotics.

*5. Beta-lactamase inhibitors (oxapenems or Klavami)).*The most effective non-competitive inhibitorβ-Lactamase of various etiologies is clavulanic acid, obtained biosynthetically. Being a weakly active antibiotic, it is widely used in clinical practice to fight againstβ-lactamase resistance of microorganisms.



Let us consider the influence of some structural changes in clavulanic acid on the inhibitory activity of the obtained derivatives. Provisions O (1) and C (2). 1-Thioanalog of clavulanic acid and its derivatives with a hydrogenated exocyclic double bond have less pronounced inhibitory properties than natural compounds. Provision C (3). The transformation of the carboxyl group into methyl or benzyl ethers does not change the biological properties of the compounds. A similar effect is observed during decarboxylation of clavulanic acid. Provision C (9). The most effective way to improve the inhibitory effect of clavulanic acid is to modify the substituents in the C (9) position of Clavam (Fig. 1). Replacing the hydroxyl group with amino-, dibenzylamino-, phenyl-, N-formylamino- leads to a significant increase in the inhibitory properties of the derivatives.

LESSON No. 1

TOPIC: Analysis of drugs from the group of antibiotics of the aromatic series.

PURPOSE: To master the methods of analysis of medicinal products from the group of aromatic antibiotics, as well as their semi-synthetic analogues.

3. TARGETS:

3.1. T o study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of antibiotics of the aromatic series and their semi- & synthetic derivatives.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the group of antibiotics of the aromatic series and their semi- & synthetic derivatives using physical, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of antibiotics of the aromatic series and their semi- & synthetic derivatives, based on their physicochemical properties.

3.9. Learn and follow the rules of safe work in a chemical laboratory.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. Antibiotics. General characteristics. Names and synonyms of antibiotics. Development of antibiotic chemistry.

2. Antibiotics as medicinal substances. Sources of receipt. Chemical structure. Nomenclature, physicochemical properties of medicinal substances from the group of antibiotics.
3. Methods of obtaining antibiotics and ways of creating new antibiotics (biological screening, modification of the "leader structure" (chemical transformation), directed synthesis).
4. Latin names, synonyms, structural formulas and chemical names of drugs from the group of aromatic antibiotics. Levomycetin (chloramphenicol) and its esters (levomycetin stearate, soluble levomycetin succinate). Synthesis methods, the relationship between structure and biological action, the role of stereoisomerism in the manifestation of biological action.
5. Use of physicochemical properties to analyze the quality of chloramphenicol antibiotics.
6. Based on the structure of the researched medicinal products, justify the identification reactions and methods of quantitative determination, give the chemistry of the corresponding reactions.
7. Justify the storage conditions of the researched medicinal products based on their structure and chemical properties.
8. The main dosage forms created on the basis of the investigated medicinal substances. Medicinal form, dosage. Application.

4.3. Test tasks:

#

1) The pharmacist-analyst conducted an identification reaction for the aromatic nitro group in chloramphenicol with sodium hydroxide solution when heated. What is observed at the same time?

A. yellow color, changing to red-orange, with subsequent precipitation of a brick-red precipitate and the smell of ammonia
B. green color and smell of ammonia
C. white sediment
D. formation of a blue complex soluble in chloroform
E. a black precipitate that dissolves when added to a water solution

#

2) Indicate how to prove the presence of a nitro group in the structure of chloramphenicol (Chloramphenicolum):

A. obtaining an azo dye after the reduction of the nitro group to the amino group
B. by the reaction of interaction with iron (III) chloride

C. according to the interaction reaction with Nessler's reagent
D. interaction with hydrochloric acid
E. interaction with a solution of potassium chloride

#

3) An analytical chemist can detect an aromatic nitro group in a chloramphenicol molecule by an azo coupling reaction after its reduction. Restoration of the indicated functional group to the amino group is carried out:

A. zinc in a hydrochloric acid environment
B. zinc in a chloroform environment
C. zinc in dioxane medium
D. zinc in a neutral environment
E. zinc in an alcoholic medium

#

4) Specify the starting substance used in the pharmaceutical industry for the synthesis of chloramphenicol:

A. acetone
B. *p*-nitroacetophenone
C. aniline
D. *p*-nitrobenzoic acid
E. benzoic acid

#

5) State the reason for the impossibility of using D - (-) - and L - (+) - erythro forms of chloramphenicol in medical practice:

A. due to high toxicity
B. due to the difficulties of chemical synthesis
C. due to low activity
D. due to the resistance of microorganisms

#

6) At a pharmaceutical enterprise, a pharmacist analyzes soluble chloramphenicol succinate. What will be observed as a result of the interaction of this medicinal substance with sodium hydroxide solution?

A. the appearance of a white precipitate
B. the appearance of the smell of ammonia
C. the appearance of a blue-violet color of the solution
D. complex salt formation
E. the formation of a red precipitate

#

7) Antibiotics are classified by the chemical structure of the carbon skeleton. Which of the following belong to the aromatic series?

A. tetracycline
B. chloramphenicol and its esters
C. penicillins
D. cephalosporins
E. streptomycin and its preparations

#

8) The chemist identified chloramphenicol stearate with concentrated hydrochloric acid. What analytical effect will be observed as a result of the reaction?

A. white precipitate
B. smell of ammonia
C. oily drops
D. red color of the solution
E. blue-violet color of the alcohol layer

#

9) Sterilize eye drops containing:

A. chloramphenicol
B. benzylpenicillin
C. phenoxymethylpenicillin
D. collargol
E. trypsin

#

10) What reagent can a pharmacist-analyst use to confirm the presence of a nitro group in the structure of chloramphenicol?

A. sodium hydroxide solution
B. copper sulfate solution
C. hydrochloric acid
D. cobalt nitrate solution
E. hydrogen peroxide solution

#

11) The presence of a nitro group in the structure of chloramphenicol can be confirmed after the reduction of the nitro group to the amino group using the formation reaction:

A. azo dye
B. iron (III) hydroxamate
C. thiochrome
D. fluorescein
E. thalleioquine

#

12) Medicinal product identified by reaction with sodium hydroxide solution when heated:

A. chloramphenicol
B. ampicillin
C. cefotaxime sodium salt
D. ascorbic acid
E. benzylpenicillin

#

13) Quantitative determination of chloramphenicol can be performed by the following method:

A. nitritometry with preliminary recovery
B. nitritometry
C. nitritometry followed by recovery
D. nitritometry with preliminary oxidation
E. complexonometry

#

14) Quantitative determination of chloramphenicol (chloramphenicol) is performed according to the requirements of the SPhU by the following method:

A. nitritometry after recovery
B. spectrophotometry
C. bromatometry
D. iodometry
E. iodatometry

#

15) Derivatives of nitrophenylalkylamines include:

A. streptomycin
B. cephaloridine
C. chloramphenicol
D. gentamicin
E. nystatin

#

16) Indicate the method by which, in accordance with the requirements of the SPhU, concomitant impurities in the substance chloramphenicol (chloramphenicol) are determined:

A. thin layer chromatography
B. iodometry
C. UV spectroscopy
D. liquid chromatography
E. HPLC

#

17) Choose a set of reagents with which, in accordance with the requirements of the State Federal Drug Administration, the identification of chloramphenicol (chloramphenicol) is carried out:

A. calcium chloride, zinc, benzoyl chloride, solution of iron (III) chloride, chloroform

B. sodium nitrite, hydrochloric acid

C. concentrated sulfuric acid

D. a solution of hydroxylamine hydrochloric acid, sodium hydroxide, a solution of iron (III) chloride

E. perhydrol, iodine solution

#

18) A mixture of D - (-) - and L - (+) - threo-isomers, that is, the racemic form of chloramphenicol, which has 50% of its activity, is called:

A. Synthomycin

B. pancreatin

C. chloramphenicol stearate

D. midecamycin

E. ephedrine

#

19) Threo-erythro-isomerism is characteristic of nitrophenylalkylamine antibiotics. Natural chloramphenicol corresponds to:

A. D - (-) - threo-isomer

B. *L*- (+) - threo-isomer

#

20) There are two asymmetric carbon atoms in the structure of chloramphenicol. An alcoholic solution of chloramphenicol rotates the layers of polarization:

A. to the right

B. to the left

C. has no optical activity

#

21) Levomycetin (chloramphenicol) exhibits weak acidic properties due to the presence in the structure of:

A. amide group and two alcohol hydroxyls

B. nitro groups

C. covalently bound chlorine atom

D. aromatic system of nitrobenzene

#

22) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, chloramphenicol and chloramphenicol disodium disuccinate impurities are determined in the chloramphenicol sodium succinate substance:

A. liquid chromatography
B. thin layer chromatography
C. iodometry
D. UV spectroscopy
E. liquid chromatography

#

23) Like other phenylalkylamines, chloramphenicol undergoes hydramine cleavage under various conditions. Thus, hydrolysis followed by oxidation with sodium periodate leads to the formation of:

A. 4-nitrobenzaldehyde, formic acid, formaldehyde and ammonia
B. 3-methyl-4-nitrobenzaldehyde, formic acid and ammonia
C. benzene, nitric acid, formaldehyde and acetic acid
D. nitrotoluenes, ammonia, methanol and formaldehyde

#

24) The residue of succinic acid in the structure of chloramphenicol sodium succinate after acid hydrolysis is detected by the reaction with:

A. with resorcinol and conc. sulfuric acid
B. with sodium nitrite and hydrochloric acid
C. with concentrated sulfuric acid
D. with a solution of hydroxylamine hydrochloric acid, sodium hydroxide, a solution of iron (III) chloride
E. with perhydrol and iodine solution

#

25) The mechanism of antimicrobial action of chloramphenicol and its preparations is based on:

A. violation of protein synthesis at the level of ribosomes
B. disruption of cell wall synthesis
C. violation of the permeability of the cytoplasmic membrane
D. disruption of RNA synthesis
E. protein denaturation of the microorganism

#

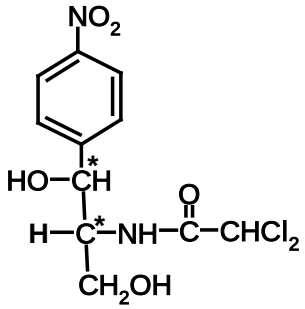
26) Indicate how to determine the presence of free stearic acid in chloramphenicol stearate:

A. by the method of neutralization using phenolphthalein
B. iodometrically

C. by the method of ion exchange chromatography
D. by the method of polarimetry
E. by the method of refractometry

4.4. Situational tasks:

1) Describe the cupriiodometric method for quantitative determination of chloramphenicol. Give the reaction equations, the formula for calculating the quantitative content.
2) Describe the reaction of chloramphenicol with sodium hydroxide. Explain how this reagent can be used to prove the presence of an aromatic nitro group, an amide group, and an aliphatic fragment in the structure of the drug?
3) Write the spatial isomers of chloramphenicol and explain which substances belong to the threo and erythro series. Indicate which of these isomers is used in medicine.
4) Write the structural formula of chloramphenicol and characterize the effect of stereoisomerism on the pharmacological activity of this compound.
5) Give the reactions and list the physicochemical properties that allow you to differentiate chloramphenicol, chloramphenicol stearate and chloramphenicol succinate soluble.
6) Give the equation of the reactions of the hydroxam test for chloramphenicol and chloramphenicol stearate.
7) Based on the chemical structure of chloramphenicol, give the reaction equations of various methods of quantitative determination of the drug.
8) Give methods for identifying the organically bound halogen atom in the chloramphenicol molecule.
9) When evaluating the quality of tablets with the specified substance:



a discrepancy in their appearance was noted in the "Description" section - the tablets were greenish-yellow in color. Give justification for the reasons for the change in the quality of the tablets according to this indicator. Suggest other tests characterizing the quality of tablets. Give reactions to establish authenticity and give justification for the methods of quantitative determination of medicinal substances in substances and tablets, give calculation formulas.

4.5. Tasks:

1) When analyzing the dosage form of the composition:

   Levomycetin 2.0

   Novocaine 1.0

   Ethanol 70% to 100.0

   4.59 ml of 0.02 M sodium nitrite solution (Kp = 1.0000) was spent on titration of the amount of novocaine and reduced chloramphenicol; 1.85 ml of 0.02 M sodium nitrite solution was spent on the same volume of the dosage form without recovery. Calculate the content of novocaine and chloramphenicol in the medicinal form. The volume of the dosage form taken for analysis is 1 ml. M.m. Levomycetin = 323.1 g / mol, M.M. of novocaine = 272.81g/mol.
2) Calculate the percentage of chloramphenicol in an aqueous solution, if A = 0.59 when measured on a spectrophotometer (cuvette 10 mm),$E_{1\text{cm}}^{1\%}$= 295.
3) During the quantitative determination of chloramphenicol, it was established that its content is 99.0%. What volume of 0.1 M sodium nitrite solution (Kp = 1.0000) was used for the titration of 0.3310 g of chloramphenicol? M.m. chloramphenicol = 323.1 g/mol.
4) The angle of rotation of a 5% solution of chloramphenicol in ethanol is + 10º. Calculate the specific rotation, if the measurement was carried out in a tube 10 cm long.
5) Calculate the percentage of chloramphenicol from the value of the specific absorption index at a wavelength of 278 nm, if the optical density of a 0.002% aqueous solution at the specified wavelength and a cuvette thickness of 9.8 mm is 0.591.
6) Calculate the content of chloramphenicol (g) in the dosage form:

   Levomycetin solution 0.01% - 10 ml

   Sodium chloride 0.09

   if 5.0 ml of the tested solution after reconstitution with zinc dust in the presence of concentrated hydrochloric acid is brought up to the mark in a volumetric flask with a capacity of 25.0 ml (solution A). The optical density of the solution obtained by appropriate processing of 1.5 ml of solution A and bringing it to a total volume of 10.0 ml at a wavelength of 364 nm in a cuvette with a layer thickness of 5 mm is 0.232; the specific absorption index of the standard solution of chloramphenicol under the same conditions is 1719.0.
7) Calculate the content of chloramphenicol in the dosage form of the composition:

   Levomycetin solution 0.015% - 10 ml

   Sodium chloride 0.09

if the optical density of 10 ml of a solution obtained from 1.5 ml of a 1: 5 dilution of the dosage form, measured at a wavelength of 364 nm in a cuvette with a layer thickness of 5 mm, is 0.430. The optical density of 10 ml of a standard solution of chloramphenicol obtained from 1.5 ml of a 0.02% solution of chloramphenicol, measured under the same conditions, is 0.285.

8) Calculate the interval of possible values of the angle of rotation of a 5% solution of chloramphenicol (levomycetin) in 95% alcohol with a cuvette thickness of 25 cm, if the specific rotation according to the QCM has a value from + 15º to + 22º.
9) Calculate the percentage content of chloramphenicol (M.m. 323.13) in the preparation if 14.02 ml of 0.1 M sodium nitrite solution (Kp = 1.0020) was spent on the titration of a weight of 0.4590 g.
10) Calculate the volume of 0.1 M sodium nitrite solution (Kp = 1.0000), which will be used for the titration of 0.5025 g of chloramphenicol (M.m. 323.13), if its percentage content in the preparation is 98.5%.
11) Determine the mass fraction of chloramphenicol (M.m. 323.13) in the medicinal product, if 16.40 ml of 0.1 M sodium nitrite solution (Kp = 0.9928) was spent on the titration of 0.5234 g of chloramphenicol.
12) Determine the volume of 0.1 M sodium nitrite solution (Kp = 0.9875), which was spent on the titration of a weight of 0.4995 g of chloramphenicol (M.m. 323.13). The percentage content of chloramphenicol in the medicinal product is 98.60%.
13) Calculate the percentage concentration of an alcoholic solution of chloramphenicol if the specific rotation is 19o, the angle of rotation is 1.95. The length of the cuvette is 190.08 mm.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 2

TOPIC: Analysis of drugs from the group of alicyclic antibiotics.

PURPOSE: To master the methods of analysis of medicinal products from the group of alicyclic antibiotics, as well as their semi-synthetic analogues.

3.1.T o study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of antibiotics of the alicyclic series and their semi- & synthetic derivatives.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the group of antibiotics of the alicyclic series and their semi- & synthetic derivatives using physical, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of antibiotics of the alicyclic series and their semi- & synthetic derivatives, based on their physicochemical properties.

3.9.Learn and follow the rules of safe work in a chemical laboratory.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. Antibiotics. General characteristics. Names and synonyms of antibiotics. Development of antibiotic chemistry.
2. Antibiotics as medicinal substances. Sources of receipt. Chemical structure. Nomenclature, physicochemical properties of medicinal substances from the group of antibiotics.

3. Methods of obtaining antibiotics and ways of creating new antibiotics (biological screening, modification of the "leader structure" (chemical transformation), directed synthesis).

4. Describe methods of analysis: biological, chemical and physicochemical methods. The concept of a unit of antibiotic activity.

5. Classification of antibioticsaccording to the method of production, spectrum, nature and mechanism of antimicrobial action, chemical.

6. To justify the need to determine abnormal toxicity, sterility, pyrogenicity, bacterial endotoxins and depressant substances in antibiotics.

7. Antibiotics of alicyclic structure:

7.1. Tetracycline, oxytetracycline. Structure, nomenclature, physical and chemical properties, analysis, storage, application.

7.2. Semi-synthetic analogues of alicyclic antibiotics: metacycline (rondomycin), doxycycline (vibramycin). Quality requirements. Methods of analysis, application, relationship between structure and biological action.

8. The relationship between chemical structure and biological action on the example of drugs from the group of alicyclic antibiotics.

9. Justify the storage conditions of the researched medicinal products based on their structure and chemical properties.

10. The main dosage forms created on the basis of the investigated medicinal substances. Medicinal form, dosage.

4.3. Work out the test tasks:

#

1) Antibiotics are ...:

A. chemical compounds of biological origin that have a harmful or harmful effect on microorganisms and macro-organisms

B. substances-inhibitors of RNA or DNA synthesis, belonging to chemotherapeutic antibacterial agents

C. substances produced by microorganisms, higher plants, animal tissues in the process of their vital activity and modification products of these substances, which selectively inhibit the growth of pathogenic microorganisms, lower fungi, some viruses and cells of malignant formations, while not having a toxic effect on the macroorganism

D. biologically active substances released from official medicinal plant raw materials

E. compounds of the steroid structure, which have a pronounced cardiotonic effect

#

2) Choose the correct definition of the concept of "unit of action" (UA) of antibiotics:

A. for unit of action of an antibiotic, the minimum amount of antibiotic is taken, which inhibits the development of the test microorganism in a certain volume of the nutrient medium

B. for UA of an antibiotic, the minimum amount of a standard test microorganism is taken, the growth of which is delayed when it is exposed to 1 mg or 1 ml of the appropriate antibiotic

C. for UA take the minimum amount of antibiotic that inhibits the development of test microorganisms on an area of 1 cm2

D. for UA take the minimum amount of antibiotic that gives a positive identification reaction

#

3) The priority of the discovery of antibiotics belongs to:

A. Fleming

B. Yermolyeva

C. Ehrlich

D. Romanovsky

E. Mendeleev

#

4) If it is necessary to identify antibiotic substances using spectroscopy in the UV or IR range of the spectrum, the control and analytical laboratory must have:

A. samples of drug substances of similar pharmacological action

B. all medicines containing this substance

C. samples of drug substances of a similar chemical structure

D. pharmacopoeial standard sample of the drug substance

E. permission of the manufacturer of the investigated substance to conduct the experiment

#

5) Indicate the methods of determining the biological activity of antibiotics and their medicinal products, according to the SPhU:

A. immunoenzymatic

B. diffusion in agar

C. turbidimetric

D. physical and chemical

E. radiometric

#

6) The reaction of antibiotics of the tetracycline series with a solution of ferric oxide chloride is due to the presence in their structure of:

A. phenolic hydroxyl
B. urea group
C. of the dimethylamine residue
D. methyl group
E. carbonyl group

#

7) The mechanism of antimicrobial action of antibiotics of the tetracycline series is based on:

A. disruption of protein synthesis at the level of ribosomes
B. disruption of cell wall synthesis
C. violations of the permeability of the cytoplasmic membrane
D. RNA synthesis disorders
E. protein denaturation of the microorganism

#

8) What reagent does a pharmacist-analyst use to determine water in tetracycline antibiotics?

A. a solution of sulfur dioxide, iodine and pyridine in methanol (Fisher's reagent)
B. anhydrous copper sulfate
C. a mixture of glacial acetic acid and acetic anhydride (1:2)
D. calcined chloride
E. alcoholic solution of picric acid

#

9) Indicate which of the antibiotics belongs to the derivatives of the alicyclic series?

