Exam questions

“Specialty Pharmaceutical Chemistry”

2024-2025

1. Drugs of heterocyclic series - pyridine and piperidine derivatives. Pyridine-3-carboxylic acid derivatives: nicotinic acid, nicotinamide, nicotinic acid diethylamide, picamilon.
2. Pyridine-4-carboxylic acid derivatives: antitubercular agents (isoniazid, ftivazid, prothionamide), antidepressants (nialamide). Dihydropyridine derivatives: nifedipine (phenigidine). Piperidine derivatives: cyclodol.
3. Quinoline derivatives. Characterization of quinoline derivatives. General method of synthesis of heterocyclic quinoline system. Quinozol, cinchofen, enteroseptol, nitroxoline, sovcain.
4. Synthetic antimalarials - quinine analogs. Plasmocide, quinocide, quinamine.
5. Pyrimidine derivatives. Relationship between structure and action in the series of pyrimidine derivatives. Uracil and its derivatives - methylthiouracil, methyluracil. Uracil derivatives - pentoxyl, fluorouracil, fluorofur, hexamidine.
6. Synthetic drugs of nucleoside nature: cytarabine, azidothymidine, iodoxuridine, lamivudine.
7. Barbituric acid derivatives. Relation between chemical structure, narcotic and anticonvulsant action in the series of barbiturates. General methods of obtaining barbiturates. Barbital, phenobarbital, ethomyl sodium, hexenal, thiopental sodium, benzonal.
8. Benzothiazine derivatives. Non-steroidal anti-inflammatory drug piroxicam. Benzothiadiazine derivatives are diuretics: chlortiazide and dichlothiazide. Chlorobenzenesulfonic acid amide derivatives. Analogs in action - derivatives of chlorobenzenesulfonic acid amide: furosemide, bufenox. Oxodoline.
9. Neuroleptic agents - derivatives of phenothiazine. Alkylamine derivatives - aminazine, propazine, triphthazine.
10. Acyl derivatives of phenothiazine - ethocyzine, ethmosine. Relationship between structure and action depending on the nature of substituents and nature of bonds.
11. Benzodiazepine derivatives as targeted drugs. General methods of obtaining. Influence of the structure of drugs on the directionality of their pharmacological action in the series: chlordiazeproxide, diazepam, oxazepam, nitrazepam, phenazepam.
12. Classification of vitamins. Vitamins of the aliphatic series. Ascorbic acid (vitamin C). Methods of obtaining, causes of instability, redox and acid-base properties.

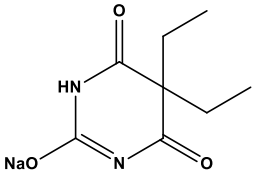
13. Vitamins of aliphatic series. Pantothenic acid (calcium pantothenate), pangamic acid (calcium pangamate - vitamin B15).
14. Vitamins of the alicyclic series. Retinols (vitamins of group A). Retinol acetate.
15. Calciferols (vitamins of group D) as transformation products of sterols. Mechanism of formation of ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Oxydevite, dioxydevite.
16. Vitamins of the aromatic series - derivatives of naphthoquinones (vitamins of the K group). Vikasol.
17. Antivitamins K. Dicoumarin, neodicoumarin, fepromarone, phenylin.
18. Vitamins of the heterocyclic series. Chromic vitamins - tocopherols (E vitamins) as medicinal and prophylactic agents. Tocopherol acetate.
19. Phenylchromanic vitamins - bioflavanoids (P vitamins). Rutin, quercetin.
20. Vitamins - derivatives of pyridine. Nicotinic acid, nicotinamide (vitamin B5 or PP).
21. Oxy-methylpyridine vitamins (B6 vitamins). Pyridoxine hydrochloride, pyridoxal phosphate.
22. Pyrimidine-thiazole vitamins (B1 vitamins). Thiamine chloride and bromide, cocarboxylase, phosphothiamine, benfotiamine. Biotransformation of vitamins. Biotransformation of B1 vitamins, stability, quality requirements, methods of analysis.
23. Pterin vitamins (folic acid group vitamins). Folic acid and its analogs. Relation between structure and biological action. Methotrexate.
24. Isoalloxazine derivatives (B2 vitamins) as medicinal and prophylactic agents. Riboflavin, riboflavin mononucleotide.
25. Pyrrole derivatives (B12 vitamins). Cyancobalamin, oxycobalamin, cobamide. Features of the structure of vitamins B12. Quality requirements, methods of analysis.
26. Alkaloids. Classification. General methods of isolation, purification and separation of alkaloids. Qualitative determination of alkaloids. General (group) reactions. Methods of quantitative determination of alkaloids.
27. Pyridine and piperidine derivatives. Lobelina hydrochloride, cytisine, pachycarpine
28. Tropane derivatives. Atropine sulfate.
29. Synthetic analogs of atropine. Homatropine hydrobromide, scopolamine hydrobromide, tropacin, aprofen, troventol. Ecgonine derivatives. Cocaine hydrochloride. Characterization of the drug.Social significance.
30. Quinoline derivatives. Quinine, quinidine, isodibut.

