MINISTRY OF HEALTH OF THE REPUBLIC OF MOLDOVA

***NICOLAE TESTEMIȚANU* STATE UNIVERSITY OF MEDICINE AND PHARMACY**

Faculty of Pharmacy

Department of Pharmaceutical and Toxicological Chemistry

Livia UNCU, Elena DONICI, Tatiana TREAPIȚÎNA,

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INORGANIC DRUG SUBSTANCES

Methodical recommendation

Chisinau, 2023

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SRL "Foxtrot"
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Approved by the Council of the Quality Management of *Nicolae Testemițanu* SUMPh
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In the methodical recommendation, the particularities of the groups of medicinal substances, inorganic derivatives in accordance with the curriculum of the discipline and the Pharmacy study program are exposed. The methodical recommendation is intended for students of the faculties of pharmacy, residents of pharmaceutical specializations, master's and doctoral students, practicing pharmacists.

Under the editorship of the author: Vladimir Valica

Tipărit la: SRL "Foxtrot"

DESCRIEREA CIP A CAMEREI NAȚIONALE A CĂRȚII DIN REPUBLICA MOLDOVA

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CONTENT

PREFACE

Pharmaceutical chemistry is a compulsory specialty subject in the Pharmacy study program, nominated in Directive 2005/36/EC of the European Parliament and of the Council on the recognition of professional qualifications at European level.

The methodological recommendation Inorganic medicinal substances includes medicinal substances from the group of inorganic compounds and is addressed to students of the Faculty of Pharmacy, in the disciplines of the Department of Pharmaceutical and Toxicological Chemistry. Students become familiar with the most important particularities of the analysis of inorganic medicinal substances (determination of physico-chemical indices, analysis of cations and anions, etc.).

Studying the topics included in the methodical recommendation will enable:

- to assess the quality of inorganic drug substances;
- to determine the impurities in inorganic drug substances;
- to detect the change in the quality of inorganic medicinal substances under the influence of different factors and to propose optimal preservation conditions.

Thus, studying the general laws and the specific peculiarities of inorganic medicinal substances allows raising the professional level of future pharmacists in order to appreciate the quality of medicinal substances.

The authors.

ABBREVIATIONS

DAN – Normative Analytical Documents

ed. – edition

etc. – etcetera

ex. – excess

FR – Romanian Pharmacopoeia

LAL – Lysate of Limulus amebocytes

PhEur – European Pharmacopoeia

INTRODUCTION

The purpose of the methodical recommendation is to train the skills regarding the complex study of inorganic medicinal substances: international common name, structural formula, relationships chemical structure - therapeutic activity, production methods, physico-chemical properties, purity control, identification and dosing of pharmaceutical substances by chemical methods classical and modern instrumental methods as well as the conditions of conservation and transport depending on the physico-chemical properties.

Recommended minimum duration

To study the topic, 4 laboratory works (16 hours) are given.

Study stages:

- control and correction of the acquisition of the material based on the subjects for the individual preparation of the student;
- students' practical work;
- recapitulation.

Objectives:

1. to acquire the comparative characteristic of the physical and physico-chemical properties of inorganic medicinal substances.
2. to accumulate skills in performing general and particular reactions for the identification of inorganic medicinal substances.
3. to acquire skills in the determination of impurities in inorganic medicinal substances and to argue their presence, arising from the physical and chemical properties of the medicinal substances.
4. to acquire skills in carrying out the quantitative determination of inorganic medicinal substances in accordance with DAN requirements.
5. to be able to establish the conditions for the preservation of inorganic medicinal substances depending on their chemical structure and physical properties.

SUBJECTS FOR INDIVIDUAL STUDENT PREPARATION BASED ON THEORETICAL MATERIAL

1. General characteristic of inorganic medicinal substances. Differences between inorganic and organic derivatives.
2. Oxygen derivatives: purified water and purified water for injections. Sources of impurities and methods of identifying impurities. Possible changes to conservation.
3. Oxygen derivatives: hydrogen peroxide and magnesium peroxide. Obtaining hydrogen peroxide. The acid-base and redox properties of hydrogen peroxide. Analysis methods. The factors that condition the degradation of peroxides. The choice of stabilizer. Conservation. Use in medicine.
4. Hydrochloric acid and its salts: sodium chloride, potassium chloride. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
5. Bromines as medicinal substances: sodium bromide, potassium bromide. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
6. Iodines as medicinal substances: sodium iodide, potassium iodide. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
7. Iodine derivatives: 5% and 10% alcoholic solutions of iodine. Physical, chemical properties and analysis methods. Stability of 5% and 10% alcoholic solutions of iodine. Explain the instability of the 10% alcoholic solution of iodine. Conservation. Use in medicine.
8. Sodium fluoride. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
9. Hydrocarbon compounds: sodium bicarbonate. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.