A. vibramycin
B. cefazolin sodium salt
C. benzylpenicillin K and Na salts
D. carfecillin sodium salt
E. Bruneomycin

#

10) Indicate which functional group in the molecule of tetracycline antibiotics causes the formation of azo dyes during azo coupling with diazonium salts?

A. phenolic hydroxyl
B. dimethylamine
C. alcohol hydroxyl
D. carboxamide group
E. methyl group

#

11) Tetracycline is an antibiotic according to its chemical structure:

A. aromatic series
B. alicyclic series
C. aliphatic series
D. heterocyclic series
E. glycosidic structure

#

12) Specify the reagent with which the reaction is absent in the express analysis of drugs of the tetracycline series:
A. sodium nitroprusside
B. *p*-dimethylaminobenzaldehyde
C. Nessler's reagent
D. diazoreactive
E. potassium acetate

#

13) The activity of tetracycline antibiotics is determined using a biological method. At the same time, they use:
A. agar diffusion method
B. experiments on rats
C. experiments on rabbits
D. hanging drop method
E. experiments on frogs

#

14) Which of the following drugs belongs to the tetracycline group of antibiotics?
A. doxycycline hyclate
B. levomycetin succinate is soluble
C. cephaloridine
D. cephapirin
E. streptomycin

#

15) A chemist analyzes doxycycline hyclate using a reaction with concentrated sulfuric acid. What color does the solution acquire after carrying out this reaction?
A. blue
B. green
C. red
D. yellow
E. black

#

16) The structure of tetracycline is based on a partially hydrogenated nucleus:

A. naphthacene
B. anthracene
C. phenanthrene
D. naphthalene
E. acridine

#

17) Methacycline hydrochloride interacts with iron (III) chloride in an alcoholic medium. What analytical effect will be observed?
A. white precipitate
B. brown color
C. green sediment
D. yellow sediment
E. blue color

#

18) In the chemical analytical laboratory, the pharmacist-analyst conducts the analysis of tetracycline hydrochloride. By which method, according to the SPhU, is this substance quantitatively determined?
A. liquid chromatography
B. alkalimetry
C. gas chromatography
D. acidimetry
E. bromatometry

#

19) At a pharmaceutical enterprise, a pharmacist conducts an analysis of methacycline hydrochloride. What compound is formed as a result of the reaction of this substance with concentrated sulfuric acid?
A. isotetracycline
B. methacycline base
C. anhydro derivative of methacycline
D. azo dye
E. maltol

#

20) In the quantitative determination of tetracycline by the photoelectrocolorimetric method, the reaction is used:
A. azo compound
B. with potassium bromide solution
C. formation of iron (III) hydroxamate
D. with Fehling's reagent

#

21) In the quantitative determination of tetracycline by the photoelectrocolorimetric method, the reaction is used:

A. with iron (III) chloride

B. with sodium edetate solution

C. formation of iron (III) hydroxamate

D. with Fehling's reagent

E. with Mayer's reagent

#

22) Select a method that cannot quantify tetracycline hydrochloride:

A. acidimetry

B. non-aqueous titration

C. biological method (diffusion in agar)

D. photoelectrocolorimeter

E. fluorimeter

#

23) To identify tetracycline, the reaction of the formation of colored anhydroderivatives under the action of concentrated sulfuric acid is used, which is based on the ability of the drug to:

A. dehydration

B. restoration

C. complex formation

D. condensation

E. esterification

#

24) The presence of dihydrate phenolic and enol hydroxyls in the oxytetracycline molecule is confirmed by the reaction:

A. with iron (III) chloride solution

B. with Dragendorff's reagent

C. with sodium nitroprusside

D. with Nessler's reagent

E. with sodium nitrite

#

25) Semi-synthetic tetracyclines include:

A. oxytetracycline

B. methacycline

C. tetracycline

D. gramicidin

E. oxacillin

#

26) Specify a set of reagents that allows you to distinguish antibiotics of the tetracycline series from each other:

A. concentrated sulfuric acid and Ehrlich's reagent (p-dimethylaminobenzaldehyde in dilute hydrochloric acid)

B. sodium nitroprusside, sodium hydroxide

C. Nessler's reagent

D. sodium nitrite, hydrochloric acid

E. potassium permanganate in the presence of conc. sulfuric acid

#

27) State the reason why the use of Ehrlich's reagent (p-dimethylaminobenzaldehyde in dilute hydrochloric acid) is limited for distinguishing tetracycline antibiotics from each other:

A. slow course of reaction (6-8 hours)

B. unstable staining of the reaction product over time

C. violent reaction flow (possible explosion)

D. all tetracyclines give the same analytical effect of the reaction

E. Ehrlich's reagent decomposes quickly

#

28) Indicate the physico-chemical method by which, according to the requirements of the SPhU, doxycycline hyclate is identified:

A. thin layer chromatography

B. HPLC

C. refractometry

D. UV spectrophotometry

E. fluorimetry

#

29) Specify the industrial method of obtaining natural tetracyclines:

A. microbiological method (deep fermentation of actinomycetes Streptomyces aureofaciens (rimosus))

B. chemical synthesis

C. allocation from plant raw materials

D. extraction from animal tissues

#

30) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, quantitative determination of tetracycline pharmacopoeial drugs is carried out:

A. liquid chromatography

B. acidimetry in non-aqueous environments

C. UV spectrophotometry

D. photoelectrocolorimetry (by reaction with a solution of iron (III) chloride)
E. thin layer chromatography

#

31) Indicate the reagent with which, in accordance with the requirements of the Federal Drug Administration, the identification of tetracycline pharmacopoeial drugs is carried out:

A. sulfuric acid
B. sodium hydroxide solution
C. iron (III) chloride solution
D. sodium nitroprusside solution
E. diazonium salts

#

32) Specify the functional group in the structure of natural tetracycline, which is responsible for the manifestation of the main properties:

A. dimethylamino group
B. phenolic hydroxyl
C. enol hydroxyl
D. methyl group
E. keto group

#

33) Specify the functional groups in the structure of natural tetracycline responsible for the manifestation of acidic properties:

A. dimethylamino group
B. phenolic hydroxyl and enol hydroxyls
C. methyl group
D. keto group
E. carboxyl group

#

34) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, concomitant impurities in pharmacopoeial preparations of tetracycline are determined:

A. liquid chromatography
B. polarimetry
C. UV spectrophotometry
D. potentiometry
E. thin layer chromatography

4.4. Situational tasks:

1) When assessing the quality of the doxycycline hydrochloride substance in samples of several series, the appearance did not meet the requirements of the Ministry of Internal Affairs under the "Description" section - the powder was wet and yellow-brown in color. What processes could cause these changes? Name these products.

2) For the quantitative analysis of the substance oxytetracycline hydrochloride, the method of acid-base titration in non-aqueous solvents can be recommended. Based on the chemical structure and acid-base properties of the proposed drug, give a justification for the use of this method in quality assessment:

a) According to the structure, characterize the acid-base properties;

b) Give a rationale for choosing a protogenic solvent for the quantitative determination of the drug in non-aqueous solvents. Write the reaction equation, specify the titration conditions;

c) Specify the additional reagent that is added during the titration of the drug. Write the reaction diagram.

3) When analyzing the substance of semi-synthetic tetracyclines, the analyst conducted a reaction to form anhydro derivatives. Name the reagent that he needs to use for this.

4) Determine the essence of photocolorimetric, polarimetric analysis in the quantitative assessment of drugs of this group?

5) Determine the interrelationship of sources and methods of obtaining with the problems of the research of medicinal substances (the content of initial, intermediate and related products, the formation of quality indicators).

4.5. Tasks:

1) Determine the quality of one of the tetracycline derivatives by specific rotation, if the angle of rotation of a solution containing 0.25 g of the analyzed sample in 25 ml of a 0.01 M hydrochloric acid solution at a cuvette length of 10 cm is -2.680. Weight loss during drying is 2.0%. Specific rotation in terms of dry matter of tetracycline hydrochloride from – 239^{o} to – 258^{o}; for tetracycline from -265^{o} to -275^{o}.

2) Calculate the approximate volume of the titrant - 0.1 mol/l perchloric acid solution (Kp = 0.9803) required for the titration of a weight of tetracycline hydrochloride weighing 0.5504 g. 1 ml of a 0.1 M perchloric acid solution corresponds to 0.04809 g of tetracycline g / x, which should be at least 99.0% in the preparation.

3) Calculate the specific absorption coefficient ($A_{1\,см}^{1\%}$) of tetracycline, if 0.05000 g of the drug was taken, dissolved in 4 ml of 0.01 M hydrochloric acid solution in a 250 ml volumetric flask, brought to the mark with water, mixed. 5 ml of this solution was added to a volumetric flask with a volume of 50 ml, brought to the

mark with water, mixed. The optical density (Ax) was determined at a wavelength of 380 nm in a cuvette with a layer thickness of 10 mm. It is equal to 0.42. The concentration of tetracycline in the drug is 98.82%.

4) Calculate the percentage concentration (C%) of a solution of tetracycline hydrochloride, if you take 0.05024 g of the drug (exactly weighed), dissolve it in 2 ml of a 0.01 M solution of hydrochloric acid in a 250 ml volumetric flask, bring it up to the mark with water, and mix. 10 ml of this solution was added to a volumetric flask with a volume of 100 ml, brought to the mark with water, mixed. The optical density (Ax) was determined at a wavelength of 380 nm in a cuvette with a layer thickness of 1 cm, it is equal to 0.78. Specific absorption index ($A_{1\,см}^{1\%}$) is equal to 389.

5) Calculate the percentage content of tetracycline (M.M. = 444.40), if 11.0 ml of 0.01 M perchloric acid solution (Kp = 0.9904) was spent on the titration of 0.0543 g of the substance. Loss in mass during drying is 8%.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 3

TOPIC: Analysis of drugs from the group of heterocyclic antibiotics.

2. PURPOSE: To master the methods of analysis of medicinal products from the group of heterocyclic antibiotics, as well as their semi-synthetic analogues

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of antibiotics of the heterocyclic series and their semi- & synthetic derivatives.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the group of antibiotics of the heterocyclic series and their semi- & synthetic derivatives using physical, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of antibiotics of the heterocyclic series and their semi- & synthetic derivatives, based on their physicochemical properties.

3.9.Learn and follow the rules of safe work in a chemical laboratory.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. Antibiotics of the heterocyclic series. β-lactam antibiotics. General characteristics. Classification, their physical and chemical properties. Relationship "structure-action" in a row β-lactam antibiotics.

2. Penicillins (penems). General characteristics. Pharmacopoeia drugs: benzylpenicillin sodium (potassium) salt. Phenoxymethylpenicillin. Features of the structure, properties, methods of analysis: general and separate.

3. Use of physicochemical properties for identification and quantification of penicillins (penems). Transformation reactions that prove their structure.

4. To justify the need to determine the transparency, color, acidity, loss in mass during drying, thermal stability, passability through the needle of a syringe of poorly water-soluble drugs in penicillin preparations.

5. Conditions and chemistry of the reactions occurring during the quantitative determination of penicillin by the iodometric method. To justify the necessity of setting up a control experiment, to explain what is its peculiarity. Other methods of quantitative determination of antibiotics of this group. Methods of quantitative assessment of the content of antibiotics in the drug. Formulas for calculating the percentage content of the amount of penicillins and the number of units.

6. Long-acting penicillin preparations. Bicillin, benzylpenicillin, novocaine salt, etc. Their properties, analysis and application in medicine.

7. Semi-synthetic penicillins, obtained on the basis of 6-aminopenicilanic acid. Ampicillin, amoxicillin, oxacillin sodium salt, Azlocillin sodium salt and others. The need to create this group of antibiotics. Methods of analysis, nature of action (unlike natural penicillins).

8. Cephemes (cephalosporins). General characteristics, chemical structure, comparative resistance to chemical reagents and enzymes. Modification of the "leader structure" of cephalosporin C, partial and directed synthesis based on 7-ACA and 7-ADCA.

9. Cepheme antibiotics are derivatives of 7-aminocephalosporanic acid (7-ACA): sodium salts of cefotaxime and cefoxitin, cephalothin and others. Properties, analysis, stability and storage.

10. Cepheme antibiotics are derivatives of 7-aminodesacetoxycephalosporanic acid (7-ADCA): cefazolin, cephalexin, ceftriaxone sodium salt and others. Properties, analysis, stability and storage.

11. Lincosamide antibiotics. General characteristics, structural features, physical and chemical properties. Lincomycin hydrochloride. Methods of analysis. Application, mechanism of action and storage.

12. Justify the storage conditions of the researched medicinal products based on their structure and chemical properties.

13. The main dosage forms created on the basis of the investigated medicinal substances. Medicinal form, dosage. Application.

4.3. Work out the test tasks:

#

1) The control and analytical laboratory received a medicinal substance - benzylpenicillin sodium salt for analysis. Indicate how, according to the SPhU, the pharmacist-analyst identifies this drug?

A. optical density is measured
B. the infrared absorption spectrum is determined
C. the pH of the solution is determined
D. reaction with Fehling's reagent
E. the specific rotation is determined

#

2) The pharmacist-analyst proves the presence of penems of the β-lactam cycle in the structure of antibiotics using the formation reaction:

A. metal hydroxamate
B. indophenol
C. azomethine dye
D. thalleiochina
E. murexide

#

3) What is the basis of the chemical structure of penicillins:

A. 6-APK (6-aminopenicillanic acid)
B. 7-APK (7-aminopenicillanic acid)
C. 8-APK (8-aminopenicillanic acid)
D. 5-APK (5-aminopenicillanic acid)
E. 4-APK (4-aminopenicillanic acid)

#

4) What causes the prolonged effect of some penicillins (bicillin, benzylpenicillin, novocaine salt, etc.)?

A. the creation of drug depots in muscle tissue due to their poor solubility
B. by increasing the dose of the injected antibiotic
C. resistance to the action of penicillinase
D. acid resistance of drugs
E. low solubility of the substance

#

5) Indicate which of the listed drugs, due to the presence of a β-lactam cycle in its structure, gives a positive reaction with a solution of hydroxylamine hydrochloride in the presence of sodium hydroxide and the subsequent addition of a solution of iron (III) chloride:

A. phenoxymethylpenicillin

B. monomycin sulfate
C. streptomycin sulfate
D. tetracycline hydrochloride

#

6) The instability of penicillins is due, first of all, to the presence in their structure of:

A. β-lactam cycle
B. urea group
C. carboxyl group
D. methyl groups
E. thiazolidine cycle

#

7) The pharmacist-analyst of the pharmacy performs the identification of oxacillin sodium salt. As a reagent, he uses a solution of hydroxylamine hydrochloric acid in the presence of a solution of sodium hydroxide and a solution of copper nitrate. What structural fragment of the drug molecule is detected using these reagents?

A. β-lactam cycle
B. thiazolidine cycle
C. isoxazole cycle
D. phenyl radical
E. urea group

#

8) Specify which of the antibiotics belongs to penem derivatives?

A. Azlocillin sodium salt
B. chloramphenicol stearate
C. streptomycin sulfate
D. azithromycin
E. Synthomycin

#

9) According to the mechanism of antimicrobial action, penems belong to antibiotics that violate:

A. synthesis of the cell wall of a microbial cell
B. permeability of the cytoplasmic membrane of a microbial cell
C. RNA synthesis of a microbial cell
D. protein synthesis at the level of ribosomes of a microbial cell
E. DNA synthesis of a microbial cell

#

10) Which of the following medicines belongs to natural penicillins?

A. ampicillin sodium salt
B. amoxicillin trihydrate
C. carbenicillin disodium salt
D. oxacillin sodium salt

E. phenoxymethylpenicillin

#

11) At a pharmaceutical enterprise, a pharmacist-analyst conducts an analysis of benzylpenicillin. Which reagents can be used to identify this substance?

A. sulfuric acid
B. Nessler's reagent
C. hydrochloric acid
D. Markey's reagent
E. sodium hydroxide

#

12) A control and analytical laboratory specialist confirms the presence of a sodium cation in the preparation "Benzylpenicillin sodium salt" by reaction with a solution of potassium pyroantimonate by the appearance of:

A. green sediment
B. yellow sediment
C. blue sediment
D. white sediment
E. purple sediment

#

13) An analytical chemist conducts an identification reaction for amoxicillin with formaldehyde in the presence of sulfuric acid. What color of the solution will be observed?

A. dark yellow
B. red
C. yellow-green
D. blue
E. red-brown

#

14) Specify the group of microorganisms on which natural penicillins have a bactericidal effect:

A. gram positive
B. gram negative
C. brucelli
D. salmonella
E. Shigella

#

15) According to the nature of antimicrobial action, penicillins belong to antibiotics:

A. have a bacteriostatic effect (bacteria are alive, but unable to reproduce)
B. have a bactericidal effect (bacteria are killed, but physically continue to be present in the environment)
C. exhibit a bacteriolytic effect (bacteria are killed, and bacterial cell walls are destroyed)

#

16) When identifying lincomycin hydrochloride, the analyst performed a reaction on the ionic composition. What ions will have a positive reaction?

A. SO_4^{2-}

B. Cl-

C. Na^+

D. Ca^{2+}

E. Hg^{2+}

#

17) The pyrogenicity test is not performed:

A. for phenoxymethylpenicillin

B. for kanamycin sulfate

C. for streptomycin sulfate

D. for benzylpenicillin sodium salt

E. for carbenicillin disodium salt

#

18) Benzylpenicillin potassium salt in aqueous solutions is incompatible:

A. with ascorbic acid

B. with novocaine

C. with sodium chloride

D. with sodium bicarbonate

#

19) Injectable solutions are not subjected to thermal sterilization:

A. benzylpenicillin sodium salt

B. glucose

C. ascorbic acid

#

20) State the reaction by which phenoxymethylpenicillin cannot be identified:

A. diazotization reaction

B. alloy with caustic alkalis followed by the addition of lead acetate

C. reaction with Markey's reagent

D. hydroxam sample

E. reaction with chromotropic acid

#

21) Quantitative determination of the amount of penicillins in the potassium salt of benzylpenicillin is carried out by the method:

A. iodometry

B. UV spectrophotometry

C. neutralization

D. photocolorimetry

E. acidimetry

#

22) What product of hydrolysis of phenoxymethylpenicillin when interacting with Markey's reagent forms an aurine dye:

A. phenol
B. formaldehyde
C. glycolic acid
D. carbon dioxide
E. ammonia

#

23) Quantitative determination of ampicillin trihydrate is carried out by the formol titration method, as it contains in its structure:

A. β-lactam cycle
B. amino acid residue
C. organically bound sulfur
D. aromatic ring

#

24) Organically bound sulfur in penicillin preparations after alloying with caustic alkalis is determined by the reaction:

A. with ammonium oxalate solution
B. with sodium nitroprusside solution
C. with sodium sulfate solution
D. with barium chloride solution
E. with potassium permanganate solution

#

25) The hydroxam test allows you to confirm the presence of benzylpenicillin in the molecule:

A. phenyl radical
B. β-Lactam cycle
C. thiazolidine cycle
D. methyl groups
E. carboxyl group

#

26) Which penicillin drug contains an amino acid residue in its structure:

A. benzylpenicillin
B. oxacillin
C. ampicillin
D. phenoxymethylpenicillin
E. chloramphenicol

#

27) Natural penicillins in industry are obtained by the method of microbiological synthesis. An obligatory component is a precursor substance, the chemical structure of which is

similar to the corresponding radical of the antibiotic in position 6. In the production of benzylpenicillin, the precursor serves as:

A. beta-dimethylcysteine
B. valine
C. phenylacetic acid
D. alpha-aminoadipic acid
E. aminoacetic acid

#

28) Natural penicillins in industry are obtained by the method of microbiological synthesis. An obligatory component is a precursor substance, the chemical structure of which is similar to the corresponding radical of the antibiotic in position 6. In the production of phenoxymethylpenicillin, the precursor serves as:

A. beta-dimethylcysteine
B. valine
C. phenoxyacetic acid
D. alpha-aminoadipic acid
E. aminoacetic acid

#

29) A chemist-analyst of the laboratory performs quantitative determination of the amount of penicillins in benzylpenicillin sodium salt using the iodometric method. what indicator does it use?

A. starch
B. phenolphthalein
C. potassium chromate
D. methyl orange
E. methyl red

#

30) Which of the indicated penicillins can be identified by the reaction with ninhydrin?

