Ministry of Health of the Russian Federation
Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

GENERAL PHARMACEUTICAL CHEMISTRY

CHEMICAL METHODS OF PHARMACOPOEIAL ANALYSIS - IDENTIFICATION OF INORGANIC DRUGS

Lesson 2 (part 1)

V term

Volgograd, 2022

Discipline

GENERAL PHARMACEUTICAL CHEMISTRY

LESSON №2

Chemical methods for the

Identification of inorganic drugs.

Chemical methods of pharmacopoeial analysis - Identification of inorganic drugs. Identification of cations, anions.

QUESTIONS FOR THE LESSON

1. Chemical elements included in the composition of medicinal substances of inorganic nature and ways of their detection.
2. Identification of inorganic medicinal substances – detection of cations.
3. Identification of inorganic medicinal substances – detection of anions.

Various inorganic compounds are used in medicine. The same element, as a rule, is part of several compounds. For example, sodium is a part of such medicinal substances as NaCl, NaCl, $NaHCO_3$, $Na_2B_4O_7$, etc. Or, for example, the element Ca – it may be part of an inorganic molecule - $CaCl_2$, $CaCO_4$, and may contain an organic structure as an anion – calcium lactate $(C_3H_5O_3)_2Ca$, calcium gluconate $(C_6H_{11}O_7)_2Ca$, etc.

These elements act as a frequently occurring structural part of various medicinal substances, and the method of detecting them is therefore unified and set out in a general regulatory document. Such a regulatory document includes the general pharmacopoeia article "General identification reactions".

The identification of inorganic medicinal substances is an authentication based on the detection by chemical reactions of cations and anions that make up their molecules. Use:

1. Precipitation reactions of anions and cations with the formation of substances insoluble in water, which can be characterized by color, solubility (in acids, alkalis, organic solvents), the ability to form complex compounds soluble in excess of reagents, etc.
2. Redox reactions.
3. Reactions of neutralization and decomposition of anions (by smell, release of oxides and dioxides).
4. Changing the color of a colorless flame.
5. Changes occurring during heating and calcination of drugs. Identification of organoelement medicinal substances.

IDENTIFICATION OF INORGANIC MEDICINAL SUBSTANCES – DETECTION OF CATIONS

Ammonium

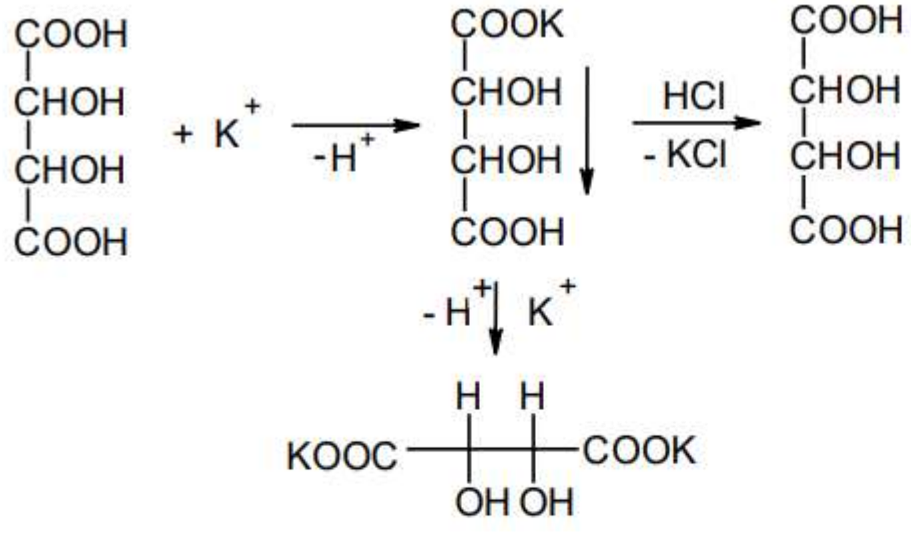
Ammonium salts are highly soluble in water. When heating solutions of ammonium salts with a solution of sodium hydroxide, ammonia is released, which can be detected by a sharp smell or by the blueness of a red litmus paper moistened with water.

$$NH_4^+ + OH^- \Longrightarrow NH_4OH \longleftrightarrow NH_3\uparrow + H_2O$$

Technique:
1 ml of ammonium salt solution is heated with 0.5 ml of caustic soda solution; ammonia is released, detectable by the smell and by the blueness of wet red litmus paper.