31. Benzylisoquinoline derivatives. Papaverine hydrochloride and Drotaverine hydrochloride (no-shpa). Analogs of papaverine in action: tifen, diprofen, aprofen.
32. Phenanthrenoisoquinoline derivatives. Morphine, codeine. Sources of obtaining morphine. Semisynthetic derivatives of morphine. Apomorphine hydrochloride, ethylmorphine hydrochloride. The problem of creation of analgesics of morphine type and its social importance. Promedol, fentanyl.
33. Indole derivatives (alkaloids of Raufolphia). Reserpine.
34. Physostegmine salicylate and its semi-synthetic analog proserine. Peculiarities of quality requirements and methods of analysis depending on redox properties and ability to isomerism. Strychnine nitrate.
35. Imidazole derivatives. Pilocarpine hydrochloride. Benzimidazole derivatives. Dibazol, omeprozole.
36. Purine derivatives. Caffeine, theophylline, theobromine. General methods of synthesis and analysis based on oxidation and hydrolytic cleavage reactions of pyrimidine and imidazole cycles.
37. Salts of purine derivatives. Diprophyllin, xanthinol nicotinate, pentoxifylline.
38. Synthetic drugs - purine derivatives. Allopurinol, etomizole, fopurin, riboxin.
39. Guanine derivatives. Acyclovir, ganciclovir.
40. Alkaloids, phenylalkylamine derivatives. Ephedrine hydrochloride, dephedrine. Guanidine derivatives. Spherofisin benzoate.
41. Hormones. Concept, biological role and classification of hormones.
42. Iodized derivatives of aromatic amino acids. Thyroid hormones: thyroxine, triiodothyronine. Complex drug - thyroidine. Antithyroid agents: diiodotyrosine.
43. Hydroxyphenylalkylamines. Adrenal medullary hormones (dopamine, adrenaline, noradrenaline and their salts). Synthetic analogs of catecholamines. Isoprenaline hydrochloride (isoprenaline). Mesaton.
44. Derivatives of substituted hydroxypropanolamines (beta-adrenoblockers). Anapriline, atenolol.
45. Biochemical role of steroids in the body. Classification and nomenclature. Cardenolides (cardiac glycosides). Compounds of digitoxigenin series: digitoxin, acetyl digitoxin, digoxin. Strophanthin. Glycosides of lily of the valley: corglycone.
46. Corticosteroids. Relationship between structure and biological activity. Mineralcorticosteroids, glucocorticosteroids.

47. Deoxycorticosterone acetate, cortisone acetate, hydrocortisone and prednisolone, fluorosubstituted compounds: dexamethasone. Compound esters of steroids.
48. Androgens and anabolics. Androgenic hormones as drugs: testosterone propionate, methyltestosterone.
49. Biological prerequisites for obtaining semi-synthetic drugs with anabolic action. Methandrostenolone, methylandrosten-diol, phenobolin. Quality requirements, methods of analysis.
50. Gestagens and their synthetic analogs. Progesterone, pregnine.
51. Estrogens. Estrone and estradiol as drug substances.
52. Estrogenic hormones. Ethinyl estradiol, mestranol, estradiol esters.
53. Synthetic analogs of estrogens of nonsteroidal structure.1 Synestrol, diethylstilbestrol. Synthetic anti-estrogenic agents - tamoxifen citrate (nolvadex).
54. Antibiotics as medicinal agents. Classification of antibiotics. Standardization of antibiotics.
55. Penicillins. General chemical structure, its peculiarities. Relation between structure and biological action. Benzylpenicillin, its salts (sodium, potassium, novocaine). Phenoxymethylpenicillin. Semisynthetic penicillins: carbenicillin dynatrium salt, amoxicillin.
56. Cephalosporins. Partial directed synthesis of cephalosporin antibiotics. Cephalexin, cephalothin. Quality requirements and methods of analysis.
57. Antibiotics of the aromatic series. Nitrophenylalkylamines. Levomycetin (chloramphenicol). Syntomycin and its esters - stearate and succinate.
58. Aminoglycoside antibiotics Streptomycin sulfate, kanamycin sulfate, gentamicin sulfate. Semisynthetic aminoglycosides. Amikacin. General quality requirements and methods of analysis.
59. Tetracyclines (partially hydrogenated naphthacene derivatives). Relationship between structure and biological action. Tetracycline, oxytetracycline and their semi-synthetic derivatives: metacycline and doxycycline. Quality requirements, methods of analysis.
60. Antitumor antibiotics of different chemical groups. Anthracycline antibiotics - rubomycin hydrochloride. Aurelic acid derivatives - olivomycin.
61. Quinoline-5,8-dione derivatives. Bruneomycin, reumycin. Actinomycins: dactinomycin.