A. ampicillin
B. benzylpenicillin
C. phenoxymethylpenicillin
D. oxacillin
E. carbenicillin

#

31) Indicate which of the indicated penicillins contains the isoxazole cycle:

A. oxacillin
B. ampicillin
C. phenoxymethylpenicillin
D. benzylpenicillin
E. carfecillin

#

32) Specify the starting compound for semi-synthetic penicillins:

A. 6-aminopenicillanic acid

B. clavulanic acid

C. penicilloic acid

D. penaldic acid

E. 7-aminocephalosporanic acid

#

33) A specialist confirms the presence of a sodium cation in ampicillin sodium salt by the appearance of a white precipitate with the solution:

A. potassium pyroantimonate

B. potassium dichromate

C. potassium permanganate

D. potassium nitrate

E. potassium chloride

#

34) Semi-synthetic penicillins include:

A. ampicillin

B. 6-aminopenicillanic acid

C. benzylpenicillin

D. phenoxymethylpenicillin

E. clavulanic acid

#

35) Specify the reaction by which the novocaine salt of benzylpenicillin can be identified:

A. detection of organically bound sulfur

B. on the primary aromatic amino group

C. with chromotropic acid

D. with sodium acetate

#

36) The β-lactamide group includes:

A. kanamycin sulfate

B. Azlocillin sodium salt

C. amikacin sulfate

D. gentamicin sulfate

E. chloramphenicol

#

37) Phenoxymethylpenicillin can be distinguished from benzylpenicillin sodium salt by:

A. reactions with chromotropic acid

B. appearance

C. solubility in water
D. hydroxam test
E. detection reactions of organically bound sulfur

#

38) All methods can be used for quantitative determination of oxacillin sodium salt, except:
A. neutralization
B. UV spectrophotometry
C. photoelectrocolorimetry (after the formation of iron (III) hydroxamate)
D. complexonometry
E. liquid chromatography

#

39) A β-lactam antibiotic that gives a ninhydrin test:
A. tetracycline
B. amoxicillin
C. streptocide
D. rifampicin
E. carfecillin

#

40) Natural penicillins include:
A. benzylpenicillin sodium salt
B. phenoxymethylpenicillin
C. ampicillin
D. oxacillin
E. carbenicillin sodium salt

#

41) The antibacterial activity of penicillins is due to:
A. the presence of a thiazolidine ring
B. the presence of a β-lactam cycle
C. spatial configuration of molecules
D. by the presence of two methyl groups
E. a sulfur heteroatom

#

42) Which of the listed drugs is acid-resistant?
A. phenoxymethylpenicillin
B. benzylpenicillin sodium salt
C. benzylpenicillin novocaine salt
D. benzylpenicillin potassium salt

#

43) Which of the drugs listed below is slightly soluble in water?

A. carfecillin sodium salt
B. benzylpenicillin novocaine salt
C. benzylpenicillin potassium salt
D. benzylpenicillin sodium salt

#

44) Molecules of penicillins contain asymmetric carbon atoms:
A. in positions 2,3,5
B. in provisions 5,6
C. in provisions 3,5,6
D. in provisions 2,3,6
E. in positions 3,5,7

#

45) Which reaction is not characteristic of ampicillin?
A. maltol test
B. hydroxam test
C. with Marqui's reagent
D. with ninhydrin
E. with chromotropic acid

#

46) Under the action of the penicillinase enzyme:
A. the thiizolidine cycle is destroyed
B. the β-lactam cycle is destroyed
C. the radical in position 6 is cleaved off
D. the radical in position 2 is cleaved off
E. the radical in position 3 is cleaved off

#

47) What are the properties of penicillins?
A. the main ones
B. acidic
C. amphoteric

#

48) The pharmacist-analyst of the pharmacy performs the identification of oxacillin sodium salt. As reagents, he uses a solution of hydroxylamine hydrochloric acid in the presence of a solution of sodium hydroxide and a solution of copper nitrate. What structural fragment of the drug molecule is identified using these reagents?
A. β-lactam cycle
B. thiazolidine cycle
C. isoxazole cycle
D. phenyl radical
E. carboxyl group

#

49) Semi-synthetic penicillin is not:

A. oxacillin sodium salt
B. carfecillin sodium salt
C. Azlocillin sodium salt
D. phenoxymethylpenicillin
E. ampicillin

#

50) For the quantitative determination of benzylpenicillin sodium salt, the method is not used:

A. complexonometry
B. iodometry
C. microbiological
D. liquid chromatography

#

51) Indicate the method of quantitative determination by which the SPhU recommends to quantitatively determine natural (benzylpenicillin sodium salt) and semi-synthetic penicillins (ampicillin, amoxicillin and their salts):

A. liquid chromatography
B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography

#

52) Indicate the reagent that, in accordance with the requirements of the SPhU, identifies natural (benzylpenicillin sodium salt) and semi-synthetic penicillins (ampicillin, amoxicillin):

A. Markey's reagent
B. Nessler's reagent
C. solution of hydroxylamine hydrochloric acid, iron (III) sulfate
D. sulfuric acid
E. copper (II) sulfate solution

#

53) Specify the method by which SPhU recommends determining concomitant impurities in natural (benzylpenicillin sodium salt) and semi-synthetic penicillins (ampicillin, amoxicillin):

A. liquid chromatography
B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography

#

54) Specify which heterocycle is the basis of lincosamide antibiotics:

A. **pyrrolidine (tetrahydropyrrol**)
B. pyrazole
C. thiophene
D. pyrimidine
E. imidazole

#

55) Specify the group of microorganisms on which lincosamide antibiotics have a bacteriostatic effect:

A. gram positive
B. gram negative
C. brucelli
D. salmonella
E. Shigella

#

56) Specify the method of quantitative determination by which the SPhU recommends quantifying lincomycin hydrochloride:

A. gas chromatography
B. liquid chromatography
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography

#

57) Indicate the set of reagents that, in accordance with the requirements of the Federal Drug Administration, identify lincomycin hydrochloride:

A. hydrochloric acid, sodium carbonate, sodium nitroprusside
B. hydrochloric acid, sodium nitrite, alkaline β-naphthol solution
C. nitric acid, alcoholic solution of potassium hydroxide
D. solution of hydroxylamine hydrochloric acid, iron (III) sulfate
E. bromine water, ammonia solution

#

58) What is the basis of the chemical structure of cephalosporins:

A. 7-ACA (7-aminocephalosporanic acid)
B. 8-ACA (8-aminocephalosporanic acid)
C. 6-ACA (6-aminocephalosporanic acid)
D. 5-ACA (5-aminocephalosporanic acid)
E. 4-ACA (4-aminocephalosporanic acid)

#

59) Indicate which of the listed antibiotics is a derivative of 7-aminocephalosporanic acid (7-ADCA)?

A. cephalexin

B. methacycline hydrochloride
C. griseofulvin
D. ampicillin trihydrate
E. streptomycin sulfate

#

60) In a chemical analytical laboratory, an analyst conducts an analysis of the antibiotic cephalothin. According to the chemical structure, this substance can be classified as an antibiotic:
A. aromatic series
B. alicyclic series
C. aliphatic series
D. polypeptide antibiotics
E. heterocyclic series

#

61) A chemist identifies cephalosporins with formaldehyde in the presence of sulfuric acid. What color does ceftriaxone sodium salt give?
A. greenish yellow
B. blue
C. light yellow
D. bright yellow
E. black

#

62) Cephalexin gives a positive ninhydrin test because it contains the residue in the molecule:
A. phenoxyacetic acid
B. phenylaminoacetic acid
C. phenylacetic acid
D. dimethoxyphenylacetic acid

#

63) The structural basis of cephalosporins is:
A. 6-membered thiazolidine and β-lactam ring
B. thiazine and lactam cycle
C. dihydrothiazine and β-lactam cycle
D. trihydrothiazine and lactam cycle
E. thiazine and lactone cycle

#

64) The difference between cephalosporins and penicillins:
A. effective against gram-negative and gram-positive microorganisms
B. effective against streptococci
C. the β-lactam ring is absent in the structure

#

65) As a result of hydrolytic cleavage of cephalothin, the following are formed:
A. 7-ACA
B. 6-APA
C. aminophenylacetamide
D. phenyl-2-acetic acid
E. acetic acid

#

66) Factors that determine the antibacterial activity of cephalosporins do not include:
A. the presence of a β-lactam cycle
B. the nature of the substitute in clause 6
C. inductive effect of the acyl substituent
D. the presence of a thiazolidine ring
E. steric effect of the molecule

#

67) As a result of hydrolytic cleavage of cephalexin, the following is formed:
A. 7-ACA
B. 7-ADCA
C. aminophenylacetamide
D. thienyl acetic acid
E. acetic acid

#

68) Cephalosporins are identified by the reaction of obtaining:
A. hydroxamate
B. maltol
C. nitro derivatives
D. iodine derivatives
E. murexide

#

69) The general method of quantitative determination of cephalosporins includes:
A. iodometry (back titration)
B. complexonometry
C. acidimetry
D. iodometry (direct titration)
E. acidimetry (substitute titration)

#

70) The β-lactamide group includes:
A. kanamycin sulfate
B. cephalexin
C. amikacin sulfate
D. gentamicin sulfate

E. chloramphenicol

#

71) Organically bound sulfur in cephalosporin antibiotics after alloying with caustic alkalis is determined by the reaction:

A. with ammonium oxalate solution
B. with sodium nitroprusside solution
C. with sodium sulfate solution
D. with potassium chloride solution
E. with potassium permanganate solution

#

72) The hydroxam test allows you to confirm the presence of cephalosporins in the molecule:

A. phenyl radical
B. β-lactam cycle
C. thiazolidine cycle
D. methyl groups
E. ethyl group

#

73) Indicate which of the indicated cephalosporins contains a furan residue:

A. cefuroxime
B. cefazolin
C. ceftriaxone
D. cefotaxime
E. cephalothin

#

74) Indicate which of the indicated cephalosporins contains heterocycles of pyridine and thiophene:

A. Cephaloridine
B. cefazolin
C. ceftriaxone
D. cefotaxime
E. cephalothin

#

75) In industry, the source for obtaining acyl derivatives of 7-ACA is:

A. cephalosporin C
B. clavulanic acid
C. aminoadipic acid
D. 7-ADCA
E. penicillins

#

76) In industry, the source for obtaining acyl derivatives of 7-ADCA is:

A. penicillins
B. cephalosporin C
C. clavulanic acid
D. aminoadipic acid
E. 7-ACA

#

77) A specialist confirms the presence of a sodium cation in ceftriaxone sodium salt by the formation of a white precipitate with a solution:

A. potassium pyroantimonate
B. potassium dichromate
C. potassium permanganate
D. potassium nitrate
E. potassium chloride

#

78) Which of the indicated cephalosporins can be identified by reaction with ninhydrin?

A. cephalexin
B. ceftriaxone
C. cephalothin
D. Cephapirin
E. cefadroxil

#

79) The pharmacist-analyst proves the presence of β-lactam cycle antibiotics in the structure of the cephalosporin series by means of the formation reaction:

A. metal hydroxamates
B. indophenol
C. azomethine dye
D. thalleiochina
E. murexide

#

80) Indicate which of the listed drugs, due to the presence of a β-lactam cycle in its structure, gives a positive reaction with a solution of hydroxylamine hydrochloride in the presence of sodium hydroxide and the subsequent addition of a solution of iron (III) chloride:

A. cephalothin
B. monomycin sulfate
C. streptomycin sulfate
D. tetracycline hydrochloride
E. papaverine hydrochloride

#

81) The instability of cephalosporins is caused, first of all, by the presence in their structure of:

A.β-lactam cycle
B. urea group
C. carboxyl group
D. methyl groups
E. thiazolidine cycle

#

82) The pharmacist-analyst of the pharmacy conducts the identification of ceftriaxone sodium salt. He uses a solution of hydroxylamine hydrochloric acid in the presence of a solution of sodium hydroxide and a solution of copper nitrate as reagents. What structural fragment of the drug molecule is detected using these reagents?

A. β-lactam cycle
B. thiazolidine cycle
C. isoxazole cycle
D. phenyl radical
E. urea group

#

83) Specify which of the antibiotics belongs to cephem derivatives?

A. azlocillin sodium salt
B. chloramphenicol stearate
C. cephalothin
D. azithromycin
E. synthomycin

#

84) Indicate which of the antibiotics belongs to the derivatives of 7-aminocephalosporanic acid (7-ACA):

A.cefotaxime
B. chloramphenicol stearate
C. cephalexin
D. azithromycin
E. Synthomycin

#

85) Indicate which of the antibiotics belongs to the derivatives of 7-aminodesacetoxycephalosporanic acid (7-ADCA):

A.cephalexin
B. cefotaxime
C. chloramphenicol stearate
D. azithromycin
E. Synthomycin

#

86) A control and analytical laboratory specialist confirms the presence of a sodium cation in the preparation "Ceftriaxone sodium salt" by reaction with a solution of potassium pyroantimonate by the appearance of:

A. green sediment
B. yellow sediment
C. blue sediment
D. white sediment
E. purple sediment

4.4. Situational tasks:

1) According to the chemical properties, explain the choice of the method of iodometric quantitative determination of the amount of penicillins:

a) Consider the chemical structure and properties of medicinal products and explain their ability to interact with iodine solution in an alkaline environment;

b) State the reactions of quantitative iodometric determination of drugs;

c) Give the formula for calculating the content of medicinal substances in preparations.

2) Give the reaction equation for the quantitative determination of the amount of penicillins in benzylpenicillin sodium salt. Explain the peculiarity of performing a control experiment. Using the reference literature, find the value of the equivalent of a standard sample of the sodium salt of benzylpenicillin per 1 ml of a 0.02 N (0.01 M) iodine solution, if the temperature of the reaction medium is 13^0C, 18^0C, 20^0C, 25^0C, respectively.

3) Explain the necessity and peculiarities of conducting a control experiment when determining the amount of penicillins by the iodometric method.

4) Describe the method of formol titration of medicinal substances using the example of ampicillin. Why not use the classic method of neutralization for this drug? Give the reaction equations, the formula for calculating the quantitative content.

5) What structural features of natural penicillins determine their lability in relation to acids and bases? How are these features used to identify benzylpenicillin preparations?

6) Describe the group of semi-synthetic penicillins and name their main representatives. State the advantages of semi-synthetic penicillins compared to natural ones.

7) Provide a scheme for the synthesis of ampicillin, indicating the chemical names of starting substances, intermediate and final products; state its pharmacological action.

8) Describe the iodometric method of quantitative determination of the amount of penicillins using the example of phenoxymethylpenicillin. What factors affect the value of the equivalent? Give the reaction equations, the formula for calculating the quantitative content.

9) Describe the photoelectrocolorimetric method of quantitative determination of medicinal substances using the example of benzylpenicillin sodium salt (after carrying out the reaction of the formation of iron (III) hydroxamate).

10) Describe the spectrophotometric method of quantitative determination of medicinal substances using an examplenatural and semi-synthetic penicillins. Explain the need to add imidazole and mercury(II) chloride.

11) Explain the features of the quantitative determination of dibenzylethylenediamine in benzathine of benzylpenicillin. Give the reaction equations, the formula for calculating the quantitative content.

12) What structural fragments of cephalexin determine its amphoteric properties?

13) Consider the regenerative properties of cephalexin and give a rationale for its interaction with Fehling's reagent. Specify the visible result and write the reaction schemes.

14) What structural features of cephalosporins determine their lability in relation to acids and bases? How are these features used to identify cephalosporin antibiotics?

15) Give the equation for the hydroxam test reaction for cephalothin.

16) Based on the chemical structure and properties of functional groups, justify the chemical properties of cephalosporin antibiotics (cephalexin, cephalothin). Confirm the answer with the chemistry of the reactions.

17) What, besides chemical, methods exist for determining the quality of antibiotics? Justify each of them, show the possibility of use for the purposes of qualitative and quantitative analysis and purity control. Give the concept of units of antibiotic activity (UA).

4.5. Tasks:

1) Calculate the specific rotation of benzylpenicillin potassium salt, if the angle of rotation of the 2% solution is +8.8o at a layer thickness of 15 cm.

2) Calculate the concentration of oxacillin sodium salt if the value of the specific rotation is $+185^{o}$, the thickness of the layer is 9 cm, the angle of rotation is $+1.7^{o}$.

3) 0.1086 g of phenoxymethylpenicillin was dissolved in 4 ml of 5% sodium bicarbonate solution in a volumetric flask with a capacity of 500 ml and the volume of the solution was brought up to the mark with water. The optical density of the obtained solution is 0.740 at a wavelength of 286 nm and a layer thickness of 10 mm. Calculate the specific absorbance of phenoxymethylpenicillin.

4) In benzylpenicillin sodium salt, the amount of penicillins is 94.5%. Calculate the volume of a 0.01 M iodine solution (Kn = 1.0000), which will be used for the titration of a measure of a medicinal substance of 0.0602 g. The measure was dissolved in water in a volumetric flask with a capacity of 100 ml, the volume of the solution was brought up to the mark with water and 5 ml of the resulting dilution was

taken for analysis. The value of the equivalent in g of a standard sample of benzylpenicillin at 20^0C is 0.0004055g. C = 1.000

5) In the quantitative determination of benzylpenicillin potassium salt by the iodometric method, 19.8 ml of 0.01 M sodium thiosulfate solution was used for the control experiment, and 14.3 ml of the same titrant was used for the titration of the tested drug (Kp = 0.9900). What is the percentage content of the drug, if T = 0.0004055 g / ml, a = 0.0503g, C = 1.045, dilution 1:20?

6) Give the reaction equation for quantitative determination of benzylpenicillin sodium salt by iodometry method. Calculate the percentage content of the drug, if a weight weighing 0.0612 g was dissolved and brought up to the mark with water in a 100 ml volumetric flask. 20 ml of 0.01 M iodine solution (Kp = 1.0100), the excess of which in the main experiment was titrated with 11.6 ml of 0.01 M sodium thiosulfate solution (Kp = 1.0200), in the control experiment - 19.4 ml of the same titrant. The titer of benzylpenicillin sodium salt (21ºC) is 0.0004000 g/ml. The moisture content of the analyzed substance is 0.5%. C = 1.00.

7) Give the reaction equation for the quantitative determination of benzylpenicillin potassium salt by the iodometric method. Calculate the content of the amount of penicillins (%) if a weight weighing 0.06024 g was dissolved and brought up to the mark with water in a volumetric flask with a capacity of 100.0 ml. 20 ml of a 0.01 M iodine solution (Кп = 0.9800) was added to a 5.0 ml aliquot, and 12.5 ml of a 0.01 M sodium thiosulfate solution (К п = 1 ,0100), in the control experiment - 19.2 ml of the same titrant. The moisture content of the analyzed sample is 0.8%. The titer of benzylpenicillin sodium salt (20^0C) is 0.0004055 g/ml. 1 mg of the sodium salt of benzylpenicillin corresponds to 1.045 mg of the potassium salt of benzylpenicillin.

8) Give the reaction equations for the quantitative determination of benzylpenicillin novocaine salt by iodometry. Calculate the content of the amount of penicillins (%) if the weight weighing 0.0809 g was dissolved and brought up to the mark with water in a volumetric flask with a volume of 200.0 ml. 20 ml of 0.01 M iodine solution (Kp = 1.0000) was added to a 10.0 ml aliquot, and 14.8 ml of 0.01 M sodium thiosulfate solution (Kp = 0, 9800), in the control experiment - 20.4 ml of the same titrant. The moisture content of the analyzed sample is 4.2%. The titer of benzylpenicillin sodium salt (15^0C) is 0.0004374 g/ml. 1 mg of sodium salt of benzylpenicillin corresponds to 1.652 mg of novocaine salt of benzylpenicillin.

9) Give the reaction equations for the quantitative determination of phenoxymethylpenicillin by the iodometric method. Calculate the content (%) if a weight weighing 0.0636 g was dissolved and brought up to the mark with water in a volumetric flask with a volume of 50.0 ml. 20 ml of 0.01 M iodine solution (K = 0.98) was added to a 2.5 ml aliquot, and 12.8 ml of 0.01 M sodium thiosulfate solution (Kp = 1, 0200), in the control experiment - 19.6 ml of the same titrant. The moisture content of

the analyzed sample is 1.5%. The titer of phenoxymethylpenicillin (18^0C) is 0.0004367 g/ml. C = 1.00.

10) Calculate the content of benzylpenicillin sodium salt in the vial in % and OD, if a weight of the drug weighing 0.0612 g was placed in a volumetric flask with a capacity of 100.0 ml, dissolved, and brought up to the mark with water. To an aliquot with a volume of 5.0 ml, 20 ml of a 0.01 M iodine solution (Kp = 1.0100) was added, and 11.6 ml of a 0.01 M sodium thiosulfate solution (Kp = 1, 0200). In the control experiment, 19.4 ml of the same titrant was used. The weight of the drug in the vial is 0.3605 mg. The titer of my substance (at the test temperature of 21^0C) is 0.0004000 g/ml. 1 unit corresponds to 0.0005988 mg of chemically pure sodium salt of benzylpenicillin.

