**Lesson 1**

**Analysis of drugs containing quinoline and quinoclidine: quinoline sulfate quinosol, quinolone, xingamine,**

**chloroquine phosphate medicinal forms.**

Quinoline was first obtained from coal tar in 1834, and later A.M. Butlerov and A.N. Vishnegradsky confirmed the presence of quinine in the molecule. This is the creation of antimalarial preparations from quinoline derivatives.

Gave impetus to conducting research in the direction of So, as a result of studying the relationship between the chemical structure and pharmacological activity of alkaloids of quinoline origin, many preparations were synthesized. These include 4-aminoquinoline derivatives, which are antipotoses and immunodepressants, as well as 8-oxyquinoline derivatives, which are effective antibacterial drugs:



One of the important achievements of the last 20 years is the development of new effective synthetic antibacterial drugs called quinolone-4 derivatives or fluoroquinolones. The characteristic feature of the chemical structure of these compounds is that the quinoline nucleus has an oxo group in the 4th position, and a fluorine atom in the 6th position:



 quinolone-4 fluoroquinolones

Fluoroquinolones have a carboxyl group in the 3rd position, and a piperazine nucleus in the 7th position (R1).

**Quinine sulfate – Quinine (Quinine) Sulfate**



*(C20H24N2O2)2 ∙ H2SO4 ∙ 2H2O*

*6'-methoxyquinolyl-(4')-[5-vinylquinuclidyl-(2)]-*

*carbinol sulfate*

*M. k. 783*

These are colorless needle crystals or white crystalline powder without odor and bitter taste. He turns yellow due to exposure to the world. Slightly soluble in water, moderately soluble in alcohol, very slightly soluble in chloroform, mineral acids, acidified water.

Definition of personality

1) The drug gives reactions 1-3 and 7 in quinine hydrochloride.

2) The specific gravity of a 3% solution of the drug in 0.1 M hydrochloric acid should be -2400 based on dry matter.

3) The drug reacts with sulfates.

Quantitative assessment

This is done in several ways.

1) The method of neutralization (alkalimetry) (the method is the same as in quinine hydrochloride (Т=0.03915 g/ml).

(Quinine base)2 ∙ H2SO4 ∙ 2H2O + 2NaOH ⟶ Na2SO4 + 4H2O + 2 (quinine base)

2) Weighing method. Quinine is converted into a base by treatment with a strong alkali of quinine-sulfate, which is extracted with chloroform; chloroform is distilled off, the residue is dried and weighed to a constant mass. The amount of quinine salt is determined by multiplying the weight of the residue by the corresponding coefficient.

The coefficient is determined by dividing the molecular mass of the quinine anhydrous salt by the molecular mass of the quinine base (324.43).

Quinine-hydrochloride 360.92: 324.43=1.112

Quinine-dihydrochloride 397.35: 324.43=1.225

Quinine sulfate 747.0: (324.43x2)=1.151

3) Anhydrous titration method: sulfate-ion is precipitated with barium perchlorate in acetic medium, then quinine-base (in the system dioxane-acetic acid (2:1)) is titrated with a solution of hydrochloric acid in anhydrous acetic acid (indicator: crystal violet).

It is used as an antimalarial agent. Tablets of 0.25 and 0.5 g are prescribed. In medical practice, quinidine, an optical isomer of quinine, is also used in the form of its sulfate salt.

**Chinosol – Chinosolum**

N

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H

2

S

O

4

O

H

2

*8-oxyquinoline-sulfate*

*(quinosol)*

 *M.k. 388.39*

**Purchase**

They are obtained by the synthesis method. Phenol is used as the main raw material for synthesis purposes. From phenol, o-nitrophenol is obtained first, and then o-aminophenol. After that, o-aminophenol combines with acrolein by the scraper method to form 8-oxyhydroxyquinoline, which is oxidized by nitrobenzene and turns into 8-oxyquinoline. Quinosol is obtained by reacting 8-oxyquinoline with dilute sulfuric acid:

O

H

H

N

O

3

O

H

N

O

2

[

H

]

O

H

N

H

2

 phenol orthonitrophenol o-aminophenol

C

C

H

C

H

2

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O

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*8-oxyhydroxyquinoline*

O

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8-oxyquinoline

Quinozol lemon is a yellow powder with a peculiar smell. Easily soluble in water, slightly soluble in alcohol, insoluble in ether and chloroform. The melting temperature is 175-1770C.

Determination of identity

Chemical reactions used to determine the identity of 8-oxyquinoline derivatives are based on the presence of phenol hydroxyl, nitro group, triple nitrogen atom and sulfuric acid in the molecule.

1. Solution of quinosol in water (1:10) with FeCl3 solution gives blue-green color iron 8-oxyquinolate (reaction related to phenol hydroxyl):

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1. sodium carbonate solution is added to 1 ml of the solution prepared in step 1; A precipitate that dissolves in the excess of the reactant is obtained:

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C

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3

+

N

a

2

S

O

4

8-oxyquinoline

+

C

O

2

+

H

2

O

N

O

H

2

+

N

a

2

C

O

3

N

O

N

a

2

8-oxyquinolinate-sodium

3) In 1 ml of the solution prepared in the 1st determination, a reaction specific to sulfates is carried out.

4) UV-spectrophotometry: solution of chonosol in 0.1 M hydrochloric acid 252; 308; It gives maximum absorption at wavelengths of 320 and 360 nm.

5) Quinozol gives azo dye with diazonium salts.

6) When the preparation is heated with a solution of citric acid in acetic anhydride, a red color is formed (reaction related to the triple nitrogen atom).