Potassium

1. ***Interaction with tartaric acid.*** Potassium salts interact with a solution of tartaric acid to form a white crystalline precipitate of an acid salt - potassium hydrotartrate. The average salt is easily soluble in water, therefore, when an excess of potassium ions is added to the precipitate acid salt, the precipitate dissolves:



The formation of a precipitate is facilitated by cooling the reaction mixture, shaking and rubbing with a glass stick against the walls of the test tube. Determination is hindered by ammonium salts, which form a precipitate with tartaric acid and therefore they must be removed beforehand.

Technique:
To 2 ml of potassium salt solution, add 1 ml of tartaric acid solution, 1 ml of sodium acetate solution, 0.5 ml of 95% alcohol and shake. Gradually, a white precipitate is formed, soluble in diluted mineral acids and solutions of caustic alkalis.

2. ***Interaction with sodium hexanitrocobalte (III).*** Potassium ions form an insoluble complex salt of potassium-sodium hexanitrocobaltate (III), soluble in mineral acids and insoluble in acetic acid. The reaction is carried out in a slightly acidic environment. Determination is hindered by ammonium salts, which must first be removed:

$$2K^+ + Na_3[Co(NO_2)_6] \longrightarrow K_2Na[Co(NO_2)_6]\downarrow + 2Na^+$$

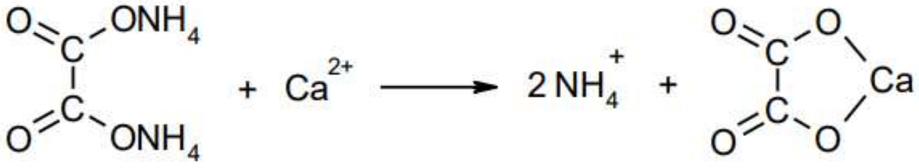
<u>*Technique:*</u>
0.5 ml of diluted acetic acid and 0.5 ml of sodium hexanitrocobaltate solution are added to 2 ml of potassium salt solution pre–calcined to remove ammonium salts - a yellow crystalline precipitate is formed.

3. ***Flame coloring.*** Potassium ions injected into the colorless flame of the burner turn it violet.

<u>*Technique:*</u>
Make a loop of thin copper wire and calcine; dip the loop in a solution or crystals of potassium salt and add to a colorless flame. The flame turns violet, and when the flame is viewed through a purple glass, it turns purple-red.

Calcium

1. ***Interaction with ammonium oxalate.*** Solutions of calcium salts with oxalate ion form a white precipitate, insoluble in acetic acid, soluble in diluted mineral acids:



<u>*Technique:*</u>
1 ml of ammonium oxalate solution is added to 1 ml of calcium salt solution; a precipitate is formed, insoluble in diluted acetic acid and ammonia solution, soluble in diluted mineral acids.

2. ***Flame coloring.*** The calcium salt, moistened with hydrochloric acid and injected into a colorless flame, turns it brick-red.

Magnesium

1. ***Interaction with sodium hydrophosphate.*** A white crystalline precipitate is formed, soluble in acetic acid:

$$MgSO_4 + Na_2HPO_4 + NH_3 \longrightarrow MgNH_4PO_4\downarrow + Na_2SO_4$$

Technique:

1 ml of ammonium chloride solution, 1 ml of ammonia solution and 0.5 ml of sodium phosphate solution are added to 1 ml of magnesium salt solution; a white crystalline precipitate is formed, soluble in diluted mineral acids and acetic acid.

Sodium

1. ***Interaction with zincuranyl acetate.*** Sodium salts form a yellow crystalline precipitate with zinc uranyl acetate. The precipitate is insoluble in acetic acid:

$$Na^{+} + Zn[(UO_2)_3(CH_3COO)_8] + CH_3COOH + 6\,H_2O \longrightarrow$$
$$\longrightarrow Na^{+} + Zn[(UO_2)_3(CH_3COO)_9]\cdot 6\,H_2O\downarrow + H^{+}$$

Technique:

1 ml of sodium salt solution is acidified with diluted acetic acid, if necessary, filtered, then 0.5 ml of zinc uranyl acetate solution is added; a yellow crystalline precipitate is formed.