11) Calculate the content of the potassium salt of benzylpenicillin in the vial in % and OD, if a weight weighing 0.06024 g was placed in a volumetric flask with a capacity of 100.0 ml, brought up to the mark with water. Along with other necessary reagents, 20.0 ml of 0.01 M iodine solution (Kp = 0.9800) was added to an aliquot with a volume of 5.0 ml. 12.5 ml of 0.01 M sodium thiosulfate solution (K n = 1.0200) was used to titrate the excess of the specified solution. 19.2 ml of the same titrant was used for the titration of the control experiment. The value of the equivalent of a standard sample of the sodium salt of benzylpenicillin at an experimental temperature of 20^0C is 0.0004055 g/ml. 1 mg of the standard sample of benzylpenicillin sodium salt corresponds to 1.045 mg of the amount of penicillins in terms of benzylpenicillin potassium salt. 1 unit corresponds to 0.0005988 mg of chemically pure sodium salt of benzylpenicillin. The weight of the drug in the vial is 0.3569 mg.

12) Calculate the % content of the amount of penicillins in benzylpenicillin of the potassium salt, if 19.8 ml of 0.01 mol / l sodium thiosulfate solution was used for the control experiment, and 14.3 ml of 0.01 mol / l thiosulfate solution was used for the titration of the weight of the drug weighing 0.0531g sodium (Kp = 0.9900).T = 0.0004055g/ml, conversion factor of benzylpenicillin potassium salt - 1.045, dilution 1:20.

13) Calculate the % content of the sum of penicillins in phenoxymethylpenicillin, if 20.1 ml of 0.01 M sodium thiosulfate solution was used for the control experiment, for titration of a weight of the drug weighing 0.0601 g - 13.1 ml of 0.01 mol / l sodium thiosulfate solution (Correction K -1.0100). T = 0.0004209g/ml, dilution 1:20. C = 1.00.

14) Calculate the volume of titrant - 0.01 M of sodium thiosulfate solution, spent on titration of a weight of benzylpenicillin sodium salt weighing 0.0531 g by the iodometric method. The volume of the control experiment is 20 ml, the percentage content of the amount of penicillins is 96.5%, K correction is 0.99. T = 0.0004055g/ml, dilution 1:20. C = 1.00.

15) Calculate the quantitative content and evaluate the quality of benzylpenicillin potassium salt, if a weight of the drug weighing 0.0487 g was dissolved in a 1000 ml volumetric flask in water. 10 ml of a solution containing imidazole and mercury chloride

was added to 2 ml of the obtained solution, after 25 min the optical density was measured. The average optical density at 325 nm is 0.616, the thickness of the cuvette is 10 mm. In parallel, the reaction was carried out with 2 ml of 0.005% standard solution of benzylpenicillin potassium salt, the measured average optical density under the same conditions was 0.623. The content of benzylpenicillin potassium salt in the preparation should be 96% and no more than 102%.

16) Calculate the weight of the weight of benzylpenicillin sodium salt, if 5.00 ml of 0.01 M sodium thiosulfate solution (K n = 1.0000) was used for the titration of an excess of 0.01 M iodine solution, the percentage content of the amount of penicillins is 99.0%, vol. the volume of the titrant in the control experiment is 20.00 ml; determination was carried out at a temperature of 21°C. T = 0.0004000, C = 1.0000, dilution 1:20.

17) Calculate the volume of 0.01 M sodium thiosulfate solution (K n = 1.000), which will be spent on the titration of an excess of 0.01 M iodine solution in the quantitative determination of benzylpenicillin potassium salt, if the weight of the drug is 0.0990, the content of the amount of penicillins is 100% , the volume of the titrant in the control experiment is 19.50 ml; determination was carried out at a temperature of 23°C T = 0.0004055, C = 1.045, dilution 1:20.

18) Calculate the percentage content of the amount of penicillins in phenoxymethylpenicillin, if the weight of the drug is 0.0685 g; volume of 0.01 M sodium thiosulfate solution (Kp = 1.0000) in the main experiment - 11.48 ml; in the control experiment - 19.80 ml; determination was carried out at a temperature of 22°C. T = 0.0004100, C = 1.0000, dilution 1:20.

19) Calculate the specific rotation and evaluate the quality of cephalothin sodium salt, if the average angle of rotation of a 5% aqueous solution of the drug is +6.54°. The length of the cuvette is 10 cm. The specific rotation should be from +124 to +134.

20) Calculate the % content of cephalothin sodium salt, if the angle of rotation of the aqueous solution of the drug is +13.08°, and the specific rotation of the drug is +130.08. The length of the cuvette is 1 dm.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 4

TOPIC: Analysis of drugs from the group of glycoside antibiotics.

PURPOSE: To master the methods of analysis of medicinal products from the group of glycoside antibiotics, as well as their semi-synthetic analogues.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of glycoside antibiotics and their semi- & synthetic derivatives.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the group of glycoside antibiotics and their semi- & synthetic derivatives using physical, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of glycoside antibiotics and their semi- & synthetic derivatives, based on their physicochemical properties.

3.9. Learn and follow the rules of safe work in a chemical laboratory.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Study questions for self-training of students:

1. Antibiotics-glycosides. General characteristics, structural features, physical and chemical properties. Streptomycin sulfate. Methods of analysis. Application, mechanism of action and storage.

2. Combined streptomycin preparations: streptosaluzide, streptomycin-chlorcalcium complex, pasomycin. Properties, features of the analysis. The necessity of creation and features of application in medical practice.
3. Aminoglycoside antibiotics: neomycin sulfate, monomycin sulfate, gentamicin sulfate, etc. Their properties, analysis and application.
4. Kanamycin sulfate, general quality requirements and methods of analysis. Semi-synthetic derivatives obtained on the basis of kanamycin: amikacin sulfate (advantages over natural analogues). Application and Medicinal form, contr-aindications.
5. Macrolide antibiotics. General characteristics, structural features, physical and chemical properties. Erythromycin, oleandomycin, midekamycin, azithromycin, roxithromycin and their dosage forms. Analysis of their structure, identification reactions, methods of quantitative determination, storage conditions.
6. Antibiotics of polypeptide structure. Gramicidin, its production, properties, analysis and application. Polymyxins.
7. Antifungal antibiotics. Griseofulvin, levorin, nystatin, amphotericin B. Properties, application, storage.
8. Antituberculosis antibiotics. Rifamycin and its semisynthetic analogues: rifampicin, rifabutin. Analysis of structure, properties, application, storage.
9. Antitumor antibiotics derived from the anthracycline series (naphthacenediones): rubomycin, doxorubicin and others; quinoline-5,8-dione derivatives: bruneomycin, olivomycin. Their properties, application, storage.
10. "Structure-activity" relationship in a series of aminoglycoside antibiotics. Medicinal form. Storage conditions.
11. Justify the storage conditions of the researched medicinal products based on their structure and chemical properties.
12. The main dosage forms created on the basis of the investigated medicinal substances. Medicinal form, dosage.

4.3. Work out the test tasks:

#

1) Which of the following reactions is most specific for streptomycin sulfate?

A. formation of copper hydroxamate
B. reaction with Fehling's reagent
C. reaction with diazonium salts
D. formation of iron (III) maltate
E. ozazone formation

#

2) The structure of the streptomycin sulfate antibiotic contains an aglycon that

contains guanidine residues. In order to identify the specified functional groups, the pharmacist-analyst needs to carry out a reaction:

A. with a solution of sodium hydroxide, bromine water and α-naphthol (Sakaguchi reaction)

B. with a solution of iron (III) chloride

C. with Fehling's reagent

D. with concentrated sulfuric acid and vanillin

E. with Marqui's reagent

#

3) In the chemical-analytical laboratory, the analyst conducts the analysis of medicinal substances of antibiotic-glycosides. Which of the following compounds belongs to this type?

A. streptomycin sulfate

B. tetracycline hydrochloride

C. phenoxymethylpenicillin

D. chloramphenicol

E. cefuroxime

#

4) At a pharmaceutical company, a pharmacist-analyst conducts an analysis of streptomycin sulfate. What quantitative method can be used to determine this substance?

A. nitritometry

B. acidimetry

C. complexonometry

D. photocolorimetry

E. bromatometry

#

5) At a pharmaceutical enterprise, a pharmacist-analyst analyzes aminoglycoside antibiotics. What color is formed when kanamycin monosulfate interacts with ninhydrin?

A. purple

B. black

C. white

D. yellow

E. green

#

6) In the laboratory, the quantitative determination of streptomycin sulfate is carried out by the method based on the maltol sample. What is this method?

A. potentiometry

B. polarography
C. polarography
D. photocolorimetry
E. fluorimetry

#

7) Ammonia is formed during alkaline hydrolysis:
A. streptomycin sulfate
B. kanamycin sulfate
C. oxacillin sodium salt
D. phenoxymethylpenicillin
E. benzylpenicillin potassium salt

#

8) The reaction with orcin gives:
A. streptomycin sulfate
B. cephalexin
C. phenoxymethylpenicillin
D. cephalothin sodium salt
E. benzylpenicillin potassium salt

#

9) The presence of an aldehyde group in the sugar part of streptomycin sulfate is confirmed by the reaction:
A. with picric acid
B. with barium chloride solution
C. withα- naphthol and sodium hypobromide
D. with Fehling's reagent
E. with formaldehyde solution

#

10) Gravimetric determination of sulfates in gentamicin sulfate is based on the reaction of precipitation of sulfates with salts:
A. ammonium
B. barium
C. sodium
D. potassium
E. lithium

#

11) Which antibiotic chemically belongs to glycosides:
A. tetracycline hydrochloride
B. doxycycline
C. benzylpenicillin sodium salt

D. carfecillin
E. gentamicin sulfate

#

12) Which of the listed antibiotics can be identified by the maltol formation reaction?

A. streptomycin sulfate
B. doxycycline hydrochloride
C. amoxicillin
D. lincomycin hydrochloride
E. kanamycin monosulfate

#

13) Specify an antibiotic that is a mixture of several substances:

A. neomycin sulfate
B. gentamicin sulfate
C. amikacin sulfate
D. erythromycin
E. cefuroxime

#

14) The salt of a nitrogen-containing organic base is:

A. streptomycin sulfate
B. phenoxymethylpenicillin
C. oxacillin sodium salt
D. cephalothin sodium salt
E. erythromycin Z

#

15) The medicinal substance is white in color, soluble in water, when heated with sodium hydroxide and the subsequent addition of hydrochloric acid and iron (III) chloride forms a purple color:

A. streptomycin sulfate
B. amoxicillin trihydrate
C. benzylpenicillin sodium salt
D. carbenicillin disodium salt

#

16) The sugar part of kanamycin is:

A. 6-amino-6-deoxy-D-glucose
B. N-methyl-α-glucosamine
C. α-streptosis
D. D-glucosamine
E. 3-amino-6-deoxy-D-glucose

#

17) According to the chemical structure, the glycoside is:

A. amikacin sulfate

B. cephalexin

C. carbenicillin disodium salt

D. phenoxymethylpenicillin

E. cefuroxime

#

18) For the quantitative determination of gentamicin sulfate, in accordance with the requirements of the SPhU, use:

A. microbiological method

B. method of spectrophotometry in the UV region

C. liquid chromatography

D. gravimetric method

E. photocolorimetry

#

19) The possibility of identifying streptomycin sulfate by the reaction of the maltol sample is due to the presence in its structure:

A. of L-streptose residue

B. of the N-methylglucosamine residue

C. guanidine groups

D. aldehyde group

E. sulfate ion

#

20) The sugar part of streptomycin is:

A. **streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose**)

B. 6-amino-6-deoxy-D-glucose

C. deoxystreptamine

D. streptidine

E. 3-amino-6-deoxy-D-glucose

#

21) According to the nature of the antimicrobial action of streptomycin sulfate, antibiotics belong to:

A. have a bacteriostatic effect (bacteria are alive, but unable to reproduce)

B. have a bactericidal effect (bacteria are killed, but physically continue to be present in the environment)

C. have a bacteriolytic effect (bacteria are killed, and bacterial cell walls are destroyed)

#

22) For the quantitative determination of streptomycin sulfate, in accordance with the requirements of the SPhU, use:

A. microbiological method
B. method of spectrophotometry in the UV region
C. liquid chromatography
D. gravimetric method
E. photocolorimetry

#

23) According to the requirements of the SPhU, one of the methods for identifying kanamycin sulfate is the determination of the melting point:

A. kanamycin picrate
B. kanamycin bases
C. kanamycin hydrolysis products
D. kanamycin hydrochloride
E. kanamycin tartrate

#

24) Gentamicin sulfate is a mixture of antibiotic sulfates produced by Micromonospora purpurea. Specify the method recommended by the Federal Drug Administration for determining the component composition of this drug:

A. liquid chromatography
B. gas chromatography
C. iodometry
D. UV spectrophotometry
E. microbiological method

#

25) The mechanism of antimicrobial action of streptomycin sulfate is based on:

A. disruption of protein synthesis at the level of ribosomes
B. disruption of cell wall synthesis
C. violations of the permeability of the cytoplasmic membrane
D. RNA synthesis disorders
E. denaturation of microorganism proteins

#

26) Specify the functional group in the structure of streptomycin sulfate, which has reducing properties:

A. aldehyde group
B. carboxyl group
C. keto group
D. methyl group

#

27) Choose an antibiotic with a polypeptide structure from the following antibiotics:

A. streptomycin sulfate
B. Gramicidin C
C. penicillin V
D. chloramphenicol
E. ceftriaxone

#

28) Which of the listed antibiotics is based on a macrocyclic lactone ring?

A. streptomycin sulfate
B. benzylpenicillin sodium salt
C. gentamicin sulfate
D. erythromycin
E. Levomycetin

#

29) Amphotericin B is highly effective:

A. antimalarial agent
B. antiprion antibiotic
C. antifungal antibiotic
D. antitumor antibiotic
E. antituberculosis antibiotic

#

30) Specify which of the antibiotics is an antitumor drug?

A. olivomycin
B. ampicillin sodium salt
C. streptomycin sulfate
D. Gramicidin C
E. erythromycin

#

31) At a pharmaceutical company, a pharmacist-analyst analyzes macrolide antibiotics. What is the basis of the structure of these compounds?

A. aromatic core
B. β-lactam cycle
C. oxazolidone cycle
D. macrocyclic lactone ring
E. dihydrothiazone cycle

#

32) Which of the following drugs belongs to polypeptide antibiotics?

A. polymyxin

B. erythromycin phosphate
C. midecamycin
D. lincomycin hydrochloride
E. gentamicin sulfate

#

33) According to the chemical classification, gramicidin and polymyxins belong to the class:
A. antibiotics of alicyclic structure
B. glycoside antibiotics
C. polypeptide antibiotics
D. antibiotics of heterocyclic structure

#

34) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, azithromycin is identified:
A. IR spectrophotometry
B. UV spectrophotometry
C. thin layer chromatography
D. interaction with p-dimethylaminobenzaldehyde in a hydrochloric acid environment
E. interaction with Fehling's reagent

#

35) Indicate the method of quantitative determination by which the State Federal Drug Administration recommends determining concomitant impurities and the quantitative content of azithromycin:
A. liquid chromatography
B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography

#

36) Indicate the reagent by which, in accordance with the requirements of the SPhU, rifampicin is identified:
A. ammonium persulfate, phosphate buffersolution
B. Nessler's reagent
C. solution of hydroxylamine hydrochloric acid, iron (III) sulfate
D. sulfuric acid
E. copper (II) sulfate solution

#

37) Specify the method of quantitative determination by which the SPhU recommends determining the quantitative content of rifampicin:

A. UV spectrophotometry
B. iodometry
C. neutralization
D. IR spectrophotometry
E. thin layer chromatography

#

38) When identifying doxorubicin hydrochloride, the analyst performed a reaction on the ionic composition. What ions will the substance have a positive reaction to?

A. SO42-
B. Cl-
C. Na+
D. Ca2+
E. Hg2+

#

39) Specify the method of quantitative determination by which the SPhU recommends to quantitatively determine doxorubicin hydrochloride:

A. liquid chromatography
B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography

#

40) What amino sugar does erythromycin contain:

A. desosamine (3-dimethylamino-4,6-dideoxypyranose)
B. deoxystreptamine
C. streptidine
D. 3-amino-6-deoxy-D-glucose
E. streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose)

#

41) Choose a polyene antibiotic from the following antibiotics:

A. streptomycin sulfate
B. Gramicidin Z
C. penicillin V
D. nystatin
E. ceftriaxone

#

42) Which of the following drugs belongs to polypeptide antibiotics?

A. polymyxin

B. erythromycin phosphate

C. midecamycin

D. amphotericin

E. gentamicin sulfate

#

43) What aglycon does nystatin contain:

A. nystatinolide

B. deoxystreptamine

C. streptidine

D. 3-amino-6-deoxy-D-glucose

E. streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose)

#

44) What amino sugar does nystatin contain:

A. mycosamine (3,6-dideoxy-3-amino-Dmannose)

B. deoxystreptamine

C. streptidine

D. 3-amino-6-deoxy-D-glucose

E. streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose)

#

45) Specify the factor that does not cause a change in the structure of polyene antibiotics, and, as a result, a loss of antibiotic activity:

A. humidity

B. light

C. high temperature

D. air oxygen

E. oxidizers

#

46) Specify which of the antibiotics is a quinoline-5,8-dione derivative?

A. Bruneomycin

B. ampicillin sodium salt

C. streptomycin sulfate

D. Gramicidin Z

E. erythromycin

#

47) Macrolide antibiotics - erythromycin and azithromycin are widely used in medical practice. Specify the spectrum of microbiological activity of these drugs:

A. broad-spectrum antibiotics

B. act mainly on gram-positive bacteria
C. act mainly on gram-negative bacteria
D. anticancer antibiotics
E. antifungal antibiotics

#

48) According to the mechanism of antimicrobial action, polymyxins belong to antibiotics that violate:

A.synthesis of the cell wall of a microbial cell
B. permeability of the cytoplasmic membrane of a microbial cell
C. RNA synthesis of a microbial cell
D. protein synthesis at the level of ribosomes of a microbial cell
E. DNA synthesis of a microbial cell

#

49) A feature of the chemical structure of anticancer antibiotics is the presence in their molecules:

A. chromoform groups of the quinoid structure
B. macrocyclic lactone ring
C. polyene chain coupling
D. thiazolidine cycle

#

50) Specify antibiotics that are active mainly against gram-negative microorganisms:

A. tetracyclines
B. aminoglycosides
C. natural penicillins
D. polypeptides
E. macrolides

4.4. Situational tasks:

1) The presence of an aldehyde group in the sugar part of streptomycin sulfate is confirmed by reaction with Fehling's reagent. Write the chemistry of the selected reaction, indicate the conditions of its implementation and the analytical effect.
2) What structural features of streptomycin sulfate are used for its quantitative determination by the photoelectrocolorimetric method? Give the corresponding reaction equations, the formula for calculating the quantitative content.
3) Describe the dosage forms of streptomycin, their pharmacological effects, advantages and disadvantages compared to streptomycin sulfate.

4) One of the identification reactions for streptomycin sulfate is the Sakaguchi reaction. What functional groups in the structure of the drug does it allow to determine? Write the chemistry, indicate the conditions and analytical effect.
5) What, besides chemical, methods exist for determining the quality of antibiotics? Justify each of them, show the possibility of use for the purposes of qualitative and quantitative analysis and purity control.
6) Give the concept of units of antibiotic activity (OU).
7) On the basis of the chemical structure and properties of functional groups, justify the chemical properties of antibiotics of the group of macrolide antibiotics. Confirm the answer with the chemistry of the reactions.
8) Consider the structural formulas of macrolide antibiotics: erythromycin, midekamycin, azithromycin. Specify the relationship between the chemical structure and the pharmacological effect of drugs.
9) Describe the group of polyene antibiotics: features of structure, analysis, storage.

4.5. Tasks:

1. Calculate the specific rotation and evaluate the quality of kanamycin monosulfate, if the average angle of rotation of a 5% aqueous solution of the drug is +6.31°. The length of the cuvette is 10 cm. The specific rotation should be from +112 to +123.
2. Calculate the percentage content of streptomycin sulfate in the preparation, if 0.2015 g of the substance was dissolved in 20 ml of water in a 50 ml volumetric flask and made up to the mark with water. Put 5 ml of the solution into a 50 ml volumetric flask and bring it up to the mark with water. 2 ml of 0.2 N sodium hydroxide solution is added to 10 ml of the solution, heated in a water bath for 4 minutes, cooled. Then add 8 ml of 1% solution of ferric ammonium alum, 0.55 N of sulfuric acid solution, mix. The optical density is measured by PhEC at a wavelength of 520 nm in a cuvette with a layer thickness of 10 mm, it is equal to 0.482. In parallel, the reaction is carried out with 10 ml of 0.04% standard solution of streptomycin sulfate A = 0.491
3. Calculate the mass of a test of streptomycin sulfate, if it is dissolved in 20 ml of water in a 100 ml volumetric flask and brought up to the mark, 10 ml of the solution is introduced into a 100 ml volumetric flask, brought up to the mark with water. Take 10 ml of the dilution, add 4 ml of 0.2N sodium hydroxide solution, heat in a water bath for 4 minutes, cool. Then 8 ml of a 1% solution of ferric ammonium alum in a 0.55 N solution of sulfuric acid was added and mixed. The optical density is measured by PhEC at a wavelength of 520 nm in a cuvette with a layer thickness of 10 mm, it is equal to 0.293. In parallel, the reaction is carried

out with 10 ml of 0.04% standard solution of streptomycin sulfate. Ao = 0.288. The content of streptomycin sulfate in the preparation is 100.02%.