10. Carbonate compounds: lithium carbonate. Obtaining. Physical, chemical properties and analysis methods. Reactions distinguishing the carbonate ion from the hydrocarbonate ion. Conservation. Use in medicine.
11. Distinguishing the carbonate ion from the hydrocarbon ion.
12. Boron compounds: boric acid, sodium tetraborate. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
13. Silver compounds: silver nitrate. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
14. Calcium compounds: calcium chloride. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
15. Magnesium compounds: magnesium sulfate. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
16. Zinc compounds: zinc sulfate. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
17. Iron (II) compounds: iron (II) sulfate. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
18. Aluminum compounds: aluminum hydroxide. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.
19. Bismuth compounds: bismuth oxide. Obtaining. Physical, chemical properties and analysis methods. Conservation. Use in medicine.

INFORMATIONAL MATERIAL

1. Drug substances from the group of oxygen derivatives

Oxygen forms bivalent compounds due to the fact that its atoms have 6 electrons in their outer electronic layer. Oxygen preparations have found wide application in medicine, being successfully used as antiseptics and disinfectants (table 1).

Table 1. **Drug substances, oxygen derivatives**

The names in the Romanian and Latin languages. Chemical formula	**Description. Solubility. Molecular mass**
Purified water ***Aqua purificata*** H_2O	Clear, colorless, odorless and tasteless liquid. M_r =18,02 g/mol
Hydrogen peroxide ***Hydrogenii peroxidum*** H_2O_2	Transparent, colorless liquid. Soluble in water. M_r = 34,01 g/mol
Magnesium peroxide ***Magnesii peroxidum*** MgO_2	White or yellowish, amorphous, light powder. Practically insoluble in water and ethanol. It dissolves in dilute mineral acids. M_r = 56,30 g/mol

Purified water

Purified water is prepared by the following methods: distillation, reverse osmosis, ion exchange, etc. It is the solvent most often used in pharmaceutical practice. Purified water must meet certain DAN requirements: it must be clear, colorless, odorless and tasteless, the pH values must be between 5.0–7.0.

In purified water, determine the dry residue after evaporating 100 ml of water. After drying at 100-105°C to constant mass, the residue must not exceed 0.001%.

Purified water must not contain reducing substances (remains of microorganisms). This determination is carried out by boiling the purified water sample with potassium permanganate in acidic medium for 10 minutes. The pink color of the solution should be maintained. If reducing substances are present in the purified water, the pink color disappears:

$$MnO_4^- + 5\bar{e} + 8H^+ \rightarrow Mn^{2+} + 4H_2O$$

Purified water easily absorbs carbon dioxide from the air, a fact that determines the need to investigate it as an impurity through the reaction with lime water. The disorder indicates the presence of carbon dioxide in the purified water sample:

$$CO_2 + H_2O \rightarrow H_2CO_3$$
$$CO_3^{2-} + Ca^{2+} \rightarrow CaCO_3\downarrow$$

The purified water must be free of nitrates and nitrites, which are determined by the yellowing of diphenylamine in concentrated sulfuric acid.

Ammonium ion impurity in purified water is allowed in an amount no greater than 0.00002%, being determined with the help of the ammonium impurity standard solution by reacting with the Nessler reagent (K2HgI4 solution in KOH). The color of the sample must not be more intense than that of the standard solution.

The purified water must be free of chlorides, being identified by the reaction with silver nitrate in the presence of nitric acid, in which no turbidity or opalescence should appear. Nitric acid performs the specific reaction:

$$Cl^- + Ag^+ \rightarrow AgCl\downarrow$$

In purified water, the absence of sulfates is determined by the reaction with barium chloride in the presence of hydrochloric acid, as a result of which no opalescence should appear:

$$SO_4^{2-} + Ba^{2+} \rightarrow BaSO_4\downarrow$$

In purified water, the lack of calcium ions is determined by the reaction with ammonium oxalate in the presence of the ammonia buffer

solution, which forms an optimal environment for the reaction (pH=6.0-7.5) and after which no opalescence should appear:

$$Ca^{2+} + (NH_4)_2C_2O_4 \rightarrow CaC_2O_4\downarrow + 2\ NH_4^+$$

The heavy metal ions are determined in purified water by the reaction with sodium sulfide in an acetic acid environment; a brown color should not appear:

$$Pb^{2+} + S^{2-} \rightarrow PbS\downarrow$$

Purified water is kept in closed vessels made of materials that do not change the properties of the water and that protect it from foreign particles and impurities.