2. ***Flame coloring.*** Sodium salt introduced into a colorless flame turns it yellow.

Iron (II)

1. ***Interaction with potassium hexacyanoferrate (III).*** Solutions of iron (II) salts with hexacyanoferrate (III) ion form a blue precipitate of iron (II) hexacyanoferrate (III) (Turnbull blue):

$$2\,Fe^{2+} + 2\,K_3[Fe(CN)_6] \longrightarrow Fe_3[Fe(CN)_6]_2\downarrow + 6\,K^{+}$$

The precipitate is insoluble in mineral acids, but soluble in alkalis with the formation of iron (II) hydroxide precipitate:

$$Fe_3[Fe(CN)_6]_2 + 6\,KOH \longrightarrow 6\,KCN + 2\,Fe(CN)_3 + 3\,Fe(OH)_2\downarrow$$

Technique:

0.5 ml of diluted hydrochloric acid and 1 ml of potassium hexacyanoferrate (III) solution are added to 2 ml of iron (II) salt solution; a blue precipitate is formed.

2. ***Interaction with sodium sulfide***. Iron (II) salts give a black precipitate with sulfide ion, soluble in hydrochloric acid:

$$Fe^{2+} + Na_2S \longrightarrow FeS\downarrow + 2\,Na^{+}$$

Technique:

1 ml of sodium sulfide solution is added to 2 ml of iron (II) salt solution; a black precipitate is formed.

Iron (III)

1. ***Interaction with potassium hexacyanoferrate (II).*** Iron (III) reacts with potassium hexacyanoferrate (II) to form a blue precipitate of iron (III) hexacyanoferrate (II) (Prussian blue).

$$4Fe^{3+} + 3K_4[Fe(CN)_6] \longrightarrow Fe_4[Fe(CN)_6]_3 + 12K^+$$

<u>Technique:</u>

0.5 ml of diluted hydrochloric acid and 1-2 drops of potassium hexacyanoferrate (II) solution are added to 2 ml of iron (III) salt solution, a blue precipitate is formed.

2. ***Interaction with ammonium rhodanide.*** The classical reaction is the interaction of iron oxide with ammonium rhodanide to form a blood-red solution as a result of obtaining iron (III) rhodanide:

$$Fe^{3+} + 3NH_4CNS \longrightarrow Fe(CNS)_3 + 3NH_4^+$$

<u>Technique:</u>

0.5 ml of diluted hydrochloric acid and 1-2 drops of ammonium rhodanide solution are added to 2 ml of iron (III) salt solution; red staining appears.

Bismuth

1. ***Interaction with sodium sulfide.*** Solutions of bismuth salts, slightly acidified with hydrochloric acid, give a brownish-black precipitate with a sulfide ion:

$$2Bi^{3+} + 3S^{2+} \longrightarrow Bi_2S_3\downarrow$$

<u>Technique:</u>

Bismuth preparations are shaken with 3 ml of diluted hydrochloric acid and 1 ml of sodium sulfide solution is added; brownish-black staining appears.

2. ***Interaction with alkali metal iodides.*** As a result of the reaction, a black precipitate is formed, soluble in excess of the reagent with the formation of an orange-yellow solution containing tetraiodovismutate. The State Pharmacopoeia recommends potassium iodide as a reagent.

$$Bi^{3+} + 3KJ \longrightarrow BiJ_3\downarrow + 3K^+$$

$$BiJ_3 + KJ \longrightarrow K[BiJ_4]$$

<u>Technique:</u>

The bismuth preparation is shaken with 5 ml of diluted sulfuric acid and filtered. 2 drops of potassium iodide solution are added to the filtrate; a black precipitate is formed, which dissolves in excess of the reagent to form a yellowish-orange solution.