4. Calculate the specific absorption rate of the medicinal product, if it is known that a sample weighing 0.0617 g was taken to prepare the solution, which was dissolved in 50 ml of solvent. 5 ml of the resulting solution was placed in a volumetric flask with a capacity of 100 ml and brought to the mark. The optical density is 0.425. The percentage content of the active substance in the preparation is 98.72%.
5. Calculate the distance from the starting line to the center of the nystatin spot if R_f = 0.84 and the distance traveled by the solvent is 10.0 cm.
6. Calculate the distance from the start line to the solvent front if R_f = 0.9 and the distance from the start line to the center of the rifampicin spot is 9.0 cm.
7. When analyzing the azithromycin substance by ascending paper chromatography, it was found that the R_f value for the specified substance is 0.84, and the path traveled by the solvent system is 10.0 cm. Determine the distance from the start line to the center of the azithromycin spot on the chromatogram.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 5

1.THEME: Final lesson on theory and practice on the topic: «Analysis of medicines of the antibiotic group. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

2.PURPOSE: To form systematic knowledge and consolidate practical skills in the analysis of the quality of medicines of the antibiotic group and their semi- & synthetic derivatives using physical, physico-chemical and chemical methods of analysis.

3. TARGETS:

3.1. Check and consolidate theoretical knowledge and practical skills in the use of physical, physicochemical and chemical methods to analyze the quality of medicines of the antibiotic group and their semi- & synthetic derivatives.

3.2. Check the protocols of laboratory work and analyze the correctness of the analysis of of medicines of antibiotic group and their semi- & synthetic derivatives in accordance with the requirements of the State Medical Research Institute, the Ministry of Health.

4. TASK FOR SELF-PREPARATION OF STUDENTS FOR THE FINAL LESSON

4.1. Control questions

1) Antibiotics. General characteristics. Names and synonyms of antibiotics. Development of antibiotic chemistry.
2) Antibiotics as medicinal substances. Sources of receipt. Chemical structure. Nomenclature, physicochemical properties of medicinal substances from the group of antibiotics.
3) Methods of obtaining antibiotics and ways of creating new antibiotics (biological screening, modification of the "leader structure" (chemical transformation), directed synthesis).
4) Describe methods of analysis: biological, chemical and physicochemical methods. The concept of a unit of antibiotic activity.
5) Classification of antibioticsaccording to the method of production, spectrum, nature and mechanism of antimicrobial action, chemical.
6) To justify the need to determine abnormal toxicity, sterility, pyrogenicity, bacterial endotoxins and depressant substances in antibiotics.

7) Latin names, synonyms, structural formulas and chemical names of drugs from the group of **aromatic antibiotics**. Levomycetin (chloramphenicol) and its esters (levomycetin stearate, soluble levomycetin succinate). Synthesis methods, the relationship between structure and biological action, the role of stereoisomerism in the manifestation of biological action.
8) Use of physicochemical properties to analyze the quality of chloramphenicol antibiotics.
9) **Antibiotics of alicyclic structure**:

   9.1. Tetracycline, oxytetracycline. Structure, nomenclature, physical and chemical properties, analysis, storage, application.

   9.2. Semi-synthetic analogues of alicyclic antibiotics: metacycline (rondomycin), doxycycline (vibramycin). Quality requirements. Methods of analysis, application, relationship between structure and biological action.
10) **Antibiotics of the heterocyclic series. β-lactam antibiotics**. General characteristics. Classification, their physical and chemical properties. Relationship "structure-action" in a row β-lactam antibiotics.
11) Penicillins (penems). General characteristics. Pharmacopoeia drugs: benzylpenicillin sodium (potassium) salt. Phenoxymethylpenicillin. Features of the structure, properties, methods of analysis: general and separate.
12) Use of physicochemical properties for identification and quantification of penicillins (penems). Transformation reactions that prove their structure.
13) To justify the need to determine the transparency, color, acidity, loss in mass during drying, thermal stability, passability through the needle of a syringe of poorly water-soluble drugs in penicillin preparations.
14) Conditions and chemistry of the reactions occurring during the quantitative determination of penicillin by the iodometric method. To justify the necessity of setting up a control experiment, to explain what is its peculiarity. Other methods of quantitative determination of antibiotics of this group. Methods of quantitative assessment of the content of antibiotics in the drug. Formulas for calculating the percentage content of the amount of penicillins and the number of units.
15) Long-acting penicillin preparations. Bicillin, benzylpenicillin, novocaine salt, etc. Their properties, analysis and application in medicine.
16) Semi-synthetic penicillins, obtained on the basis of 6-aminopenicilanic acid. Ampicillin, amoxicillin, oxacillin sodium salt, Azlocillin sodium salt and others. The need to create this group of antibiotics. Methods of analysis, nature of action (unlike natural penicillins).
17) **Cephemes (cephalosporins).** General characteristics, chemical structure, comparative resistance to chemical reagents and enzymes. Modification of the

"leader structure" of cephalosporin C, partial and directed synthesis based on 7-ACA and 7-ADCA.

18) Cepheme antibiotics are derivatives of 7-aminocephalosporanic acid (7-ACA): sodium salts of cefotaxime and cefoxitin, cephalothin and others. Properties, analysis, stability and storage.

19) Cepheme antibiotics are derivatives of 7-aminodesacetoxycephalosporanic acid (7-ADCA): cefazolin, cephalexin, ceftriaxone sodium salt and others. Properties, analysis, stability and storage.

20) Lincosamide antibiotics. General characteristics, structural features, physical and chemical properties. Lincomycin hydrochloride. Methods of analysis. Application, mechanism of action and storage.

21) **Antibiotics-glycosides**. General characteristics, structural features, physical and chemical properties. Streptomycin sulfate. Methods of analysis. Application, mechanism of action and storage.

22) Combined streptomycin preparations: streptosaluzide, streptomycin-chlorcalcium complex, pasomycin. Properties, features of the analysis. The necessity of creation and features of application in medical practice.

23) Aminoglycoside antibiotics: neomycin sulfate, monomycin sulfate, gentamicin sulfate, etc. Their properties, analysis and application.

24) Kanamycin sulfate, general quality requirements and methods of analysis. Semi-synthetic derivatives obtained on the basis of kanamycin: amikacin sulfate (advantages over natural analogues). Application and medicinal form, contr-aindications.

25) Macrolide antibiotics. General characteristics, structural features, physical and chemical properties. Erythromycin, oleandomycin, midekamycin, azithromycin, roxithromycin and their dosage forms. Analysis of their structure, identification reactions, methods of quantitative determination, storage conditions.

26) Antibiotics of polypeptide structure. Gramicidin, its production, properties, analysis and application. Polymyxins.

27) Antifungal antibiotics. Griseofulvin, levorin, nystatin, amphotericin B. Properties, application, storage.

28) Antituberculosis antibiotics. Rifamycin and its semisynthetic analogues: rifampicin, rifabutin. Analysis of structure, properties, application, storage.

29) Antitumor antibiotics derived from the anthracycline series (naphtrantracendiones): rubomycin, doxorubicin and others; quinoline-5,8-dione derivatives: bruneomycin, olivomycin. Their properties, application, storage.

30) "Structure-activity" relationship in a series of aminoglycoside antibiotics. Medicinal form. Storage conditions.

31) Based on the structure of the researched medicinal products, justify the identification reactions and methods of quantitative determination, give the chemistry of the corresponding reactions.
32) The relationship between chemical structure and biological action on the example of drugs from the group of antibiotics and their semi- & synthetic derivatives.
33) Justify the storage conditions of the researched medicinal products based on their structure and chemical properties.
34) The main dosage forms created on the basis of the investigated medicinal substances. Medicinal form, dosage. Application.

4.2. Test tasks for the final lesson

#

1) The pharmacist-analyst conducted an identification reaction for the aromatic nitro group in chloramphenicol with sodium hydroxide solution when heated. What is observed at the same time?

A. yellow color, changing to red-orange, with subsequent precipitation of a brick-red precipitate and the smell of ammonia
B. green color and smell of ammonia
C. white sediment
D. formation of a blue complex soluble in chloroform
E. a black precipitate that dissolves when added to a water solution

#

2) Indicate how to prove the presence of a nitro group in the structure of chloramphenicol (Chloramphenicolum):

A. obtaining an azo dye after the reduction of the nitro group to the amino group
B. by the reaction of interaction with iron (III) chloride
C. according to the interaction reaction with Nessler's reagent
D. interaction with hydrochloric acid
E. interaction with a solution of potassium chloride

#

3) An analytical chemist can detect an aromatic nitro group in a chloramphenicol molecule by an azo coupling reaction after its reduction. Restoration of the indicated functional group to the amino group is carried out:

A. zinc in a hydrochloric acid environment
B. zinc in a chloroform environment
C. zinc in dioxane medium
D. zinc in a neutral environment
E. zinc in an alcoholic medium

#

4) Specify the starting substance used in the pharmaceutical industry for the synthesis of chloramphenicol:

A. acetone

B. *p*-nitroacetophenone

C. aniline

D. *p*-nitrobenzoic acid

E. benzoic acid

#

5) State the reason for the impossibility of using D - (-) - and L - (+) - erythro forms of chloramphenicol in medical practice:

A. due to high toxicity

B. due to the difficulties of chemical synthesis

C. due to low activity

D. due to the resistance of microorganisms

#

6) At a pharmaceutical enterprise, a pharmacist analyzes soluble chloramphenicol succinate. What will be observed as a result of the interaction of this medicinal substance with sodium hydroxide solution?

A. the appearance of a white precipitate

B. the appearance of the smell of ammonia

C. the appearance of a blue-violet color of the solution

D. complex salt formation

E. the formation of a red precipitate

#

7) Antibiotics are classified by the chemical structure of the carbon skeleton. Which of the following belong to the aromatic series?

A. tetracycline

B. chloramphenicol and its esters

C. penicillins

D. cephalosporins

E. streptomycin and its preparations

#

8) The chemist identified chloramphenicol stearate with concentrated hydrochloric acid. What analytical effect will be observed as a result of the reaction?

A. white precipitate

B. smell of ammonia

C. oily drops

D. red color of the solution

E. blue-violet color of the alcohol layer
#
9) Sterilize eye drops containing:
A. chloramphenicol
B. benzylpenicillin
C. phenoxymethylpenicillin
D. collargol
E. trypsin
#
10) What reagent can a pharmacist-analyst use to confirm the presence of a nitro group in the structure of chloramphenicol?
A. sodium hydroxide solution
B. copper sulfate solution
C. hydrochloric acid
D. cobalt nitrate solution
E. hydrogen peroxide solution
#
11) The presence of a nitro group in the structure of chloramphenicol can be confirmed after the reduction of the nitro group to the amino group using the formation reaction:
A. azo dye
B. iron (III) hydroxamate
C. thiochrome
D. fluorescein
E. thalleioquine
#
12) Medicinal product identified by reaction with sodium hydroxide solution when heated:
A. chloramphenicol
B. ampicillin
C. cefotaxime sodium salt
D. ascorbic acid
E. benzylpenicillin
#
13) Quantitative determination of chloramphenicol can be performed by the following method:
A. nitritometry with preliminary recovery
B. nitritometry
C. nitritometry followed by recovery

D. nitritometry with preliminary oxidation
E. complexonometry
#
14) Quantitative determination of chloramphenicol (chloramphenicol) is performed according to the requirements of the SPhU by the following method:
A. nitritometry after recovery
B. spectrophotometry
C. bromatometry
D. iodometry
E. iodatometry
#
15) Derivatives of nitrophenylalkylamines include:
A. streptomycin
B. cephaloridine
C. chloramphenicol
D. gentamicin
E. nystatin
#
16) Indicate the method by which, in accordance with the requirements of the SPhU, concomitant impurities in the substance chloramphenicol (chloramphenicol) are determined:
A. thin layer chromatography
B. iodometry
C. UV spectroscopy
D. liquid chromatography
E. HPLC
#
17) Choose a set of reagents with which, in accordance with the requirements of the State Federal Drug Administration, the identification of chloramphenicol (chloramphenicol) is carried out:
A. calcium chloride, zinc, benzoyl chloride, solution of iron (III) chloride, chloroform
B. sodium nitrite, hydrochloric acid
C. concentrated sulfuric acid
D. a solution of hydroxylamine hydrochloric acid, sodium hydroxide, a solution of iron (III) chloride
E. perhydrol, iodine solution
#

18) A mixture of D - (-) - and L - (+) - threo-isomers, that is, the racemic form of chloramphenicol, which has 50% of its activity, is called:

A. Synthomycin

B. pancreatin

C. chloramphenicol stearate

D. midecamycin

E. ephedrine

#

19) Threo-erythro-isomerism is characteristic of nitrophenylalkylamine antibiotics. Natural chloramphenicol corresponds to:

A. D - (-) - threo-isomer

B. *L*- (+) - threo-isomer

#

20) There are two asymmetric carbon atoms in the structure of chloramphenicol. An alcoholic solution of chloramphenicol rotates the layers of polarization:

A. to the right

B. to the left

C. has no optical activity

#

21) Levomycetin (chloramphenicol) exhibits weak acidic properties due to the presence in the structure of:

A. amide group and two alcohol hydroxyls

B. nitro groups

C. covalently bound chlorine atom

D. aromatic system of nitrobenzene

#

22) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, chloramphenicol and chloramphenicol disodium disuccinate impurities are determined in the chloramphenicol sodium succinate substance:

A. liquid chromatography

B. thin layer chromatography

C. iodometry

D. UV spectroscopy

E. liquid chromatography

#

23) Like other phenylalkylamines, chloramphenicol undergoes hydramine cleavage under various conditions. Thus, hydrolysis followed by oxidation with sodium periodate leads to the formation of:

A. 4-nitrobenzaldehyde, formic acid, formaldehyde and ammonia
B. 3-methyl-4-nitrobenzaldehyde, formic acid and ammonia
C. benzene, nitric acid, formaldehyde and acetic acid
D. nitrotoluenes, ammonia, methanol and formaldehyde
#
24) The residue of succinic acid in the structure of chloramphenicol sodium succinate after acid hydrolysis is detected by the reaction with:
A. with resorcinol and conc. sulfuric acid
B. with sodium nitrite and hydrochloric acid
C. with concentrated sulfuric acid
D. with a solution of hydroxylamine hydrochloric acid, sodium hydroxide, a solution of iron (III) chloride
E. with perhydrol and iodine solution
#
25) The mechanism of antimicrobial action of chloramphenicol and its preparations is based on:
A. violation of protein synthesis at the level of ribosomes
B. disruption of cell wall synthesis
C. violation of the permeability of the cytoplasmic membrane
D. disruption of RNA synthesis
E. protein denaturation of the microorganism
#
26) Indicate how to determine the presence of free stearic acid in chloramphenicol stearate:
A. by the method of neutralization using phenolphthalein
B. iodometrically
C. by the method of ion exchange chromatography
D. by the method of polarimetry
E. by the method of refractometry
#
27) Antibiotics are ...:
A. chemical compounds of biological origin that have a harmful or harmful effect on microorganisms and macro-organisms
B. substances-inhibitors of RNA or DNA synthesis, belonging to chemotherapeutic antibacterial agents
C. substances produced by microorganisms, higher plants, animal tissues in the process of their vital activity and modification products of these substances, which selectively inhibit the growth of pathogenic microorganisms, lower fungi,

some viruses and cells of malignant formations, while not having a toxic effect on the macroorganism

D. biologically active substances released from official medicinal plant raw materials

E. compounds of the steroid structure, which have a pronounced cardiotonic effect

#

28) Choose the correct definition of the concept of "unit of action" (UA) of antibiotics:

A. for unit of action of an antibiotic, the minimum amount of antibiotic is taken, which inhibits the development of the test microorganism in a certain volume of the nutrient medium

B. for UA of an antibiotic, the minimum amount of a standard test microorganism is taken, the growth of which is delayed when it is exposed to 1 mg or 1 ml of the appropriate antibiotic

C. for UA take the minimum amount of antibiotic that inhibits the development of test microorganisms on an area of 1 cm2

D. for UA take the minimum amount of antibiotic that gives a positive identification reaction

#

29) The priority of the discovery of antibiotics belongs to:

A. Fleming

B. Yermolyeva

C. Ehrlich

D. Romanovsky

E. Mendeleev

#

30) If it is necessary to identify antibiotic substances using spectroscopy in the UV or IR range of the spectrum, the control and analytical laboratory must have:

A. samples of drug substances of similar pharmacological action

B. all medicines containing this substance

C. samples of drug substances of a similar chemical structure

D. pharmacopoeial standard sample of the drug substance

E. permission of the manufacturer of the investigated substance to conduct the experiment

#

31) Indicate the methods of determining the biological activity of antibiotics and their medicinal products, according to the SPhU:

A. immunoenzymatic

B. diffusion in agar

C. turbidimetric

D. physical and chemical
E. radiometric
#
32) The reaction of antibiotics of the tetracycline series with a solution of ferric oxide chloride is due to the presence in their structure of:
A. phenolic hydroxyl
B. urea group
C. of the dimethylamine residue
D. methyl group
E. carbonyl group
#
33) The mechanism of antimicrobial action of antibiotics of the tetracycline series is based on:
A. disruption of protein synthesis at the level of ribosomes
B. disruption of cell wall synthesis
C. violations of the permeability of the cytoplasmic membrane
D. RNA synthesis disorders
E. protein denaturation of the microorganism
#
34) What reagent does a pharmacist-analyst use to determine water in tetracycline antibiotics?
A. a solution of sulfur dioxide, iodine and pyridine in methanol (Fisher's reagent)
B. anhydrous copper sulfate
C. a mixture of glacial acetic acid and acetic anhydride (1:2)
D. calcined chloride
E. alcoholic solution of picric acid
#
35) Indicate which of the antibiotics belongs to the derivatives of the alicyclic series?
A. vibramycin
B. cefazolin sodium salt
C. benzylpenicillin K and Na salts
D. carfecillin sodium salt
E. Bruneomycin
#
36) Indicate which functional group in the molecule of tetracycline antibiotics causes the formation of azo dyes during azo coupling with diazonium salts?
A. phenolic hydroxyl

B. dimethylamine
C. alcohol hydroxyl
D. carboxamide group
E. methyl group
#
37) Tetracycline is an antibiotic according to its chemical structure:
A. aromatic series
B. alicyclic series
C. aliphatic series
D. heterocyclic series
E. glycosidic structure
#
38) Specify the reagent with which the reaction is absent in the express analysis of drugs of the tetracycline series:
A. sodium nitroprusside
B. *p*-dimethylaminobenzaldehyde
C. Nessler's reagent
D. diazoreactive
E. potassium acetate
#
39) The activity of tetracycline antibiotics is determined using a biological method. At the same time, they use:
A. agar diffusion method
B. experiments on rats
C. experiments on rabbits
D. hanging drop method
E. experiments on frogs
#
40) Which of the following drugs belongs to the tetracycline group of antibiotics?
A. doxycycline hyclate
B. levomycetin succinate is soluble
C. cephaloridine
D. cephapirin
E. streptomycin
#
41) A chemist analyzes doxycycline hyclate using a reaction with concentrated sulfuric acid. What color does the solution acquire after carrying out this reaction?
A. blue
B. green

C. red
D. yellow
E. black
#
42) The structure of tetracycline is based on a partially hydrogenated nucleus:
A. naphthacene
B.anthracene
C.phenanthrene
D.naphthalene
E.acridine
#
43) Methacycline hydrochloride interacts with iron (III) chloride in an alcoholic medium. What analytical effect will be observed?
A. white precipitate
B. brown color
C. green sediment
D. yellow sediment
E. blue color
#
44) In the chemical analytical laboratory, the pharmacist-analyst conducts the analysis of tetracycline hydrochloride. By which method, according to the SPhU, is this substance quantitatively determined?
A. liquid chromatography
B. alkalimetry
C. gas chromatography
D. acidimetry
E. bromatometry
#
45) At a pharmaceutical enterprise, a pharmacist conducts an analysis of methacycline hydrochloride. What compound is formed as a result of the reaction of this substance with concentrated sulfuric acid?
A. isotetracycline
B. methacycline base
C. anhydro derivative of methacycline
D. azo dye
E. maltol
#
46) In the quantitative determination of tetracycline by the photoelectrocolorimetric method, the reaction is used:

A. azo compound
B. with potassium bromide solution
C. formation of iron (III) hydroxamate
D. with Fehling's reagent
#
47) In the quantitative determination of tetracycline by the photoelectrocolorimetric method, the reaction is used:
A. with iron (III) chloride
B. with sodium edetate solution
C. formation of iron (III) hydroxamate
D. with Fehling's reagent
E. with Mayer's reagent
#
48) Select a method that cannot quantify tetracycline hydrochloride:
A. acidimetry
B. non-aqueous titration
C. biological method (diffusion in agar)
D. photoelectrocolorimeter
E. fluorimeter
#
49) To identify tetracycline, the reaction of the formation of colored anhydroderivatives under the action of concentrated sulfuric acid is used, which is based on the ability of the drug to:
A. dehydration
B. restoration
C. complex formation
D. condensation
E. esterification
#
50) The presence of dihydrate phenolic and enol hydroxyls in the oxytetracycline molecule is confirmed by the reaction:
A. with iron (III) chloride solution
B. with Dragendorff's reagent
C. with sodium nitroprusside
D. with Nessler's reagent
E. with sodium nitrite
#
51) Semi-synthetic tetracyclines include:
A. oxytetracycline

B. methacycline
C. tetracycline
D. gramicidin
E. oxacillin
#
52) Specify a set of reagents that allows you to distinguish antibiotics of the tetracycline series from each other:
A. concentrated sulfuric acid and Ehrlich's reagent (p-dimethylaminobenzaldehyde in dilute hydrochloric acid)
B. sodium nitroprusside, sodium hydroxide
C. Nessler's reagent
D. sodium nitrite, hydrochloric acid
E. potassium permanganate in the presence of conc. sulfuric acid
#
53) State the reason why the use of Ehrlich's reagent (p-dimethylaminobenzaldehyde in dilute hydrochloric acid) is limited for distinguishing tetracycline antibiotics from each other:
A. slow course of reaction (6-8 hours)
B. unstable staining of the reaction product over time
C. violent reaction flow (possible explosion)
D. all tetracyclines give the same analytical effect of the reaction
E. Ehrlich's reagent decomposes quickly
#
54) Indicate the physico-chemical method by which, according to the requirements of the SPhU, doxycycline hyclate is identified:
A. thin layer chromatography
B. HPLC
C. refractometry
D. UV spectrophotometry
E. fluorimetry
#
55) Specify the industrial method of obtaining natural tetracyclines:
A. microbiological method (deep fermentation of actinomycetes Streptomyces aureofaciens (rimosus))
B. chemical synthesis
C. allocation from plant raw materials
D. extraction from animal tissues
#

56) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, quantitative determination of tetracycline pharmacopoeial drugs is carried out:

A. liquid chromatography
B. acidimetry in non-aqueous environments
C. UV spectrophotometry
D. photoelectrocolorimetry (by reaction with a solution of iron (III) chloride)
E. thin layer chromatography

#

57) Indicate the reagent with which, in accordance with the requirements of the Federal Drug Administration, the identification of tetracycline pharmacopoeial drugs is carried out:

A. sulfuric acid
B. sodium hydroxide solution
C. iron (III) chloride solution
D. sodium nitroprusside solution
E. diazonium salts

#

58) Specify the functional group in the structure of natural tetracycline, which is responsible for the manifestation of the main properties:

A. dimethylamino group
B. phenolic hydroxyl
C. enol hydroxyl
D. methyl group
E. keto group

#

59) Specify the functional groups in the structure of natural tetracycline responsible for the manifestation of acidic properties:

A. dimethylamino group
B. phenolic hydroxyl and enol hydroxyls
C. methyl group
D. keto group
E. carboxyl group

#

60) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, concomitant impurities in pharmacopoeial preparations of tetracycline are determined:

A. liquid chromatography
B. polarimetry

C. UV spectrophotometry
D. potentiometry
E. thin layer chromatography

#
61) The control and analytical laboratory received a medicinal substance - benzylpenicillin sodium salt for analysis. Indicate how, according to the SPhU, the pharmacist-analyst identifies this drug?
A. optical density is measured
B. the infrared absorption spectrum is determined
C. the pH of the solution is determined
D. reaction with Fehling's reagent
E. the specific rotation is determined
#
62) The pharmacist-analyst proves the presence of penems of the β-lactam cycle in the structure of antibiotics using the formation reaction:
A. metal hydroxamate
B. indophenol
C. azomethine dye
D. thalleiochina
E. murexide
#
63) What is the basis of the chemical structure of penicillins:
A. 6-APK (6-aminopenicillanic acid)
B. 7-APK (7-aminopenicillanic acid)
C. 8-APK (8-aminopenicillanic acid)
D. 5-APK (5-aminopenicillanic acid)
E. 4-APK (4-aminopenicillanic acid)
#
64) What causes the prolonged effect of some penicillins (bicillin, benzylpenicillin, novocaine salt, etc.)?
A. the creation of drug depots in muscle tissue due to their poor solubility
B. by increasing the dose of the injected antibiotic
C. resistance to the action of penicillinase
D. acid resistance of drugs
E. low solubility of the substance
#
65) Indicate which of the listed drugs, due to the presence of a β-lactam cycle in its structure, gives a positive reaction with a solution of hydroxylamine hydrochloride in

the presence of sodium hydroxide and the subsequent addition of a solution of iron (III) chloride:

A. phenoxymethylpenicillin

B. monomycin sulfate

C. streptomycin sulfate

D. tetracycline hydrochloride

#

66) The instability of penicillins is due, first of all, to the presence in their structure of:

A. β-lactam cycle

B. urea group

C. carboxyl group

D. methyl groups

E. thiazolidine cycle

#

67) The pharmacist-analyst of the pharmacy performs the identification of oxacillin sodium salt. As a reagent, he uses a solution of hydroxylamine hydrochloric acid in the presence of a solution of sodium hydroxide and a solution of copper nitrate. What structural fragment of the drug molecule is detected using these reagents?

A. β-lactam cycle

B. thiazolidine cycle

C. isoxazole cycle

D. phenyl radical

E. urea group

#

68) Specify which of the antibiotics belongs to penem derivatives?

A. Azlocillin sodium salt

B. chloramphenicol stearate

C. streptomycin sulfate

D. azithromycin

E. Synthomycin

#

69) According to the mechanism of antimicrobial action, penems belong to antibiotics that violate:

A. synthesis of the cell wall of a microbial cell

B. permeability of the cytoplasmic membrane of a microbial cell

C. RNA synthesis of a microbial cell

D. protein synthesis at the level of ribosomes of a microbial cell

E. DNA synthesis of a microbial cell

#

70) Which of the following medicines belongs to natural penicillins?

A. ampicillin sodium salt

B. amoxicillin trihydrate

C. carbenicillin disodium salt

D. oxacillin sodium salt

E. phenoxymethylpenicillin

#

71) At a pharmaceutical enterprise, a pharmacist-analyst conducts an analysis of benzylpenicillin. Which reagents can be used to identify this substance?

A. sulfuric acid

B. Nessler's reagent

C. hydrochloric acid

D. Markey's reagent

E. sodium hydroxide

#

72) A control and analytical laboratory specialist confirms the presence of a sodium cation in the preparation "Benzylpenicillin sodium salt" by reaction with a solution of potassium pyroantimonate by the appearance of:

A. green sediment

B. yellow sediment

C. blue sediment

D. white sediment

E. purple sediment

#

73) An analytical chemist conducts an identification reaction for amoxicillin with formaldehyde in the presence of sulfuric acid. What color of the solution will be observed?

A. dark yellow

B. red

C. yellow-green

D. blue

E. red-brown

#

74) Specify the group of microorganisms on which natural penicillins have a bactericidal effect:

A. gram positive

B. gram negative

C. brucelli

D. salmonella
E. Shigella
#
75) According to the nature of antimicrobial action, penicillins belong to antibiotics:
A. have a bacteriostatic effect (bacteria are alive, but unable to reproduce)
B. have a bactericidal effect (bacteria are killed, but physically continue to be present in the environment)
C. exhibit a bacteriolytic effect (bacteria are killed, and bacterial cell walls are destroyed)
#
76) When identifying lincomycin hydrochloride, the analyst performed a reaction on the ionic composition. What ions will have a positive reaction?
A. SO_4^{2-}
B. Cl-
C. Na^+
D. Ca^{2+}
E. Hg^{2+}
#
77) The pyrogenicity test is not performed:
A. for phenoxymethylpenicillin
B. for kanamycin sulfate
C. for streptomycin sulfate
D. for benzylpenicillin sodium salt
E. for carbenicillin disodium salt
#
78) Benzylpenicillin potassium salt in aqueous solutions is incompatible:
A. with ascorbic acid
B. with novocaine
C. with sodium chloride
D. with sodium bicarbonate
#
79) Injectable solutions are not subjected to thermal sterilization:
A. benzylpenicillin sodium salt
B. glucose
C. ascorbic acid
#
80) State the reaction by which phenoxymethylpenicillin cannot be identified:
A. diazotization reaction

B. alloy with caustic alkalis followed by the addition of lead acetate
C. reaction with Markey's reagent
D. hydroxam sample
E. reaction with chromotropic acid
#
81) Quantitative determination of the amount of penicillins in the potassium salt of benzylpenicillin is carried out by the method:
A. iodometry
B. UV spectrophotometry
C. neutralization
D. photocolorimetry
E. acidimetry
#
82) What product of hydrolysis of phenoxymethylpenicillin when interacting with Markey's reagent forms an aurine dye:
A. phenol
B. formaldehyde
C. glycolic acid
D. carbon dioxide
E. ammonia
#
83) Quantitative determination of ampicillin trihydrate is carried out by the formol titration method, as it contains in its structure:
A. β-lactam cycle
B. amino acid residue
C. organically bound sulfur
D. aromatic ring
#
84) Organically bound sulfur in penicillin preparations after alloying with caustic alkalis is determined by the reaction:
A. with ammonium oxalate solution
B. with sodium nitroprusside solution
C. with sodium sulfate solution
D. with barium chloride solution
E. with potassium permanganate solution
#
85) The hydroxam test allows you to confirm the presence of benzylpenicillin in the molecule:
A. phenyl radical

B. β-Lactam cycle
C. thiazolidine cycle
D. methyl groups
E. carboxyl group
#
86) Which penicillin drug contains an amino acid residue in its structure:
A. benzylpenicillin
B. oxacillin
C. ampicillin
D. phenoxymethylpenicillin
E. chloramphenicol
#
87) Natural penicillins in industry are obtained by the method of microbiological synthesis. An obligatory component is a precursor substance, the chemical structure of which is similar to the corresponding radical of the antibiotic in position 6. In the production of benzylpenicillin, the precursor serves as:
A. beta-dimethylcysteine
B. valine
C. phenylacetic acid
D. alpha-aminoadipic acid
E. aminoacetic acid
#
88) Natural penicillins in industry are obtained by the method of microbiological synthesis. An obligatory component is a precursor substance, the chemical structure of which is similar to the corresponding radical of the antibiotic in position 6. In the production of phenoxymethylpenicillin, the precursor serves as:
A. beta-dimethylcysteine
B. valine
C. phenoxyacetic acid
D. alpha-aminoadipic acid
E. aminoacetic acid
#
89) A chemist-analyst of the laboratory performs quantitative determination of the amount of penicillins in benzylpenicillin sodium salt using the iodometric method. what indicator does it use?
A. starch
B. phenolphthalein
C. potassium chromate
D. methyl orange

E. methyl red
#
90) Which of the indicated penicillins can be identified by the reaction with ninhydrin?
A. ampicillin
B. benzylpenicillin
C. phenoxymethylpenicillin
D. oxacillin
E. carbenicillin
#
91) Indicate which of the indicated penicillins contains the isoxazole cycle:
A. oxacillin
B. ampicillin
C. phenoxymethylpenicillin
D. benzylpenicillin
E. carfecillin
#
92) Specify the starting compound for semi-synthetic penicillins:
A. 6-aminopenicillanic acid
B. clavulanic acid
C. penicilloic acid
D. penaldic acid
E. 7-aminocephalosporanic acid
#
93) A specialist confirms the presence of a sodium cation in ampicillin sodium salt by the appearance of a white precipitate with the solution:
A. potassium pyroantimonate
B. potassium dichromate
C. potassium permanganate
D. potassium nitrate
E. potassium chloride
#
94) Semi-synthetic penicillins include:
A. ampicillin
B. 6-aminopenicillanic acid
C. benzylpenicillin
D. phenoxymethylpenicillin
E. clavulanic acid
#

95) Specify the reaction by which the novocaine salt of benzylpenicillin can be identified:
A. detection of organically bound sulfur
B. on the primary aromatic amino group
C. with chromotropic acid
D. with sodium acetate
#
96) The β-lactamide group includes:
A. kanamycin sulfate
B. Azlocillin sodium salt
C. amikacin sulfate
D. gentamicin sulfate
E. chloramphenicol
#
97) Phenoxymethylpenicillin can be distinguished from benzylpenicillin sodium salt by:
A. reactions with chromotropic acid
B. appearance
C. solubility in water
D. hydroxam test
E. detection reactions of organically bound sulfur
#
98) All methods can be used for quantitative determination of oxacillin sodium salt, except:
A. neutralization
B. UV spectrophotometry
C. photoelectrocolorimetry (after the formation of iron (III) hydroxamate)
D. complexonometry
E. liquid chromatography
#
99) A β-lactam antibiotic that gives a ninhydrin test:
A. tetracycline
B. amoxicillin
C. streptocide
D. rifampicin
E. carfecillin
#
100) Natural penicillins include:
A. benzylpenicillin sodium salt

B. phenoxymethylpenicillin
C. ampicillin
D. oxacillin
E. carbenicillin sodium salt
#
101) The antibacterial activity of penicillins is due to:
A. the presence of a thiazolidine ring
B. the presence of a β-lactam cycle
C. spatial configuration of molecules
D. by the presence of two methyl groups
E. a sulfur heteroatom
#
102) Which of the listed drugs is acid-resistant?
A. phenoxymethylpenicillin
B. benzylpenicillin sodium salt
C. benzylpenicillin novocaine salt
D. benzylpenicillin potassium salt
#
103) Which of the drugs listed below is slightly soluble in water?
A. carfecillin sodium salt
B. benzylpenicillin novocaine salt
C. benzylpenicillin potassium salt
D. benzylpenicillin sodium salt
#
104) Molecules of penicillins contain asymmetric carbon atoms:
A. in positions 2,3,5
B. in provisions 5,6
C. in provisions 3,5,6
D. in provisions 2,3,6
E. in positions 3,5,7
#
105) Which reaction is not characteristic of ampicillin?
A. maltol test
B. hydroxam test
C. with Marqui's reagent
D. with ninhydrin
E. with chromotropic acid
#
106) Under the action of the penicillinase enzyme:

A. the thiizolidine cycle
B. the β-lactam cycle is destroyed
C. the radical in position 6 is cleaved off
D. the radical in position 2 is cleaved off
E. the radical in position 3 is cleaved off
#
107) What are the properties of penicillins?
A. the main ones
B. acidic
C. amphoteric
#
108) The pharmacist-analyst of the pharmacy performs the identification of oxacillin sodium salt. As reagents, he uses a solution of hydroxylamine hydrochloric acid in the presence of a solution of sodium hydroxide and a solution of copper nitrate. What structural fragment of the drug molecule is identified using these reagents?
A. β-lactam cycle
B. thiazolidine cycle
C. isoxazole cycle
D. phenyl radical
E. carboxyl group
#
109) Semi-synthetic penicillin is not:
A. oxacillin sodium salt
B. carfecillin sodium salt
C. Azlocillin sodium salt
D. phenoxymethylpenicillin
E. ampicillin
#
110) For the quantitative determination of benzylpenicillin sodium salt, the method is not used:
A. complexonometry
B. iodometry
C. microbiological
D. liquid chromatography
#
111) Indicate the method of quantitative determination by which the SPhU recommends to quantitatively determine natural (benzylpenicillin sodium salt) and semi-synthetic penicillins (ampicillin, amoxicillin and their salts):
A. liquid chromatography

B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography
#
112) Indicate the reagent that, in accordance with the requirements of the SPhU, identifies natural (benzylpenicillin sodium salt) and semi-synthetic penicillins (ampicillin, amoxicillin):
A. Markey's reagent
B. Nessler's reagent
C. solution of hydroxylamine hydrochloric acid, iron (III) sulfate
D. sulfuric acid
E. copper (II) sulfate solution
#
113) Specify the method by which SPhU recommends determining concomitant impurities in natural (benzylpenicillin sodium salt) and semi-synthetic penicillins (ampicillin, amoxicillin):
A. liquid chromatography
B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography
#
114) Specify which heterocycle is the basis of lincosamide antibiotics:
A. **pyrrolidine (tetrahydropyrrol**)
B. pyrazole
C. thiophene
D. pyrimidine
E. imidazole
#
115) Specify the group of microorganisms on which lincosamide antibiotics have a bacteriostatic effect:
A. gram positive
B. gram negative
C. brucelli
D. salmonella
E. Shigella
#

116) Specify the method of quantitative determination by which the SPhU recommends quantifying lincomycin hydrochloride:

A. gas chromatography
B. liquid chromatography
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography

#

117) Indicate the set of reagents that, in accordance with the requirements of the Federal Drug Administration, identify lincomycin hydrochloride:

A. hydrochloric acid, sodium carbonate, sodium nitroprusside
B. hydrochloric acid, sodium nitrite, alkaline β-naphthol solution
C. nitric acid, alcoholic solution of potassium hydroxide
D. solution of hydroxylamine hydrochloric acid, iron (III) sulfate
E. bromine water, ammonia solution

#

118) What is the basis of the chemical structure of cephalosporins:

A. 7-ACA (7-aminocephalosporanic acid)
B. 8-ACA (8-aminocephalosporanic acid)
C. 6-ACA (6-aminocephalosporanic acid)
D. 5-ACA (5-aminocephalosporanic acid)
E. 4-ACA (4-aminocephalosporanic acid)

#

119) Indicate which of the listed antibiotics is a derivative of 7-aminocephalosporanic acid (7-ADCA)?

A. cephalexin
B. methacycline hydrochloride
C. griseofulvin
D. ampicillin trihydrate
E. streptomycin sulfate

#

120) In a chemical analytical laboratory, an analyst conducts an analysis of the antibiotic cephalothin. According to the chemical structure, this substance can be classified as an antibiotic:

A. aromatic series
B. alicyclic series
C. aliphatic series
D. polypeptide antibiotics
E. heterocyclic series

#

121) A chemist identifies cephalosporins with formaldehyde in the presence of sulfuric acid. What color does ceftriaxone sodium salt give?