Situation tasks

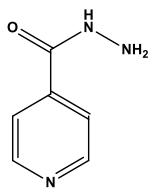
1. Intern Provisor-analyst quality control pharmaceutical enterprise received a substance of the following structure:

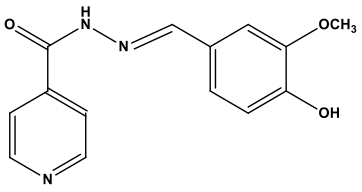


When assessing the quality of the drug indicators “Solubility”, “Transparency and color”, “Free alkali content” did not meet the requirements of regulatory documentation. The solution of the preparation opalesced immediately and the quantitative content of “free alkali” is much higher than specified in the normative documentation. The trainee needs to:

- Give a justification of the reasons for the change in its quality by this indicator according to its storage conditions and properties.
- Provide other tests characterizing its quality.
- Give the name of this medicinal substance.
- Characterize its physical and chemical properties.
- According to its chemical properties, propose identification reactions and methods of quantification.

2. Provisor-analyst of the pharmaceutical company delivered substances of drugs, received for obtaining tablets of medicinal substances of several series of the following structure:



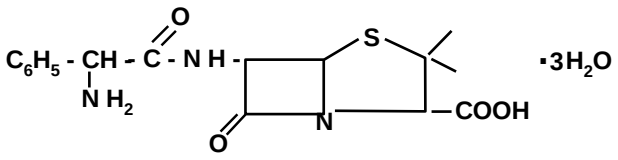


When determining the impurity of isonicotinic acid hydrazide in sample No. 2 according to the method of the State Pharmacopoeia stable blue staining on iodo-starch paper with sodium nitrite solution was not observed. The Provisor-Analyst should:

- Make a conclusion about compliance of the impurity content with the requirements of the State Pharmacopoeia. Suggest other tests to characterize the quality of these drugs.
- Give the Russian, Latin and rational names of the drug. Characterize its physical and chemical properties.
- According to the chemical properties, propose identification reactions and methods of quantification. Write equations of reactions.

3. The quality control department of a pharmaceutical company received the substance Aminazine.
   - Give the chemical formula of the compound and characterize it according to the indicators “Description” and “Solubility”.
   - When determining the content of 2-chlorophenothiazine impurity in the test drug, it was found that the coloration of the test drug was more intense than that of the reference solution.
   - Write the formula of 2-chlorophenothiazine. How is the test for this impurity performed? What stage of synthesis is the major source of this impurity?
   - Give identification reactions and methods for quantification of aminazine.

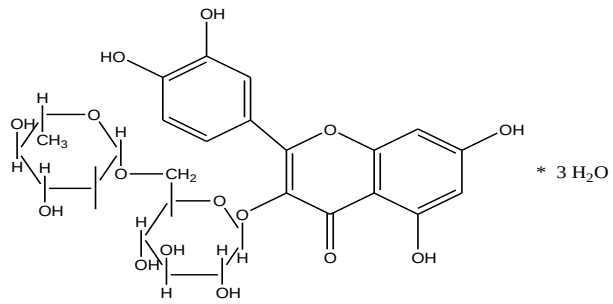
4. When assessing the quality of a pharmaceutical substance of the following chemical structure:



in samples of one series of indicators “Description” and “Solubility” did not meet the requirements of the pharmacopoeial article - the powder was damped and difficult to dissolve in water. Give a justification of the reasons for the change in its quality according to these indicators in accordance with the chemical properties of the substance.