Mercury (II)

1. **Interaction with alkalis.** When alkalis act on aqueous solutions of mercury (II) salts, a yellow precipitate of mercury (II) oxide is formed:

$$HgCl_2 + 2NaOH \longrightarrow HgO\downarrow + 2NaCl + H_2O$$

<u>Technique:</u>

0.5 ml of caustic soda solution is added to 2 ml of mercury oxide salt solution; a yellow precipitate is formed.

2. **Interaction with potassium iodide.** When potassium iodide acts on a solution of mercury (II) chloride, a red precipitate of mercury (II) iodide is formed. If potassium iodide is taken in excess, then the precipitate formed dissolves to form a colorless solution of potassium tetraiodomercurate:

$$HgCl_2 + 2KJ \longrightarrow HgJ_2\downarrow + 2KCl$$

$$HgJ_2 + 2KJ \longrightarrow K_2[HgJ_4]$$

<u>Technique:</u>

To 1 ml of a solution of mercury oxide salt, a solution of potassium iodide is carefully added drop by drop; a red precipitate is formed, soluble in excess of the reagent.

3. **Interaction with sodium sulfide.** Mercury (II) salts are precipitated by sulfide ion from aqueous solutions in the form of a black precipitate insoluble in nitric acid:

$$HgCl_2 + Na_2S \longrightarrow HgS\downarrow + 2NaCl$$

<u>Technique:</u>

0.5 ml of sodium sulfide solution is added to the solution of mercury oxide salt; a brown-black precipitate is formed, insoluble in diluted nitric acid.

Zinc

1. **Interaction with potassium hexacyanoferrate.** Zinc salts with ferrocyanide ion form a white gelatinous precipitate of potassium zinc hexacyanoferrate (II), insoluble in dilute hydrochloric acid.

$$3ZnSO_4 + 2K_4[Fe(CN)_6] \longrightarrow K_2Zn_3[Fe(CN)_6]_2\downarrow + 3K_2SO_4$$

<u>Technique:</u>

0.5 ml of potassium ferrocyanide solution is added to 2 ml of zinc salt solution; a white precipitate is formed, insoluble in diluted hydrochloric acid.

2. ***Interaction with sodium sulfide.*** Solutions of zinc salts form a white zinc sulfide precipitate with a sulfide ion, easily soluble in dilute hydrochloric acid and insoluble in acetic acid:

$$Zn^{2+} + S^{2-} \longrightarrow ZnS\downarrow$$

$$ZnS + 2HCl \longrightarrow ZnCl_2 + H_2S\uparrow$$

Technique:

0.5 ml of sodium sulfide or hydrogen sulfide solution is added to 2 ml of zinc salt solution; a white precipitate is formed, insoluble in acetic acid and easily soluble in diluted hydrochloric acid.

Silver

1. ***Interaction with chlorides.*** Solutions of silver salts with chloride ion form a white curd precipitate of silver chloride, insoluble in nitric acid, soluble in solutions of ammonia and ammonium carbonate to form diamminserebr chloride.

$$Ag^{+} + Cl^{-} \longrightarrow AgCl\downarrow$$

$$AgCl + 2NH_4OH \longrightarrow [Ag(NH_3)_2]Cl + 2H_2O$$

$$AgCl + (NH_4)_2CO_3 \longrightarrow [Ag(NH_3)_2]Cl + CO_2\uparrow + H_2O$$

Technique:

2-3 drops of diluted hydrochloric acid or sodium chloride solution are added to 1 ml of silver salt solution; a white curd precipitate is formed, insoluble in nitric acid, soluble in ammonia solution.

2. ***The "silver mirror" reaction***. An ammonia solution of silver salt (diamminserebra hydroxide) reacts with aldehydes that reduce silver to metallic, forming a plaque on the walls of the test tube (silver mirror reaction):

$$2[Ag(NH_3)_2]OH + CH_2O \longrightarrow 2Ag\downarrow + CO_2\uparrow + 4NH_3\uparrow + H_2O$$

Technique:

An ammonia solution is added to 1 ml of silver salt solution until the precipitate formed at the beginning is dissolved, then 2-3 drops of formaldehyde solution are added and heated; a shiny coating of metallic silver is formed on the walls.