A. greenish yellow

B. blue

C. light yellow

D. bright yellow

E. black

#

122) Cephalexin gives a positive ninhydrin test because it contains the residue in the molecule:

A. phenoxyacetic acid

B. phenylaminoacetic acid

C. phenylacetic acid

D. dimethoxyphenylacetic acid

#

123) The structural basis of cephalosporins is:

A. 6-membered thiazolidine and β-lactam ring

B. thiazine and lactam cycle

C. dihydrothiazine and β-lactam cycle

D. trihydrothiazine and lactam cycle

E. thiazine and lactone cycle

#

124) The difference between cephalosporins and penicillins:

A. effective against gram-negative and gram-positive microorganisms

B. effective against streptococci

C. the β-lactam ring is absent in the structure

#

125) As a result of hydrolytic cleavage of cephalothin, the following are formed:

A. 7-ACA

B. 6-APA

C. aminophenylacetamide

D. phenyl-2-acetic acid

E. acetic acid

#

126) Factors that determine the antibacterial activity of cephalosporins do not include:

A. the presence of a β-lactam cycle

B. the nature of the substitute in clause 6

C. inductive effect of the acyl substituent
D. **the presence of a thiazolidine ring**
E. steric effect of the molecule
#
127) As a result of hydrolytic cleavage of cephalexin, the following is formed:
A. 7-ACA
B. **7-ADCA**
C. aminophenylacetamide
D. thienyl acetic acid
E. acetic acid
#
128) Cephalosporins are identified by the reaction of obtaining:
A. **hydroxamate**
B. maltol
C. nitro derivatives
D. iodine derivatives
E. murexide
#
129) The general method of quantitative determination of cephalosporins includes:
A. **iodometry (back titration)**
B. complexonometry
C. acidimetry
D. iodometry (direct titration)
E. acidimetry (substitute titration)
#
130) The β-lactamide group includes:
A. kanamycin sulfate
B. **cephalexin**
C. amikacin sulfate
D. gentamicin sulfate
E. chloramphenicol
#
131) Organically bound sulfur in cephalosporin antibiotics after alloying with caustic alkalis is determined by the reaction:
A. with ammonium oxalate solution
B. **with sodium nitroprusside solution**
C. with sodium sulfate solution
D. with potassium chloride solution
E. with potassium permanganate solution

#

132) The hydroxam test allows you to confirm the presence of cephalosporins in the molecule:

A. phenyl radical

B. **β-lactam cycle**

C. thiazolidine cycle

D. methyl groups

E. ethyl group

#

133) Indicate which of the indicated cephalosporins contains a furan residue:

A. cefuroxime

B. cefazolin

C. ceftriaxone

D. cefotaxime

E. cephalothin

#

134) Indicate which of the indicated cephalosporins contains heterocycles of pyridine and thiophene:

A. **Cephaloridine**

B. cefazolin

C. ceftriaxone

D. cefotaxime

E. cephalothin

#

135) In industry, the source for obtaining acyl derivatives of 7-ACA is:

A. **cephalosporin C**

B. clavulanic acid

C. aminoadipic acid

D. 7-ADCA

E. penicillins

#

136) In industry, the source for obtaining acyl derivatives of 7-ADCA is:

A. **penicillins**

B. cephalosporin C

C. clavulanic acid

D. aminoadipic acid

E. 7-ACA

#

137) A specialist confirms the presence of a sodium cation in ceftriaxone sodium

salt by the formation of a white precipitate with a solution:

A. potassium pyroantimonate
B. potassium dichromate
C. potassium permanganate
D. potassium nitrate
E. potassium chloride

#

138) Which of the indicated cephalosporins can be identified by reaction with ninhydrin?

A. cephalexin
B. ceftriaxone
C. cephalothin
D. Cephapirin
E. cefadroxil

#

139) The pharmacist-analyst proves the presence of β-lactam cycle antibiotics in the structure of the cephalosporin series by means of the formation reaction:

A. metal hydroxamates
B. indophenol
C. azomethine dye
D. thalleiochina
E. murexide

#

140) Indicate which of the listed drugs, due to the presence of a β-lactam cycle in its structure, gives a positive reaction with a solution of hydroxylamine hydrochloride in the presence of sodium hydroxide and the subsequent addition of a solution of iron (III) chloride:

A. cephalothin
B. monomycin sulfate
C. streptomycin sulfate
D. tetracycline hydrochloride
E. papaverine hydrochloride

#

141) The instability of cephalosporins is caused, first of all, by the presence in their structure of:

A. β-lactam cycle
B. urea group
C. carboxyl group
D. methyl groups
E. thiazolidine cycle

#
142) The pharmacist-analyst of the pharmacy conducts the identification of ceftriaxone sodium salt. He uses a solution of hydroxylamine hydrochloric acid in the presence of a solution of sodium hydroxide and a solution of copper nitrate as reagents. What structural fragment of the drug molecule is detected using these reagents?

A. β-lactam cycle
B. thiazolidine cycle
C. isoxazole cycle
D. phenyl radical
E. urea group

#
143) Specify which of the antibiotics belongs to cephem derivatives?

A. azlocillin sodium salt
B. chloramphenicol stearate
C. cephalothin
D. azithromycin
E. synthomycin

#
144) Indicate which of the antibiotics belongs to the derivatives of 7-aminocephalosporanic acid (7-ACA):

A. cefotaxime
B. chloramphenicol stearate
C. cephalexin
D. azithromycin
E. Synthomycin

#
145) Indicate which of the antibiotics belongs to the derivatives of 7-aminodesacetoxycephalosporanic acid (7-ADCA):

A. cephalexin
B. cefotaxime
C. chloramphenicol stearate
D. azithromycin
E. Synthomycin

#
146) A control and analytical laboratory specialist confirms the presence of a sodium cation in the preparation "Ceftriaxone sodium salt" by reaction with a solution of potassium pyroantimonate by the appearance of:

A. green sediment
B. yellow sediment
C. blue sediment

D. white sediment
E. purple sediment
#
147) Which of the following reactions is most specific for streptomycin sulfate?
A. formation of copper hydroxamate
B. reaction with Fehling's reagent
C. reaction with diazonium salts
D. formation of iron (III) maltate
E. ozazone formation
#
148) The structure of the streptomycin sulfate antibiotic contains an aglycon that contains guanidine residues. In order to identify the specified functional groups, the pharmacist-analyst needs to carry out a reaction:
A. with a solution of sodium hydroxide, bromine water andα-naphthol (Sakaguchi reaction)
B. with a solution of iron (III) chloride
C. with Fehling's reagent
D. with concentrated sulfuric acid and vanillin
E. with Marqui's reagent
#
149) In the chemical-analytical laboratory, the analyst conducts the analysis of medicinal substances of antibiotic-glycosides. Which of the following compounds belongs to this type?
A. streptomycin sulfate
B. tetracycline hydrochloride
C. phenoxymethylpenicillin
D. chloramphenicol
E. cefuroxime
#
150) At a pharmaceutical company, a pharmacist-analyst conducts an analysis of streptomycin sulfate. What quantitative method can be used to determine this substance?
A. nitritometry
B. acidimetry
C. complexonometry
D. photocolorimetry
E. bromatometry
#
151) At a pharmaceutical enterprise, a pharmacist-analyst analyzes aminoglycoside antibiotics. What color is formed when kanamycin monosulfate interacts with ninhydrin?

A. purple
B. black
C. white
D. yellow
E. green
#
152) In the laboratory, the quantitative determination of streptomycin sulfate is carried out by the method based on the maltol sample. What is this method?
A. potentiometry
B. polarography
C. polarography
D. photocolorimetry
E. fluorimetry
#
153) Ammonia is formed during alkaline hydrolysis:
A. streptomycin sulfate
B. kanamycin sulfate
C. oxacillin sodium salt
D. phenoxymethylpenicillin
E. benzylpenicillin potassium salt
#
154) The reaction with orcin gives:
A. streptomycin sulfate
B. cephalexin
C. phenoxymethylpenicillin
D. cephalothin sodium salt
E. benzylpenicillin potassium salt
#
155) The presence of an aldehyde group in the sugar part of streptomycin sulfate is confirmed by the reaction:
A. with picric acid
B. with barium chloride solution
C. withα- naphthol and sodium hypobromide
D. with Fehling's reagent
E. with formaldehyde solution
#
156) Gravimetric determination of sulfates in gentamicin sulfate is based on the reaction of precipitation of sulfates with salts:
A. ammonium
B. barium
C. sodium

D. potassium
E. lithium
#
157) Which antibiotic chemically belongs to glycosides:
A. tetracycline hydrochloride
B. doxycycline
C. benzylpenicillin sodium salt
D. carfecillin
E. gentamicin sulfate
#
158) Which of the listed antibiotics can be identified by the maltol formation reaction?
A. streptomycin sulfate
B. doxycycline hydrochloride
C. amoxicillin
D. lincomycin hydrochloride
E. kanamycin monosulfate
#
159) Specify an antibiotic that is a mixture of several substances:
A. neomycin sulfate
B. gentamicin sulfate
C. amikacin sulfate
D. erythromycin
E. cefuroxime
#
160) The salt of a nitrogen-containing organic base is:
A. streptomycin sulfate
B. phenoxymethylpenicillin
C. oxacillin sodium salt
D. cephalothin sodium salt
E. erythromycin Z
#
161) The medicinal substance is white in color, soluble in water, when heated with sodium hydroxide and the subsequent addition of hydrochloric acid and iron (III) chloride forms a purple color:
A. streptomycin sulfate
B. amoxicillin trihydrate
C. benzylpenicillin sodium salt
D. carbenicillin disodium salt
#
162) The sugar part of kanamycin is:

A. 6-amino-6-deoxy-D-glucose
B. N-methyl-α-glucosamine
C. α-streptosis
D. D-glucosamine
E. 3-amino-6-deoxy-D-glucose
#
163) According to the chemical structure, the glycoside is:
A. amikacin sulfate
B. cephalexin
C. carbenicillin disodium salt
D. phenoxymethylpenicillin
E. cefuroxime
#
164) For the quantitative determination of gentamicin sulfate, in accordance with the requirements of the SPhU, use:
A. microbiological method
B. method of spectrophotometry in the UV region
C. liquid chromatography
D. gravimetric method
E. photocolorimetry
#
165) The possibility of identifying streptomycin sulfate by the reaction of the maltol sample is due to the presence in its structure:
A. of L-streptose residue
B. of the N-methylglucosamine residue
C. guanidine groups
D. aldehyde group
E. sulfate ion
#
166) The sugar part of streptomycin is:
A. **streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose**)
B. 6-amino-6-deoxy-D-glucose
C. deoxystreptamine
D. streptidine
E. 3-amino-6-deoxy-D-glucose
#
167) According to the nature of the antimicrobial action of streptomycin sulfate, antibiotics belong to:
A. have a bacteriostatic effect (bacteria are alive, but unable to reproduce)
B. have a bactericidal effect (bacteria are killed, but physically continue to be present in the environment)

C. have a bacteriolytic effect (bacteria are killed, and bacterial cell walls are destroyed)
#
168) For the quantitative determination of streptomycin sulfate, in accordance with the requirements of the SPhU, use:
A. microbiological method
B. method of spectrophotometry in the UV region
C. liquid chromatography
D. gravimetric method
E. photocolorimetry
#
169) According to the requirements of the SPhU, one of the methods for identifying kanamycin sulfate is the determination of the melting point:
A. kanamycin picrate
B. kanamycin bases
C. kanamycin hydrolysis products
D. kanamycin hydrochloride
E. kanamycin tartrate
#
170) Gentamicin sulfate is a mixture of antibiotic sulfates produced by Micromonospora purpurea. Specify the method recommended by the Federal Drug Administration for determining the component composition of this drug:
A. liquid chromatography
B. gas chromatography
C. iodometry
D. UV spectrophotometry
E. microbiological method
#
171) The mechanism of antimicrobial action of streptomycin sulfate is based on:
A. disruption of protein synthesis at the level of ribosomes
B. disruption of cell wall synthesis
C. violations of the permeability of the cytoplasmic membrane
D. RNA synthesis disorders
E. denaturation of microorganism proteins
#
172) Specify the functional group in the structure of streptomycin sulfate, which has reducing properties:
A. aldehyde group
B. carboxyl group
C. keto group
D. methyl group

#
173) Choose an antibiotic with a polypeptide structure from the following antibiotics:
A. streptomycin sulfate
B. Gramicidin C
C. penicillin V
D. chloramphenicol
E. ceftriaxone
#
174) Which of the listed antibiotics is based on a macrocyclic lactone ring?
A. streptomycin sulfate
B. benzylpenicillin sodium salt
C. gentamicin sulfate
D. erythromycin
E. Levomycetin
#
175) Amphotericin B is highly effective:
A. antimalarial agent
B. antiprion antibiotic
C. antifungal antibiotic
D. antitumor antibiotic
E. antituberculosis antibiotic
#
176) Specify which of the antibiotics is an antitumor drug?
A. olivomycin
B. ampicillin sodium salt
C. streptomycin sulfate
D. Gramicidin C
E. erythromycin
#
177) At a pharmaceutical company, a pharmacist-analyst analyzes macrolide antibiotics. What is the basis of the structure of these compounds?
A. aromatic core
B. β-lactam cycle
C. oxazolidone cycle
D. macrocyclic lactone ring
E. dihydrothiazone cycle
#
178) Which of the following drugs belongs to polypeptide antibiotics?
A. polymyxin
B. erythromycin phosphate

C. midecamycin
D. lincomycin hydrochloride
E. gentamicin sulfate
#
179) According to the chemical classification, gramicidin and polymyxins belong to the class:
A. antibiotics of alicyclic structure
B. glycoside antibiotics
C. polypeptide antibiotics
D. antibiotics of heterocyclic structure
#
180) Indicate the method by which, in accordance with the requirements of the Federal Drug Administration, azithromycin is identified:
A. IR spectrophotometry
B. UV spectrophotometry
C. thin layer chromatography
D. interaction with p-dimethylaminobenzaldehyde in a hydrochloric acid environment
E. interaction with Fehling's reagent
#
181) Indicate the method of quantitative determination by which the State Federal Drug Administration recommends determining concomitant impurities and the quantitative content of azithromycin:
A. liquid chromatography
B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography
#
182) Indicate the reagent by which, in accordance with the requirements of the SPhU, rifampicin is identified:
A. ammonium persulfate, phosphate buffersolution
B. Nessler's reagent
C. solution of hydroxylamine hydrochloric acid, iron (III) sulfate
D. sulfuric acid
E. copper (II) sulfate solution
#
183) Specify the method of quantitative determination by which the SPhU recommends determining the quantitative content of rifampicin:
A. UV spectrophotometry
B. iodometry

C. neutralization
D. IR spectrophotometry
E. thin layer chromatography
#
184) When identifying doxorubicin hydrochloride, the analyst performed a reaction on the ionic composition. What ions will the substance have a positive reaction to?
A. SO_4^{2-}
B. $\mathbf{Cl^-}$
C. Na^+
D. Ca^{2+}
E. Hg^{2+}
#
185) Specify the method of quantitative determination by which the SPhU recommends to quantitatively determine doxorubicin hydrochloride:
A. liquid chromatography
B. iodometry
C. neutralization
D. UV spectrophotometry
E. thin layer chromatography
#
186) What amino sugar does erythromycin contain:
A. desosamine (3-dimethylamino-4,6-dideoxypyranose)
B. deoxystreptamine
C. streptidine
D. 3-amino-6-deoxy-D-glucose
E. streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose)
#
187) Choose a polyene antibiotic from the following antibiotics:
A. streptomycin sulfate
B. Gramicidin Z
C. penicillin V
D. nystatin
E. ceftriaxone
#
188) Which of the following drugs belongs to polypeptide antibiotics?
A. polymyxin
B. erythromycin phosphate
C. midecamycin
D. amphotericin
E. gentamicin sulfate
#

189) What aglycon does nystatin contain:

A. nystatinolide

B. deoxystreptamine

C. streptidine

D. 3-amino-6-deoxy-D-glucose

E. streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose)

#

190) What amino sugar does nystatin contain:

A. mycosamine (3,6-dideoxy-3-amino-Dmannose)

B. deoxystreptamine

C. streptidine

D. 3-amino-6-deoxy-D-glucose

E. streptobiosamine disaccharide (N-methyl-α-glucosamine and L-streptose)

#

191) Specify the factor that does not cause a change in the structure of polyene antibiotics, and, as a result, a loss of antibiotic activity:

A. humidity

B. light

C. high temperature

D. air oxygen

E. oxidizers

#

192) Specify which of the antibiotics is a quinoline-5,8-dione derivative?

A. Bruneomycin

B. ampicillin sodium salt

C. streptomycin sulfate

D. Gramicidin Z

E. erythromycin

#

193) Macrolide antibiotics - erythromycin and azithromycin are widely used in medical practice. Specify the spectrum of microbiological activity of these drugs:

A. broad-spectrum antibiotics

B. act mainly on gram-positive bacteria

C. act mainly on gram-negative bacteria

D. anticancer antibiotics

E. antifungal antibiotics

#

194) According to the mechanism of antimicrobial action, polymyxins belong to antibiotics that violate:

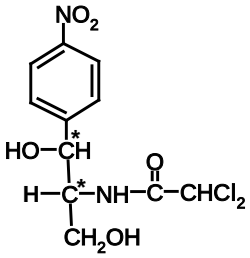
A. synthesis of the cell wall of a microbial cell

B. permeability of the cytoplasmic membrane of a microbial cell

C. RNA synthesis of a microbial cell
D. protein synthesis at the level of ribosomes of a microbial cell
E. DNA synthesis of a microbial cell
#
195) A feature of the chemical structure of anticancer antibiotics is the presence in their molecules:
A. chromoform groups of the quinoid structure
B. macrocyclic lactone ring
C. polyene chain coupling
D. thiazolidine cycle
#
196) Specify antibiotics that are active mainly against gram-negative microorganisms:
A. tetracyclines
B. aminoglycosides
C. natural penicillins
D. polypeptides
E. macrolides

4.3. Situational tasks:

1) Describe the cupriiodometric method for quantitative determination of chloramphenicol. Give the reaction equations, the formula for calculating the quantitative content.
2) Describe the reaction of chloramphenicol with sodium hydroxide. Explain how this reagent can be used to prove the presence of an aromatic nitro group, an amide group, and an aliphatic fragment in the structure of the drug?
3) Write the spatial isomers of chloramphenicol and explain which substances belong to the threo and erythro series. Indicate which of these isomers is used in medicine.
4) Write the structural formula of chloramphenicol and characterize the effect of stereoisomerism on the pharmacological activity of this compound.
5) Give the reactions and list the physicochemical properties that allow you to differentiate chloramphenicol, chloramphenicol stearate and chloramphenicol succinate soluble.
6) Give the equation of the reactions of the hydroxam test for chloramphenicol and chloramphenicol stearate.
7) Based on the chemical structure of chloramphenicol, give the reaction equations of various methods of quantitative determination of the drug.
8) Give methods for identifying the organically bound halogen atom in the chloramphenicol molecule.
9) When evaluating the quality of tablets with the specified substance:



a discrepancy in their appearance was noted in the "Description" section - the tablets were greenish-yellow in color. Give justification for the reasons for the change in the quality of the tablets according to this indicator. Suggest other tests characterizing the quality of tablets. Give reactions to establish authenticity and give justification for the methods of quantitative determination of medicinal substances in substances and tablets, give calculation formulas.

10) When assessing the quality of the doxycycline hydrochloride substance in samples of several series, the appearance did not meet the requirements of the Ministry of Internal Affairs under the "Description" section - the powder was wet and yellow-brown in color. What processes could cause these changes? Name these products.

11) For the quantitative analysis of the substance oxytetracycline hydrochloride, the method of acid-base titration in non-aqueous solvents can be recommended. Based on the chemical structure and acid-base properties of the proposed drug, give a justification for the use of this method in quality assessment:

a) According to the structure, characterize the acid-base properties;

b) Give a rationale for choosing a protogenic solvent for the quantitative determination of the drug in non-aqueous solvents. Write the reaction equation, specify the titration conditions;

c) Specify the additional reagent that is added during the titration of the drug. Write the reaction diagram.

12) When analyzing the substance of semi-synthetic tetracyclines, the analyst conducted a reaction to form anhydro derivatives. Name the reagent that he needs to use for this.

13) Determine the essence of photocolorimetric, polarimetric analysis in the quantitative assessment of drugs of this group?

14) Determine the interrelationship of sources and methods of obtaining with the problems of the research of medicinal substances (the content of initial, intermediate and related products, the formation of quality indicators).

15) According to the chemical properties, explain the choice of the method of iodometric quantitative determination of the amount of penicillins:

a) Consider the chemical structure and properties of medicinal products and explain their ability to interact with iodine solution in an alkaline environment;

b) State the reactions of quantitative iodometric determination of drugs;

c) Give the formula for calculating the content of medicinal substances in preparations.

16) Give the reaction equation for the quantitative determination of the amount of penicillins in benzylpenicillin sodium salt. Explain the peculiarity of performing a control experiment. Using the reference literature, find the value of the equivalent of a standard sample of the sodium salt of benzylpenicillin per 1 ml of a 0.02 N (0.01 M) iodine solution, if the temperature of the reaction medium is 130C, 180C, 200C, 250C, respectively.

17) Explain the necessity and peculiarities of conducting a control experiment when determining the amount of penicillins by the iodometric method.

18) Describe the method of formol titration of medicinal substances using the example of ampicillin. Why not use the classic method of neutralization for this drug? Give the reaction equations, the formula for calculating the quantitative content.

19) What structural features of natural penicillins determine their lability in relation to acids and bases? How are these features used to identify benzylpenicillin preparations?

20) Describe the group of semi-synthetic penicillins and name their main representatives. State the advantages of semi-synthetic penicillins compared to natural ones.

21) Provide a scheme for the synthesis of ampicillin, indicating the chemical names of starting substances, intermediate and final products; state its pharmacological action.

22) Describe the iodometric method of quantitative determination of the amount of penicillins using the example of phenoxymethylpenicillin. What factors affect the value of the equivalent? Give the reaction equations, the formula for calculating the quantitative content.

23) Describe the photoelectrocolorimetric method of quantitative determination of medicinal substances using the example of benzylpenicillin sodium salt (after carrying out the reaction of the formation of iron (III) hydroxamate).