Purified water for injections

Purified water for injections must meet the requirements, which also apply to purified water. Apart from this, purified water for injections must be pyrogenic and sterile.

Determination of pyrogenicity is carried out in accordance with the general pharmacopoeial monograph of FR ed. X "Pyrogenic impurities" (IX.F.10) which is based on rectal temperature tracking in rabbits. To determine the pyrogenicity of injectable preparations, including purified water for injections, in PhEur ed. 10 the LAL test (bacterial endotoxins) is regulated. The LAL test is based on the possibility of the amebocyte lysate (blood cells) of Limulus polyphemus to react with bacterial endotoxins (lipopolysaccharides). The reaction between endotoxins and lysate forms a turbidity of the reactant mixture and increases its coagulation until the formation of a dense gel. This result denotes the presence of endotoxins. The main advantage of this method compared to the rabbit test is its high sensitivity. Also, the analysis does not require much time, because the result can be read in 30-60 minutes.

Purified water for injections is used freshly prepared or stored at a temperature from 5ºC to 10ºC or from 80ºC to 95ºC in closed vessels, prepared from materials that do not change its properties and prevent contamination with mechanical and microbiological impurities, but not more than 24 hours, being kept in aseptic conditions.

Hydrogen peroxide

Hydrogen peroxide is found in small amounts in rain water, snow and in the air, coming from electrical discharges in the atmosphere. It was discovered by Thenard in 1818.

FR ed. X formalizes two Pharmacopoeia Monographs:

- ✓ Solutio hydrogenii peroxydati concentrata, concentrated hydrogen peroxide solution, known as perhydrol, which has a content of 29-31% hydrogen peroxide.
- ✓ Solutio hydrogenii peroxydati diluta, diluted hydrogen peroxide solution, which has a 3% hydrogen peroxide content and is obtained by diluting perhydrol with purified water.

Acid-base properties. Hydrogen peroxide is a very weak acid, but compared to water, it has stronger acid properties:

$$H_2O_2 \leftrightarrow H^+ + HO^-_2$$

Redox properties. Hydrogen peroxide can be both oxidizing and reducing:

$$H_2^+O_2^{2-} + 2\bar{e} + 2H^+ \rightarrow 2H_2O$$

$$H_2^+O_2^{2-} - 2\bar{e} \rightarrow 2H^+ + O_2\uparrow$$

Hydrogen peroxide is an oxidant in both acidic and basic solutions. However, in acidic solutions, oxidation proceeds more slowly. The oxidizing properties of hydrogen peroxide are well observed in the reaction with potassium iodide solution:

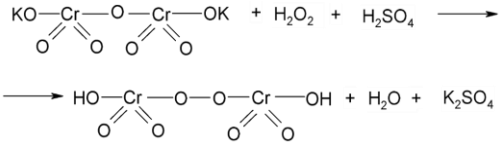
$$H_2O_2 + 2KI + H_2SO_4 \rightarrow I_2 + 2H_2O + K_2SO_4$$

The reducing properties of hydrogen peroxide are observed in reactions with strong oxidants such as potassium permanganate in an acidic environment:

$$5H_2O_2 + 2KMnO_4 + 3H_2SO4 \rightarrow 2MnSO_4 + 5O_2\uparrow + K_2SO_4 + 8H_2O$$

The specific reaction for identifying hydrogen peroxide is the formation reaction of blue colored perchromic acids. These, however, are very unstable in water, and their characteristic blue color will disappear easily and the analytical effect will not be observed. To solve the problem, a non-polar solvent will be added: diethyl ether, in which

perchromic acids dissolve easily and are stable. The analytical effect can be observed by coloring the ether layer in blue:



The quantitative determination of hydrogen peroxide is done by the permanganateometric method in an acidic environment:

$$5H_2O_2 + 2KMnO_4 + 3H_2SO_4 \rightarrow K_2SO_4 + 2MnSO_4 + 5O_2\uparrow + 8H_2O$$

Storage of hydrogen peroxide. Hydrogen peroxide is slightly stable. It easily decomposes into water and oxygen, releasing heat:

$$H_2O_2 — ½O_2 + H_2O$$

Since hydrogen peroxide is both oxidizing and reducing, it easily participates in the disproportionation reaction (autooxidation–autoreduction), as a result, its decomposition takes place:

$$H_2O_2 + H_2O_2 \rightarrow 2H_2O + O_2\uparrow$$

The decomposition of hydrogen peroxide takes place in the presence of traces of heavy metal ions, high temperature, light, and pH. Thus, these factors must be taken into account, as well as the chemical properties of hydrogen peroxide. The following storage requirements will be observed: store in neutral, dark glass vials, in a cool place, away from light and with the cap completely loose. Perhydrol is not stored in full containers because the danger of explosion is much greater. It is transported without shaking, usually in plastic containers.