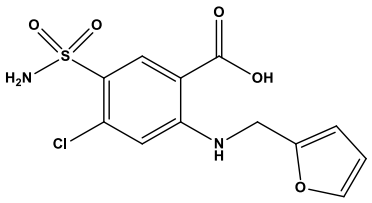
   - Give the name of the substance, characterize its chemical structure and the indicators “Description” and “Solubility”.
   - What class of compounds does this substance belong to and how is it produced in industry?
   - According to the chemical structure, suggest identification reactions and quantification methods. Explain how the organically bound sulfur and aliphatic amino group can be detected in the molecule of this substance. Write the equations of the reactions.
   - Explain how this substance can be detected by UV spectrophotometry.
   - What other methods are known to you for the quantitative determination of this substance?

5. A pharmaceutical substance of the following chemical structure was received for quality control in the control department of a pharmaceutical company for the manufacture of tablets:



- Name this pharmaceutical substance, characterize the chemical structure, specify the functional groups.
- When the substance was tested for one of the impurities, the optical density readings exceeded the norm specified in the pharmacopoeial article. Name this impurity and justify the change in the content of this impurity.
- According to the chemical structure, suggest identification reactions and quantification methods. Write the equations of the reactions.
- Why can spectrophotometric method be used to analyze this substance? Explain your answer.

6. The quality control department of a pharmaceutical company received a substance of the following structure:



- To which group of biologically active compounds does this substance belong? Give the name of this drug substance.
- Characterize it according to the indicators “Description” and “Solubility”.
- Give the reactions of identification and quantification of the compound.
- When analyzed by HPLC using a column filled with octadecylsilyl silica gel (C18), it was found that the peaks of 2 foreign impurities exceeded the peak area of the impurity 2-chloro-4-[(furan-2-ylmethyl)amino]-5-sulfamoyl-benzoic acid (impurity A). What type

of HPLC method was used? What conclusion can be drawn from the results of the analysis? Write the formula of impurity A and explain which synthesis step is its main source.

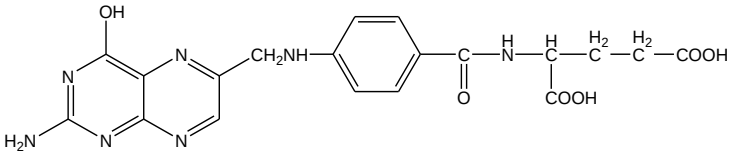
7. Provide justification for a set of tests to assess the quality of the pharmaceutical substance ergocalciferol. For this purpose:

   – Give the structural formula of ergocalciferol, characterize its structure and physical properties.
   – Explain the possibility of using IR and UV spectrophotometry for identification of ergocalciferol. What spectral characteristics are used for this purpose? What is the difference between UV absorption spectrum and IR spectrum?
   – Provide a method for calculating the content of ergocalciferol from a standard sample by UV spectrophotometry. What is called a standard sample?
   – In what diseases and in what dosage forms is ergocalciferol used?

8. Give a rationale for a set of tests to assess the quality of the pharmaceutical substance retinol acetate. For this purpose:

   – Give the structural formula, characterize the features of the chemical structure of retinol acetate. Describe the external signs of the substance.
   – Explain the possibility of using spectrophotometric method to determine the identification of retinol acetate. What optical characteristics are used for this purpose? Give definitions of these characteristics. What qualitative reaction can be used to identify retinol acetate?
   – What is the essence of spectrophotometric quantification of retinol?
   – Explain the storage conditions of retinol acetate.

9. The quality control department of a pharmaceutical company received for analysis a pharmaceutical substance with the following chemical structure:



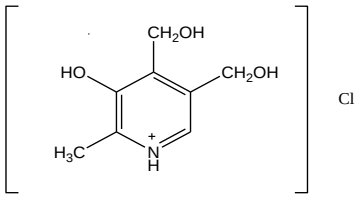
   – Name this substance and characterize the chemical structure, name the functional groups.

– When assessing the quality of this medicinal product in samples of one series, the appearance did not meet the requirements of the section "Description" - the powder was wet and dirty green in color. Give a justification of the reasons for changes in its quality according to this indicator in accordance with the methods of obtaining and properties.