7) Quinosol gives internal complex compounds with many metals (Mg, Cd, Cu (II), Zn, Al and other colors (this reaction is also given by nitroxoline). Quinosol and other 8-oxyquinoline derivatives are dihydro derivatives in the presence of dilute hydrochloric acid and zinc When a few drops of perhydrol or bromine water are added to the filtrate, a red-violet color is gradually obtained as a result of the formation of the quinoid structure:



Adding 1 drop of copper sulfate solution to the reaction mixture accelerates the reaction. Thus, 8-oxyquinoline derivatives can be distinguished from 8-aminoquinoline derivatives because 8-aminoquinoline derivatives do not form colored products as a result of this reaction.

8) Due to the strong nitrogen atom in the quinosol molecule, it precipitates with many precipitating reagents (Dragendorf, Mayer, picric acid, Wagner, etc.) and K2Cr2O7 solution.

9) IR-spectroscopy: the IR-spectrum of quinosol taken in the 4000-400 cm-1 range should be the same as the spectrum of the standard sample.

Determination of purity

Acidity, sulfate ash, heavy metals and arsenic are tested for DF.

Quantification

1) It is determined by the method of neutralization (alkalimetry). Titration 0.1 M

It is carried out with NaOH solution (indicator - phenolphthalein; T=0.01942 g/ml).

X

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+

2

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a

O

H

N

O

H

2

+

N

a

2

S

O

4

+

2

H

2

O

20 ml of chloroform is added to dissolve the quinosol base.

2) On the contrary, it is carried out by the method of bromatometry. As a result of the method reaction 7-

based on the formation of bromine derivatives. An excess of 0.1 M potassium bromate solution is determined by iodometry in the presence of potassium bromide:

KBrO3 + H2SO4 + 3H2SO4 $\rightarrow $ 3Br2 + 3K2SO4 + 3H2O



Br2 + 2Na2S2O3 $\rightarrow $ I2 + 2 KBr

I2 + 2Na2S2O3 $\rightarrow $ 2NaI + Na2S4O6

As an antiseptic (1:1000 and 1:2000), solutions are used for washing hands and wounds, 5-10% ointments, 1-2% sprays. Since quinosol gives insoluble compounds with metals, medical instruments cannot be disinfected with its solutions. It is packed in the amount of 10 g.

**Chloroquine Phosphate (Chingamine) – Chloroquine Phosphate (Chingaminum) (Delagil, Resochin)**



It is a white, odorless, bitter-tasting crystalline powder. It changes color under the influence of light. Easily soluble in water, slightly soluble in alcohol, chloroform, ether. Aqueous solutions have an acidic reaction (pH=3.5-4.5).

Determination of identity

1) Add a 1% solution of picric acid to the solution of the preparation in water

they do. The obtained yellow precipitate is separated, washed with water, alcohol and ether, dried,

they determine the melting temperature. The melting point of chloroquine picrate is 204-207 0C.

The melting temperature of the preparation is 214.5-2180C.

2) 0.001% solution of chloroquine phosphate in 0.01 M hydrochloric acid 257,

It gives maximum absorption at wavelengths of 329 and 343 nm.

1. Gives the reaction related to phosphates:

H3PO4 + 12(NH4)2MoO4 + 21HNO3→

→21NH4NO3 + 12H2O + (NH4)3PO4 ∙ 12MoO3↓

Sarı

Quantitative assessment

1) Water titration method. Preparation and other dissolve in anhydrous acetic acid and titrate with 0.1 M HClO4 until green color (indicator - violet crystal; T=0.02580 g/ml).

2) Determination of both the identity and quantity of the drug is carried out by the YEMX method. Preservation of the main peak of the test solution and standard sample

The duration should be identical.

Parallel determination is carried out with a standard sample of the preparation.

3) Spectrophotometry method. This is the purpose of the drug tablets given. Optical densities of preparations and solutions of standard samples at 343 nm

it is measured in wavelength. Xingamine is a very effective antimalarial drug. It is available in tablets of 0.25 g and 5% solution for injections in the amount of 5 ml. Hydroxychloroquine-sulfate is a drug similar in action to syngamin.

**Chloroquine Phosphate (Hingamine) – Chloroquine Phosphate (Hingamine) (Delagil, Resochin)**



It is a white, odorless, bitter-tasting crystalline powder. It changes color under the influence of light. Easily soluble in water, slightly soluble in alcohol, chloroform, ether. Aqueous solutions have an acidic reaction (pH=3.5-4.5).

Determination of identity

1) Add a 1% solution of picric acid to the solution of the preparation in water they do. The obtained yellow precipitate is separated, washed with water, alcohol and ether, dried, they determine the melting temperature. The melting point of chloroquine picrate is 204-207 0C.

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2) 0.001% solution of chloroquine phosphate in 0.01 M hydrochloric acid 257,

It gives maximum absorption at wavelengths of 329 and 343 nm.

1. Gives the reaction related to phosphates:

H3PO4 + 12(NH4)2MoO4 + 21HNO3→

→21NH4NO3 + 12H2O + (NH4)3PO4 ∙ 12MoO3↓

sarı

Quantification

1) Aqueous titration method. The preparation etc. dissolve in anhydrous acetic acid and titrate with 0.1 M HClO4 until green (indicator - violet crystal; T=0.02580 g/ml).

2) Determinations of both the identity and quantity of the preparation are carried out by the YEMX method. Retention of the main peak of the test solution and the standard sample

The duration should be the same.

Parallel determination is carried out with a standard sample of the drug.

3) Spectrophotometry method. Such an appointment is for tablets of the drug given. Optical densities of the preparation and standard sample solutions at 343 nm measured in wavelength.

Xingamine is a very effective antimalarial drug. It is available in 0.25 g tablets and 5% solution for injection in the amount of 5 ml.

Hydroxychloroquine-sulphate is a drug close to xingamine in terms of its effect.