Therapeutic action and uses in medical practice. Hydrogen peroxide is an antiseptic and a bactericide. In the presence of blood, it decomposes into water and oxygen under the influence of the catalase enzyme, with the formation of an abundant foam, which also has a direct bactericidal action. It is also used as a disinfectant of the oral cavity in association with chamomile infusion. Hydrogen peroxide helps to remove dressings by the effervescence it produces. It is well tolerated and has no irritating action.

2. Drug substances from the group of halogen derivatives and their compounds with alkali metals

Halogens in the form of various compounds are part of the structure of vital tissues and play an important role in the activity of the human body. Thus, fluorine is found in the bone tissue (in the enamel of the teeth), chlorine and chlorides are found in significant quantities in all body tissues, bromine is located in the pituitary gland, and iodine – in the thyroid gland. The insufficiency of these elements can cause serious diseases. Among the halogens in the molecular state, only iodine is used in medical practice. Salts of halogenated acids: chlorides, bromides, iodides, in which the halogen has an oxidation state of -1, are widely used. From the salts of oxygenated acids, hypochlorites are used, in which the halogen has the +1 oxidation state (table 2).

Table 2. **Drug substances, derivatives of halogens and their compounds with alkali metals**

The names in the Romanian and Latin languages. Chemical formula	**Physical properties. Solubility. Molecular mass**
Sodium chloride ***Natrii chloridum*** NaCl	Colorless crystals or white crystalline powder, odorless, salty taste. Slightly soluble in water, soluble in glycerol, practically insoluble in ethyl alcohol. M_r = 58,44 g/mol
Potassium chloride ***Kalii chloridum*** KCl	Colorless crystals or white crystalline powder, odorless, salty taste. Easily soluble in water, practically insoluble in ethyl alcohol. M_r = 74,5 g/mol
Sodium bromide ***Natrii bromidum*** NaBr	Small, colorless, transparent or opaque crystals or white or almost white crystalline powder, odorless, salty taste, slightly hygroscopic. Slightly soluble in water, insoluble in ethyl alcohol. M_r = 102,9 g/mol

The names in the Romanian and Latin languages. Chemical formula	**Physical properties. Solubility. Molecular mass**
Potassium bromide ***Kalii bromidum*** KBr	Colorless crystals or white crystalline powder, odorless, salty taste. Easily soluble in water and glycerol, slightly soluble in ethyl alcohol. M_r = 119,0 g/mol
Sodium iodide ***Natrii iodidum*** NaI	Colorless crystals or white or almost white crystalline powder, odorless, salty and slightly bitter taste, hygroscopic. Very slightly soluble in water, slightly soluble in ethyl alcohol. M_r = 149,9 g/mol
Potassium iodide ***Kalii iodidum*** KI	Colorless crystals or white crystalline powder, odorless, with salty and slightly bitter taste. Very slightly soluble in water, slightly soluble in glycerol, soluble in ethyl alcohol. M_r = 166,0 g/mol
Alcoholic solution of iodine 5% ***Solutio Iodi spirituosa 5%*** Iodine 5 g Potassium iodide 2 g Water and ethanol 95% (1:1) up to 100 ml	Clear, brown solution with a characteristic odor of iodine and alcohol.
Alcoholic solution of iodine 10% ***Solutio Iodi spirituosa 10%*** Iodine 10 g Ethanol 95% up to 100 ml	Clear, brown solution with characteristic smell. When water is added, a microcrystalline precipitate of iodine is deposited.
Sodium fluoride ***Natrii floridum*** NaF	Colorless crystals or white or almost white crystalline powder. Soluble in water, practically insoluble in ethyl alcohol. M_r = 41,99 g/mol

Halogens in molecular state are oxidants:

$$I_2 + 2\bar{e} \rightarrow 2I^-$$

The oxidative properties of iodine are used in the analysis of iodine and its preparations and determine the storage conditions of iodine and its alcoholic solutions.