– Based on the chemical structure, suggest identification reactions. Write reaction equations to identify phenolic hydroxyl, aromatic and aliphatic amino groups.

– List the methods of quantitative determination of this substance, explain the essence of one of them.

10. The Test Center received a pharmaceutical substance with the following chemical structure:



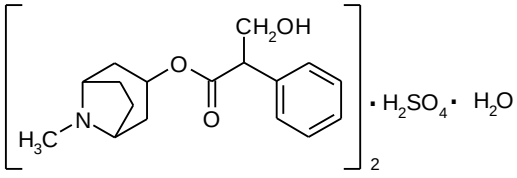
– Name this substance and characterize its chemical structure, name the functional groups.

– When determining the impurity "methyl ether" in the samples of one series, blue coloring appeared. Give a justification of the reasons for the change in its quality by this indicator according to the methods of obtaining and properties.

– According to the chemical structure, suggest identification reactions and methods of quantitative determination. Write the equations of the reactions.

– Explain how chemical properties affect the nature of spectra of this in different solvents? What medicinal preparations of this substance are known to you?

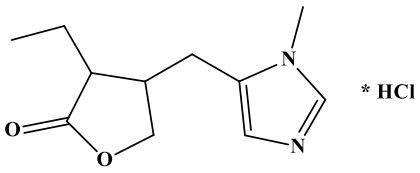
11. The center for quality control of medicines received for analysis a medicinal substance of several series from manufacturing plants with the following chemical structure:



When measuring the angle of rotation of this medicinal substance in samples of one series, the readings exceeded the regulated norm in accordance with the regulatory documentation. Give the justification of rationing of this indicator and suggest other tests characterizing its quality.

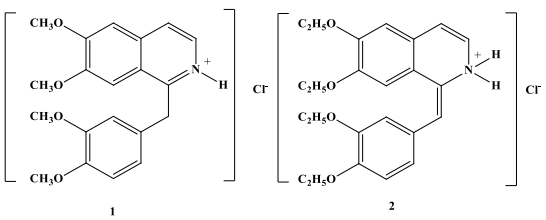
- Give the name of the drug.
- Characterize physico-chemical properties (appearance, solubility, spectral and optical characteristics) and their use for quality assessment.
- According to the chemical properties, suggest identification reactions and quantification methods.

12. Under conditions of industrial production, a preparation (in the form of a 1% solution) containing the following compound substance is obtained:



- To what class and group of compounds does this substance belong? What structural fragments does it contain?
- What is the purpose of performing the hydroxamic assay and the Legall reaction on this compound? On which fragment of the structure is this reaction performed? Give other reactions for identification of this substance.
- What methods of quantitative determination can be used for this substance?
- What are the peculiarities of storage and use of this substance?

13. The analytical laboratory of a chemical-pharmaceutical enterprise received for analysis drug substances with the following structures:



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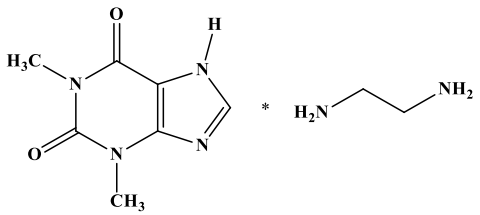
- When evaluating the quality of substance 1 in samples of one series, the pH value of the solution did not meet the requirements of the State Pharmacopoeia - it was less than 3.0. Give a justification of the reasons for the change of its quality by this indicator in accordance with its properties. Suggest other tests characterizing its quality.

- Give the name of the medicinal product. Characterize physico-chemical properties (appearance, solubility, spectral and optical characteristics) and their use for quality assessment.
- According to the chemical properties, suggest identification reactions and quantification methods. Suggest general and differentiating reactions for their detection. Write the equations of the reactions.
- Suggest methods of quantification, give formulas for calculating the drug substance content. What environmental factors affect the stability of drugs? Suggest rational storage conditions and methods of stabilization in dosage form.

14. A chemical-pharmaceutical company received a drug substance of several series with the following chemical structure for obtaining a solution for injection:



- To prepare a solution for injection from samples of one series, the technologists found incomplete dissolution of the medicinal substance in the water for injection. Give a justification for this according to the properties. Suggest other tests characterizing its quality.
- Give the name of the drug. Characterize the physico-chemical properties (appearance, solubility, spectral and optical characteristics) and their use for quality assessment.
- According to the chemical properties, suggest identification reactions and quantification methods. Write the equations of the reactions.