24) Describe the spectrophotometric method of quantitative determination of medicinal substances using an examplenatural and semi-synthetic penicillins. Explain the need to add imidazole and mercury(II) chloride.

25) Explain the features of the quantitative determination of dibenzylethylenediamine in benzathine of benzylpenicillin. Give the reaction equations, the formula for calculating the quantitative content.

26) What structural fragments of cephalexin determine its amphoteric properties?

27) Consider the regenerative properties of cephalexin and give a rationale for its interaction with Fehling's reagent. Specify the visible result and write the reaction schemes.

28) What structural features of cephalosporins determine their lability in relation to acids and bases? How are these features used to identify cephalosporin antibiotics?

29) Give the equation for the hydroxam test reaction for cephalothin.

30) Based on the chemical structure and properties of functional groups, justify the chemical properties of cephalosporin antibiotics (cephalexin, cephalothin). Confirm the answer with the chemistry of the reactions.

31) What, besides chemical, methods exist for determining the quality of antibiotics? Justify each of them, show the possibility of use for the purposes of qualitative and quantitative analysis and purity control. Give the concept of units of antibiotic activity (UA).

32) The presence of an aldehyde group in the sugar part of streptomycin sulfate is confirmed by reaction with Fehling's reagent. Write the chemistry of the selected reaction, indicate the conditions of its implementation and the analytical effect.

33) What structural features of streptomycin sulfate are used for its quantitative determination by the photoelectrocolorimetric method? Give the corresponding reaction equations, the formula for calculating the quantitative content.

34) Describe the dosage forms of streptomycin, their pharmacological effects, advantages and disadvantages compared to streptomycin sulfate.

35) One of the identification reactions for streptomycin sulfate is the Sakaguchi reaction. What functional groups in the structure of the drug does it allow to determine? Write the chemistry, indicate the conditions and analytical effect.

36) What, besides chemical, methods exist for determining the quality of antibiotics? Justify each of them, show the possibility of use for the purposes of qualitative and quantitative analysis and purity control.

37) Give the concept of units of antibiotic activity (OU).

38) On the basis of the chemical structure and properties of functional groups, justify the chemical properties of antibiotics of the group of macrolide antibiotics. Confirm the answer with the chemistry of the reactions.

39) Consider the structural formulas of macrolide antibiotics: erythromycin, midekamycin, azithromycin. Specify the relationship between the chemical structure and the pharmacological effect of drugs.

40) Describe the group of polyene antibiotics: features of structure, analysis, storage.

4.4. Tasks:

1) When analyzing the dosage form of the composition:

Levomycetin 2.0

Novocaine 1.0

Ethanol 70% to 100.0

4.59 ml of 0.02 M sodium nitrite solution (Kp = 1.0000) was spent on titration of the amount of novocaine and reduced chloramphenicol; 1.85 ml of 0.02 M sodium nitrite solution was spent on the same volume of the dosage form without recovery. Calculate the content of novocaine and chloramphenicol in the medicinal form. The volume of the dosage form taken for analysis is 1 ml. M.m. Levomycetin = 323.1 g / mol, M.M. of novocaine = 272.81g/mol.

2) Calculate the percentage of chloramphenicol in an aqueous solution, if A = 0.59 when measured on a spectrophotometer (cuvette 10 mm), $E_{1\text{cm}}^{1\%}$ = 295.

3) During the quantitative determination of chloramphenicol, it was established that its content is 99.0%. What volume of 0.1 M sodium nitrite solution (Kp = 1.0000) was used for the titration of 0.3310 g of chloramphenicol? M.m. chloramphenicol = 323.1 g/mol.

4) The angle of rotation of a 5% solution of chloramphenicol in ethanol is + 10o. Calculate the specific rotation, if the measurement was carried out in a tube 10 cm long.

5) Calculate the percentage of chloramphenicol from the value of the specific absorption index at a wavelength of 278 nm, if the optical density of a 0.002% aqueous solution at the specified wavelength and a cuvette thickness of 9.8 mm is 0.591.

6) Calculate the content of chloramphenicol (g) in the dosage form:

Levomycetin solution 0.01% - 10 ml

Sodium chloride 0.09

if 5.0 ml of the tested solution after reconstitution with zinc dust in the presence of concentrated hydrochloric acid is brought up to the mark in a volumetric flask with a capacity of 25.0 ml (solution A). The optical density of the solution obtained by appropriate processing of 1.5 ml of solution A and bringing it to a total volume of 10.0 ml at a wavelength of 364 nm in a cuvette with a layer thickness of 5 mm is 0.232; the specific absorption index of the standard solution of chloramphenicol under the same conditions is 1719.0.

7) Calculate the content of chloramphenicol in the dosage form of the composition:

Levomycetin solution 0.015% - 10 ml

Sodium chloride 0.09

if the optical density of 10 ml of a solution obtained from 1.5 ml of a 1: 5 dilution of the dosage form, measured at a wavelength of 364 nm in a cuvette with a layer thickness of 5 mm, is 0.430. The optical density of 10 ml of a standard solution

of chloramphenicol obtained from 1.5 ml of a 0.02% solution of chloramphenicol, measured under the same conditions, is 0.285.

8) Calculate the interval of possible values of the angle of rotation of a 5% solution of chloramphenicol (levomycetin) in 95% alcohol with a cuvette thickness of 25 cm, if the specific rotation according to the QMC has a value from + 15º to + 22º.

9) Calculate the percentage content of chloramphenicol (M.m. 323.13) in the preparation if 14.02 ml of 0.1 M sodium nitrite solution (Kp = 1.0020) was spent on the titration of a weight of 0.4590 g.

10) Calculate the volume of 0.1 M sodium nitrite solution (Kp = 1.0000), which will be used for the titration of 0.5025 g of chloramphenicol (M.m. 323.13), if its percentage content in the preparation is 98.5%.

11) Determine the mass fraction of chloramphenicol (M.m. 323.13) in the medicinal product, if 16.40 ml of 0.1 M sodium nitrite solution (Kp = 0.9928) was spent on the titration of 0.5234 g of chloramphenicol.

12) Determine the volume of 0.1 M sodium nitrite solution (Kp = 0.9875), which was spent on the titration of a weight of 0.4995 g of chloramphenicol (M.m. 323.13). The percentage content of chloramphenicol in the medicinal product is 98.60%.

13) Calculate the percentage concentration of an alcoholic solution of chloramphenicol if the specific rotation is 19o, the angle of rotation is 1.95. The length of the cuvette is 190.08 mm.

14) Determine the quality of one of the tetracycline derivatives by specific rotation, if the angle of rotation of a solution containing 0.25 g of the analyzed sample in 25 ml of a 0.01 M hydrochloric acid solution at a cuvette length of 10 cm is -2.68o. Weight loss during drying is 2.0%. Specific rotation in terms of dry matter of tetracycline hydrochloride from – 239o to – 258o; for tetracycline from -265o to -275o.

15) Calculate the approximate volume of the titrant - 0.1 mol/l perchloric acid solution (Kp = 0.9803) required for the titration of a weight of tetracycline hydrochloride weighing 0.5504 g. 1 ml of a 0.1 M perchloric acid solution corresponds to 0.04809 g of tetracycline g / x, which should be at least 99.0% in the preparation.

16) Calculate the specific absorption coefficient ($A_{1\,см}^{1\%}$) of tetracycline, if 0.05000 g of the drug was taken, dissolved in 4 ml of 0.01 M hydrochloric acid solution in a 250 ml volumetric flask, brought to the mark with water, mixed. 5 ml of this solution was added to a volumetric flask with a volume of 50 ml, brought to the mark with water, mixed. The optical density (Ax) was determined at a

wavelength of 380 nm in a cuvette with a layer thickness of 10 mm. It is equal to 0.42. The concentration of tetracycline in the drug is 98.82%.

17) Calculate the percentage concentration (C%) of a solution of tetracycline hydrochloride, if you take 0.05024 g of the drug (exactly weighed), dissolve it in 2 ml of a 0.01 M solution of hydrochloric acid in a 250 ml volumetric flask, bring it up to the mark with water, and mix. 10 ml of this solution was added to a volumetric flask with a volume of 100 ml, brought to the mark with water, mixed. The optical density (Ax) was determined at a wavelength of 380 nm in a cuvette with a layer thickness of 1 cm, it is equal to 0.78. Specific absorption index ($A_{1\,см}^{1\%}$) is equal to 389.

18) Calculate the percentage content of tetracycline (M.M. = 444.40), if 11.0 ml of 0.01 M perchloric acid solution (Kp = 0.9904) was spent on the titration of 0.0543 g of the substance. Loss in mass during drying is 8%.

19) Calculate the specific rotation of benzylpenicillin potassium salt, if the angle of rotation of the 2% solution is $+8.8^{o}$ at a layer thickness of 15 cm.

20) Calculate the concentration of oxacillin sodium salt if the value of the specific rotation is $+185^{o}$, the thickness of the layer is 9 cm, the angle of rotation is $+1.7^{o}$.

21) 0.1086 g of phenoxymethylpenicillin was dissolved in 4 ml of 5% sodium bicarbonate solution in a volumetric flask with a capacity of 500 ml and the volume of the solution was brought up to the mark with water. The optical density of the obtained solution is 0.740 at a wavelength of 286 nm and a layer thickness of 10 mm. Calculate the specific absorbance of phenoxymethylpenicillin.

22) In benzylpenicillin sodium salt, the amount of penicillins is 94.5%. Calculate the volume of a 0.01 M iodine solution (Kn = 1.0000), which will be used for the titration of a measure of a medicinal substance of 0.0602 g. The measure was dissolved in water in a volumetric flask with a capacity of 100 ml, the volume of the solution was brought up to the mark with water and 5 ml of the resulting dilution was taken for analysis. The value of the equivalent in g of a standard sample of benzylpenicillin at 200C is 0.0004055g. C = 1,000

23) In the quantitative determination of benzylpenicillin potassium salt by the iodometric method, 19.8 ml of 0.01 M sodium thiosulfate solution was used for the control experiment, and 14.3 ml of the same titrant was used for the titration of the tested drug (Kp = 0.9900). What is the percentage content of the drug, if T = 0.0004055 g / ml, a = 0.0503g, C = 1.045, dilution 1:20?

24) Give the reaction equation for quantitative determination of benzylpenicillin sodium salt by iodometry method. Calculate the percentage content of the drug, if a weight weighing 0.0612 g was dissolved and brought up to the mark with water

in a 100 ml volumetric flask. 20 ml of 0.01 M iodine solution (Kp = 1.0100), the excess of which in the main experiment was titrated with 11.6 ml of 0.01 M sodium thiosulfate solution (Kp = 1.0200), in the control experiment - 19.4 ml of the same titrant. The titer of benzylpenicillin sodium salt (21oC) is 0.0004000 g/ml. The moisture content of the analyzed substance is 0.5%. C = 1.00.

25) Give the reaction equation for the quantitative determination of benzylpenicillin potassium salt by the iodometric method. Calculate the content of the amount of penicillins (%) if a weight weighing 0.06024 g was dissolved and brought up to the mark with water in a volumetric flask with a capacity of 100.0 ml. 20 ml of a 0.01 M iodine solution (Кп = 0.9800) was added to a 5.0 ml aliquot, and 12.5 ml of a 0.01 M sodium thiosulfate solution (К п = 1 ,0100), in the control experiment - 19.2 ml of the same titrant. The moisture content of the analyzed sample is 0.8%. The titer of benzylpenicillin sodium salt (20^0C) is 0.0004055 g/ml. 1 mg of the sodium salt of benzylpenicillin corresponds to 1.045 mg of the potassium salt of benzylpenicillin.

26) Give the reaction equations for the quantitative determination of benzylpenicillin novocaine salt by iodometry. Calculate the content of the amount of penicillins (%) if the weight weighing 0.0809 g was dissolved and brought up to the mark with water in a volumetric flask with a volume of 200.0 ml. 20 ml of 0.01 M iodine solution (Kp = 1.0000) was added to a 10.0 ml aliquot, and 14.8 ml of 0.01 M sodium thiosulfate solution (Kp = 0, 9800), in the control experiment - 20.4 ml of the same titrant. The moisture content of the analyzed sample is 4.2%. The titer of benzylpenicillin sodium salt (15^0C) is 0.0004374 g/ml. 1 mg of sodium salt of benzylpenicillin corresponds to 1.652 mg of novocaine salt of benzylpenicillin.

27) Give the reaction equations for the quantitative determination of phenoxymethylpenicillin by the iodometric method. Calculate the content (%) if a weight weighing 0.0636 g was dissolved and brought up to the mark with water in a volumetric flask with a volume of 50.0 ml. 20 ml of 0.01 M iodine solution (K = 0.98) was added to a 2.5 ml aliquot, and 12.8 ml of 0.01 M sodium thiosulfate solution (Kp = 1, 0200), in the control experiment - 19.6 ml of the same titrant. The moisture content of the analyzed sample is 1.5%. The titer of phenoxymethylpenicillin (18^0C) is 0.0004367 g/ml. C = 1.00.

28) Calculate the content of benzylpenicillin sodium salt in the vial in % and OD, if a weight of the drug weighing 0.0612 g was placed in a volumetric flask with a capacity of 100.0 ml, dissolved, and brought up to the mark with water. To an aliquot with a volume of 5.0 ml, 20 ml of a 0.01 M iodine solution (Kp = 1.0100) was added, and 11.6 ml of a 0.01 M sodium thiosulfate solution (Kp = 1, 0200). In the control experiment, 19.4 ml of the same titrant was used. The weight of the

drug in the vial is 0.3605 mg. The titer of my substance (at the test temperature of 21^0C) is 0.0004000 g/ml. 1 unit corresponds to 0.0005988 mg of chemically pure sodium salt of benzylpenicillin.

29) Calculate the content of the potassium salt of benzylpenicillin in the vial in % and OD, if a weight weighing 0.06024 g was placed in a volumetric flask with a capacity of 100.0 ml, brought up to the mark with water. Along with other necessary reagents, 20.0 ml of 0.01 M iodine solution (Kp = 0.9800) was added to an aliquot with a volume of 5.0 ml. 12.5 ml of 0.01 M sodium thiosulfate solution (K n = 1.0200) was used to titrate the excess of the specified solution. 19.2 ml of the same titrant was used for the titration of the control experiment. The value of the equivalent of a standard sample of the sodium salt of benzylpenicillin at an experimental temperature of 20◦C is 0.0004055 g/ml. 1 mg of the standard sample of benzylpenicillin sodium salt corresponds to 1.045 mg of the amount of penicillins in terms of benzylpenicillin potassium salt. 1 unit corresponds to 0.0005988 mg of chemically pure sodium salt of benzylpenicillin. The weight of the drug in the vial is 0.3569 mg.

30) Calculate the % content of the amount of penicillins in benzylpenicillin of the potassium salt, if 19.8 ml of 0.01 mol / l sodium thiosulfate solution was used for the control experiment, and 14.3 ml of 0.01 mol / l thiosulfate solution was used for the titration of the weight of the drug weighing 0.0531g sodium (Kp = 0.9900).T = 0.0004055g/ml, conversion factor of benzylpenicillin potassium salt - 1.045, dilution 1:20.

31) Calculate the % content of the sum of penicillins in phenoxymethylpenicillin, if 20.1 ml of 0.01 M sodium thiosulfate solution was used for the control experiment, for titration of a weight of the drug weighing 0.0601 g - 13.1 ml of 0.01 mol / l sodium thiosulfate solution (K = 1.0100). T = 0.0004209g/ml, dilution 1:20. C = 1.00.

32) Calculate the volume of titrant - 0.01 M of sodium thiosulfate solution, spent on titration of a weight of benzylpenicillin sodium salt weighing 0.0531 g by the iodometric method. The volume of the control experiment is 20 ml, the percentage content of the amount of penicillins is 96.5%, K correction is 0.99. T = 0.0004055g/ml, dilution 1:20. C = 1.00.

33) Calculate the quantitative content and evaluate the quality of benzylpenicillin potassium salt, if a weight of the drug weighing 0.0487 g was dissolved in a 1000 ml volumetric flask in water. 10 ml of a solution containing imidazole and mercury chloride was added to 2 ml of the obtained solution, after 25 min the optical density was measured. The average optical density at 325 nm is 0.616, the thickness of the cuvette is 10 mm. In parallel, the reaction was carried out with 2 ml of 0.005% standard solution of benzylpenicillin potassium salt, the measured

average optical density under the same conditions was 0.623. The content of benzylpenicillin potassium salt in the preparation should be 96% and no more than 102%.

34) Calculate the weight of the weight of benzylpenicillin sodium salt, if 5.00 ml of 0.01 M sodium thiosulfate solution (K n = 1.0000) was used for the titration of an excess of 0.01 M iodine solution, the percentage content of the amount of penicillins is 99.0%, vol. the volume of the titrant in the control experiment is 20.00 ml; determination was carried out at a temperature of 21°S. T = 0.0004000, C = 1.0000, dilution 1:20.

35) Calculate the volume of 0.01 M sodium thiosulfate solution (K n = 1.000), which will be spent on the titration of an excess of 0.01 M iodine solution in the quantitative determination of benzylpenicillin potassium salt, if the weight of the drug is 0.0990, the content of the amount of penicillins is 100% , the volume of the titrant in the control experiment is 19.50 ml; determination was carried out at a temperature of 23°C T = 0.0004055, C = 1.045, dilution 1:20.

36) Calculate the percentage content of the amount of penicillins in phenoxymethylpenicillin, if the weight of the drug is 0.0685 g; volume of 0.01 M sodium thiosulfate solution (Kp = 1.0000) in the main experiment - 11.48 ml; in the control experiment - 19.80 ml; determination was carried out at a temperature of 22°S. T = 0.0004100, C = 1.0000, dilution 1:20.

37) Calculate the specific rotation and evaluate the quality of cephalothin sodium salt, if the average angle of rotation of a 5% aqueous solution of the drug is +6.54°. The length of the cuvette is 10 cm. The specific rotation should be from +124 to +134.

38) Calculate the % content of cephalothin sodium salt, if the angle of rotation of the aqueous solution of the drug is +13.08°, and the specific rotation of the drug is +130.08. The length of the cuvette is 1 dm.

39) Calculate the specific rotation and evaluate the quality of kanamycin monosulfate, if the average angle of rotation of a 5% aqueous solution of the drug is +6.31°. The length of the cuvette is 10 cm. The specific rotation should be from +112 to +123.

40) Calculate the percentage content of streptomycin sulfate in the preparation, if 0.2015 g of the substance was dissolved in 20 ml of water in a 50 ml volumetric flask and made up to the mark with water. Put 5 ml of the solution into a 50 ml volumetric flask and bring it up to the mark with water. 2 ml of 0.2 N sodium hydroxide solution is added to 10 ml of the solution, heated in a water bath for 4 minutes, cooled. Then add 8 ml of 1% solution of ferric ammonium alum, 0.55 N of sulfuric acid solution, mix. The optical density is measured by PhEC at a wavelength of 520 nm in a cuvette with a layer thickness of 10 mm, it is equal to

0.482. In parallel, the reaction is carried out with 10 ml of 0.04% standard solution of streptomycin sulfate A = 0.491

41) Calculate the mass of a test of streptomycin sulfate, if it is dissolved in 20 ml of water in a 100 ml volumetric flask and brought up to the mark, 10 ml of the solution is introduced into a 100 ml volumetric flask, brought up to the mark with water. Take 10 ml of the dilution, add 4 ml of 0.2N sodium hydroxide solution, heat in a water bath for 4 minutes, cool. Then 8 ml of a 1% solution of ferric ammonium alum in a 0.55 N solution of sulfuric acid was added and mixed. The optical density is measured by PhEC at a wavelength of 520 nm in a cuvette with a layer thickness of 10 mm, it is equal to 0.293. In parallel, the reaction is carried out with 10 ml of 0.04% standard solution of streptomycin sulfate. Ao = 0.288. The content of streptomycin sulfate in the preparation is 100.02%.

42) Calculate the specific absorption rate of the medicinal product, if it is known that a sample weighing 0.0617 g was taken to prepare the solution, which was dissolved in 50 ml of solvent. 5 ml of the resulting solution was placed in a volumetric flask with a capacity of 100 ml and brought to the mark. The optical density is 0.425. The percentage content of the active substance in the preparation is 98.72%.

43) Calculate the distance from the starting line to the center of the nystatin spot if $R_f = 0.84$ and the distance traveled by the solvent is 10.0 cm.

44) Calculate the distance from the start line to the solvent front if $R_f = 0.9$ and the distance from the start line to the center of the rifampicin spot is 9.0 cm.

45) When analyzing the azithromycin substance by ascending paper chromatography, it was found that the R_f value for the specified substance is 0.84, and the path traveled by the solvent system is 10.0 cm. Determine the distance from the start line to the center of the azithromycin spot on the chromatogram.

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