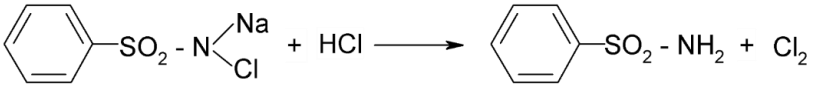
Halogens are reducing agents:

$$2I^- - 2\bar{e} \rightarrow I_2$$

Compared to chlorides and bromines, iodines give up electrons more easily, being stronger reducing agents. This property is used for the analysis of chlorides, bromides and iodines when they are simultaneously found in mixtures. Likewise, the reducing properties of halogens are also applied to purity analysis, when the impurity of one halogen is determined in the presence of another, which serves as a medicinal preparation. For example, iodide impurities in potassium bromide can be determined by reaction with iron (III) chloride, which, being a weak oxidizer, will not react with potassium bromide, but with iodide impurities, which have stronger reducing properties than the bromines.

Bromines and iodides can be identified by oxidation reactions to molecular bromine and iodine. Molecular halogens are extracted with chloroform and color it brown (molecular bromine) or purple (molecular iodine).

For the determination of the bromide ion, chloramine in the presence of hydrochloric acid is recommended as an oxidant.



$$2\,NaBr + Cl_2 \longrightarrow Br_2\uparrow + 2\,NaCl$$

For the determination of the iodide ion, sodium nitrite in an acidic medium is recommended as an oxidant:

$$2I^- + 2NaNO_2 + 2H_2SO_4 \rightarrow I_2\uparrow + 2NO + K_2SO_4 + Na_2SO_4 + 2H_2O$$

Halogens are strong oxidizers. Oxidative activity decreases from fluorine to iodine.

The common reaction for the identification of halides is the reaction of the formation of precipitates of silver halide insoluble in nitric acid, which differ by color and solubility in ammonia solution and ammonium carbonate. Silver chloride is soluble in ammonia solution and ammonium carbonate, silver bromide – in ammonia solution, silver iodide is

insoluble in ammonia solution and ammonium carbonate. All three silver halides are soluble in sodium thiosulfate solution with the formation of the complex $Na_3[Ag(S_2O_3)_2]$.

Iodine and its preparations

Iodine is presented in the form of plates or crystalline powder of a black-black color with a metallic luster. Iodine is volatile at room temperature. It will be stored in well-closed containers, in a cool place and away from light. In the pharmacy, it must be kept separately from other preparations.

When heated in a dry test tube, iodine evaporates, its vapors have a characteristic violet color. The color of the vapors is also the solution of iodine in chloroform, in which it is well soluble, which is used to release iodine from iodides in order to identify them. Iodine is well soluble in potassium iodide solution:

$$KI + I_2 \rightarrow KI_3$$

This property is used in the quantitative determination to improve the solubility of iodine in water, and also in the preparation of the 5% alcoholic solution of iodine.

To determine the identity of iodine, its property to color starch blue is used.

Iodine must not contain iodine cyanide impurities, which are determined by the Berlin blue reaction. Sulfuric acid is added to the solution to discolor the iodine:

$$I_2 + H_2SO_3 + H_2O \rightarrow H_2SO_4 + 2HI$$

Then the lack of iodine cyanide impurity is investigated. If iodine cyanide is present in the analyzed iodine sample, the blue color will appear as a result of the following reactions:

$$ICN + 2NaOH \rightarrow NaCN + NaOI + H_2O$$

$$6NaCN + FeSO_4 \rightarrow Na_4[Fe(CN)_6] + Na_2SO_4$$

$$3\ Na_4[Fe(CN)_6] + 4FeCl_3 \rightarrow Fe_4[Fe(CN)_6]_3\downarrow + 12NaCl$$

Alcoholic solutions of iodine

The 10% alcoholic solution of iodine is prepared by dissolving iodine in 95% alcohol. The preparation is unstable and easily altered. When stored, iodine easily undergoes an oxidation-reduction reaction with alcohol:

$$C_2H_5OH + I_2 \rightarrow CH_3COH + 2HI$$

The degree of degradation of the preparation is regulated by the pharmacopoeia by determining the maximum content of hydroiodic acid when titrating with sodium hydroxide solution.

The 10% alcoholic solution of iodine is prepared for a period of up to 1 month. The quantitative determination is checked periodically, no less often than once a quarter.

The 5% alcoholic solution of iodine is more stable when stored.