15. The quality control department of a pharmaceutical company received the active pharmaceutical substance Digoxin.

- To which group of biologically active compounds does this substance belong? Give the Latin name of this medicinal substance.
- What fragments are included in the sugar residue of this compound? Name the aglycone included in its composition. What reactions can be used to determine the presence of aglycone, steroid fragment and saccharide residue? Give structural formulas of aglycone and monosaccharides equations of reactions.
- What biological quality control methods can be used for this substance and what are they?

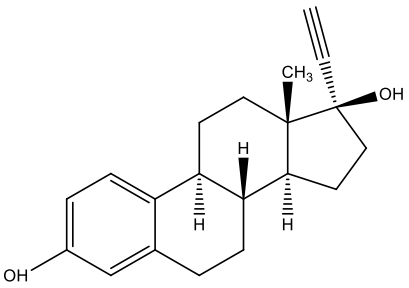
16. The quality control department of a pharmaceutical company received the substance “Cortisone acetate”.

- Give the structural formula of the drug. What class of steroidal compounds does cortisone acetate belong to?
- When analyzing the indicator “specific rotation” it was found that this indicator has a value of +170º (0.5% in acetone). What can be the reason for the deviation of this parameter from the values stipulated by the pharmacopoeial article?
- What reactions can be used to confirm the presence of ester and alpha-ketol groups in the composition of this substance? Write equations of chemical reactions.
- During the TLC analysis of the substance on the chromatogram there were detected spots of cortisone acetate, cortisone and one extraneous spot. What conclusion can be drawn from this analysis? What system is used for chromatography?

17. The quality control department of a pharmaceutical company received a substance “Methyltestosterone”.

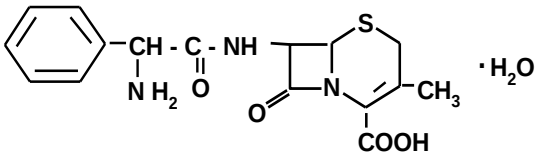
- Give the chemical formula of the compound and characterize it according to the indicators “Description” and “Solubility”.
- When determining the specific absorption index of the substance, it was found that this parameter at a wavelength of 240 nm (for 0.001% solution in 95% ethanol) was equal to 570. What interval of the specific absorption index is specified in the Pharmacopoeial Article? What can be the reason for the discrepancy between the obtained and required values?
- The presence of which functional group can be established using hydroxylamine hydrochloride? How is the product obtained identified? Write the equation of the reaction.
- The presence of which functional group can be determined using acetylation reaction? How is the resulting product identified? Write the equation of the reaction.

18. The quality control department of a pharmaceutical company received a substance of the following structure:



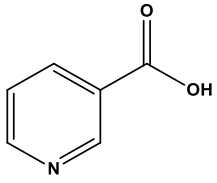
- To which group of biologically active compounds does this substance belong? Give the Russian and Latin names of this medicinal substance.
- When adding m-dinitrobenzene solution and alcoholic solution of caustic potassium to the alcoholic solution of the drug and holding it for an hour, a coloration appeared, more intense than in the control experiment. What impurity is the presence of such an effect in this reaction?
- Give the reactions of identification of ethinyl estradiol.

19. Justify a set of tests to assess the quality of a pharmaceutical substance, the chemical structure of which is given below:



- Give the name of this substance, characterize its structural fragments (heterocycle and functional groups) and physical properties.
- On the basis of the chemical structure, give the equations of the identification reaction of the substance. Explain the amphoteric properties of the substance.
- Suggest physicochemical methods for analyzing this substance.
- How are antibiotics biologically standardized?
- In what diseases is this chemotherapeutic agent used?

20. The quality control department of a pharmaceutical company received a substance of the following structure:



- To which group of biologically active compounds does this substance belong? Give the Russian and Latin names of this drug substance.
- When 2 ml of diphenylamine solution was added to 0.01 g of the preparation, blue coloring appeared. What impurity does this coloring indicate? Give the equation of the reaction.
- Specify the methods of identification and quantification of the drug.

Considered at the meeting of the department of Pharmaceutical and Toxicological Chemistry, pharmacognosy and botany "28" August 2024, protocol No1

Head of the Department  Ozerov A.A.