Compounds of halogens with alkali metals

Obtaining halogen compounds with alkali metals. Sodium chloride is the only halogen compound extremely widespread in nature in the form of salt deposits and dissolved in lakes and seas. The salt obtained from the deposits is purified by treatment with barium chloride solution, for the precipitation of sulfates and phosphates. Then, after settling, it is treated with an excess of sodium carbonate to precipitate the remains of magnesium, calcium and barium. After a new settling, it is neutralized with hydrochloric acid to remove carbonates. Potassium chloride is separated from ores by the flotation method and purified analogously to sodium chloride. Bromines and iodides are obtained by various methods. One of them consists in treating ferrous-ferric bromide (iodide) with sodium carbonate solution.

Chemical properties and methods of analysis of compounds of halogens with alkali metals. The identification of medicinal substances derived from halogens with heavy metals consists in determining the corresponding cations and anions.

Identification of the sodium cation (Na^+):

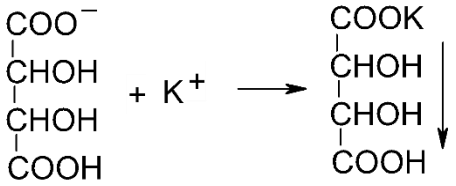
- ✓ yellow coloration of the flame;

- ✓ the reaction with zinc uranyl acetate in the presence of dilute acetic acid. A yellow-green crystalline precipitate is formed:

$$NaCl + Zn[(UO_2)_3(CH_3COO)_8] + CH_3COOH + 9H_2O \rightarrow$$
$$\rightarrow Na[Zn(UO_2)_3(CH_3COO)_9]\cdot 9H_2O\downarrow + HCl$$

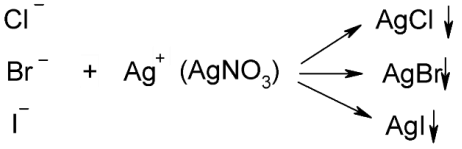
Identifying the potassium cation (K^+):

- ✓ flame color in purple, and when examined through a blue glass in red-purple;
- ✓ the reaction with tartaric acid in a neutral or weakly acetic environment with the formation of a white crystalline precipitate, easily soluble in mineral acids and alkaline hydroxides, insoluble in acetic acid and ethyl alcohol:



Identification of chloride (Cl^-), bromide (Br^-) and iodide (I^-) anions. It is determined by the reaction with silver nitrate. Different precipitates are formed according to color and solubility in nitric acid and ammonia solution:

a) silver chloride is a white, casey precipitate, insoluble in dilute nitric acid, soluble in ammonia solution;
b) silver bromide is a yellowish, caseous precipitate, insoluble in nitric acid, soluble in ammonia solution;
c) silver iodide is a yellow precipitate, insoluble in ammonia solution:



All silver halides are soluble in sodium thiosulfate solution.

The assay of drug substances from the halogen group is carried out by the argentometric method.

Medicinal substances, chloride and bromide derivatives are determined by the Mohr argentometric method. The preparations are titrated with silver nitrate in a neutral environment in the presence of potassium chromate as an indicator. At the equivalence point, the excess titrant reacts with the indicator, forming a red-orange precipitate:

$$2AgNO_3 + K_2CrO_4 \rightarrow Ag_2CrO_4\downarrow + 2KNO_3$$

Bromines are also dosed by the Wolhard argentometric method:

$$NaBr + AgNO_3\ (ex) \rightarrow AgBr\downarrow + NaNO_3 + AgNO_{3rest}$$

$$AgNO_{3rest} + NH_4SCN \rightarrow AgSCN\downarrow + NH_4NO_3$$

$$NH_4SCN + Fe(SO_4)_2NH_4 \rightarrow Fe(SCN)_3 + 2(NH_4)_2SO_4$$

Medicinal substances, iodine derivatives are quantitatively determined by the Fajans argentometric method, by titrating with a 0.1 mol/l silver nitrate solution in the presence of sodium eosinate as an indicator. Through this reaction, silver iodide is obtained in the form of colloidal particles with strong adsorption properties. Positively charged, these particles attach to their surface the anions of the negatively charged indicator and at the equivalence point, the color of the precipitate changes from yellow to pink.

The medical use of drug substances derived from halogens is different. Sodium chloride plays an important role in regulating osmosis and diffusion in the human body. Sodium bromide and potassium bromide are used as sedative substances internally and intravenously in the form of 5, 10 and 20% solutions. Iodines are used in case of iodine deficiency in the body.

Medicinal substances derived from halogens *are stored* in a dry place, in well-closed containers. For bromines and iodides, it is necessary to preserve them in dark colored glass, because in the presence of light and moisture they decompose.

3. Drug substances from the group of carbonates, hydrocarbons and boron derivatives

Carbonates and hydrocarbon compounds. Carbonic acid, being a dibasic acid, can form two types of salts - neutral (carbonates) and acids (hydrocarbons). Both neutral and acidic salts in aqueous solutions have a basic reaction, due to hydrolysis (table 3).

Boron compounds. Natural ores that contain boric acid (sasolina) and sodium tetraborate (borax, chernita) or that decompose to form these substances serve as the raw material for obtaining these preparations. In this case, the principle of the production method is that the ores (borax, chernite, asharite, borocalcite) are processed with mineral acids and transformed into boric acid, and when processed with sodium carbonate – into sodium tetraborate (table 3).

Calcium compounds. Calcium is found in the Earth's crust approximately 3.6% mostly in the form of chalk, marble, limestone, gypsum. It is part of bone tissue, blood and muscles; blood coagulation occurs only in the presence of calcium ions (table 3).

Magnesium compounds. Magnesium is found in the earth's crust in an amount of about 2.1%. It is found only in the form of compounds, for example: magnesite, dolomite, chizerite, various silicates (talc, serpentine, asbestos, etc.). Among the magnesium compounds used in medicine are: Magnesium sulfate (table 3).

Table 3. **Compounds of carbonates, hydrocarbons, boron, calcium and magnesium**

Names in Latin and Romanian. Chemical formula	Physical properties. Solubility
Sodium hudrocarbonate ***Natrii hydrocarbonas*** $NaHCO_3$	White, crystalline powder; the aqueous solution has a neutral reaction. Hardly soluble in water. M_r = 84,0 g/mol

Names in Latin and Romanian. Chemical formula	Physical properties. Solubility
Lithium carbonate ***Lithii carbonas*** Li_2CO_3	White, light powder. Hardly soluble in water, insoluble in absolute alcohol and ether. M_r = 73,9 g/mol
Boric acid ***Acidum boricum*** H_3BO_3	Crystalline powder or lamellae greasy to the touch, odorless, colorless and glossy. Dissolve in cold water 1:25, in hot water 1:3, in 25 parts of alcohol. M_r = 73,9 g/mol
Sodium tetraborate (Borax) ***Natrii tetraboras*** $Na_2B_4O_7 \cdot 10H_2O$	Colorless, transparent, very slightly efflorescent crystals or white crystalline powder. It dissolves in water and glycerin, very easily dissolves in hot water, insoluble in ethyl alcohol. M_r = 381,4 g/mol
Calcium chloride ***Calcii chloridum*** $CaCl_2 \cdot 6H_2O$	Colorless prismatic crystals, odorless, bitter taste; the crystals are very hygroscopic and deliquescent in air. It is dissolved in 0.25 parts of water, lowering the temperature of the solution. M_r = 219,1 g/mol
Magnesium sulphate ***Magnesii sulphas*** $MgSO_4 \cdot 7H_2O$	Prismatic crystals, colorless, efflorescent only in dry and warm air. Soluble in 1 part of cold water and 0.3 parts of hot water, forming transparent solutions with a bitter taste, with a neutral reaction, insoluble in alcohol. M_r = 246,5 g/mol

Carbonate and hydrocarbon compounds. *Obtaining sodium bicarbonate.* Sodium bicarbonate is obtained as an intermediate product in the preparation of sodium carbonate in the chemical industry

according to the ammoniacal method proposed by Solvay. The concentrated solution of kitchen salt is saturated with ammonia while cooling and at the same time, under pressure, a stream of carbon dioxide is passed through the solution. Ammonia reacts with carbon dioxide. The obtained ammonium hydrocarbonate reacts with sodium chloride. Sodium bicarbonate, being hardly soluble in water, falls into the precipitate. To purify the sodium bicarbonate precipitated by the ammonium chloride, the solution is decanted, which is then calcined. Thus, ammonia compounds and carbon dioxide volatilize. Sodium carbonate is obtained in the residue. The newly formed carbon dioxide is used in the reaction with ammonia, which is obtained by heating the solution containing NH_4Cl with $CaCO_3$. The sodium carbonate obtained does not contain water of crystallization and after recrystallization from water, hydrate $Na_2CO_3 \cdot 10H_2O$ is obtained. When the hydrate obtained is saturated with carbon dioxide, sodium bicarbonate is formed.

The following methods are used *to identify* sodium bicarbonate:

- ✓ identification of the sodium ion (*see* Compounds of halogens with alkali metals).
- ✓ identification of the hydrocarbon ion through the carbon dioxide release reaction by heating the solution in a water bath or when treated with hydrochloric acid:

$$NaHCO_3 + HCl \rightarrow NaCl + CO_2\uparrow + H_2O$$

Determination of purity. DAN does not allow the presence of traces of heavy metals and ammonium salts. Traces of chlorides, sulfates, potassium and arsenic are allowed.

Assay is done by the neutralization method. The sample is titrated with hydrochloric acid in the presence of the methyl orange indicator.

Sodium bicarbonate is *used in medicine* internally in the form of powder and mineral waters as an antacid remedy, as well as externally in the form of gargles, washes, inhalations.

Store Sodium bicarbonate in well-closed containers, in a cool and dry place.

Lithium carbonate is obtained from various minerals: spodumene $LiAl(Si_2O_6)$, cynvaldied $KLiFiAl[Si_3AlO_{10}](F,OH)_2$, lepidolitis.

The mineral is processed with concentrated sulfuric acid. Aluminum is precipitated with ammonia and ammonium sulfide, and the aqueous extraction is processed with sodium carbonate. As a result, lithium carbonate is obtained, which is then subjected to purification.

The identity of lithium carbonate is determined by the identification reactions of the lithium ion and the carbonate ion.

The preparation will not contain *impurities* of heavy metals, barium salts and alkaline metals. Traces of chlorides, sulfates, calcium and iron are allowed in quantities that do not exceed the concentration in the standard solutions.

Assay is done by the method of neutralization with hydrochloric acid solution (methyl orange indicator).

Lithium carbonate is *used in medicine* as a diuretic remedy in the form of powder 0.1-0.3 g several times a day.

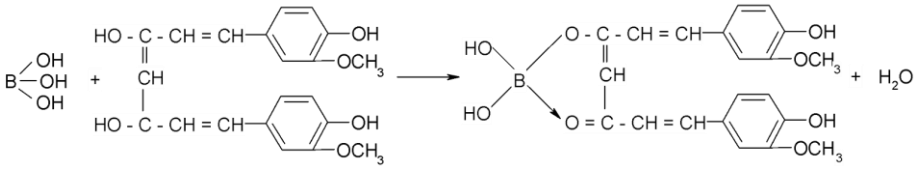
Store in tightly closed containers.

Boron compounds. *Boric acid.* The industrial method of obtaining boric acid consists in the decomposition of ash under the action of sulfuric acid at a temperature of 100-110^{0}C. The obtained mixture is separated by sublimation of boric acid at a temperature of 400-500^{0}C.

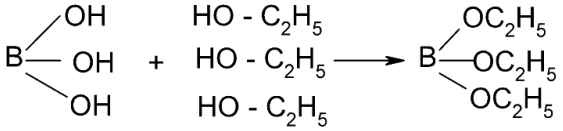
Boric acid for medical use is obtained by decomposing borax or borocalcite with a hot solution of hydrochloric acid. The precipitate that is deposited by cooling is recrystallized from water.

Identification of boric acid:

- ✓ reaction with curcumin paper. Curcumin paper, moistened with a solution of boric acid, acidulated with hydrochloric acid and then dried, is colored red-brown, which passes through moistening with ammonia in black-greenish:



- ✓ the formation reaction of boroethyl ether which burns with a flame with a green edge:

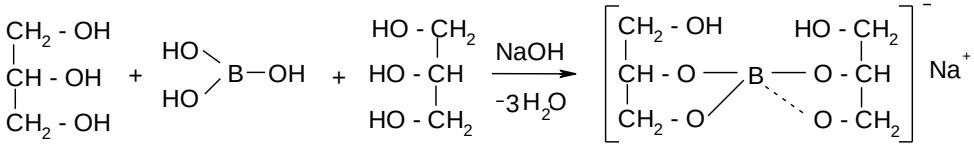


Quantitative determination. Boric acid is a weak acid. When titrating boric acid with sodium hydroxide, the equivalence point is at pH 11.0. In this pH region it is difficult to choose a sufficient indicator. On the other hand, upon the action of hydroxides with boric acid, tetraboric acid salts and, finally, metaboric acid salts are formed. Therefore, when titrating boric acid with sodium hydroxide, the sodium salt of metaboric acid hydrolyzes easily:

$$H_3BO_3 + NaOH \rightarrow NaBO_2 + 2\ H_2O$$

$$NaBO_2 + 2\ H_2O \leftrightarrow H_3BO_3 + NaOH$$

Following hydrolysis, the alkaline reaction will appear earlier than the equivalence point is reached and the result of the determination will always be smaller. So it is impossible to titrate boric acid with the 0.1 mol/l sodium hydroxide solution with the necessary precision. To increase the acidic properties of boric acid, the property of the acid to form a complex monobasic acid with glycerin is used – diglycerinboric acid which can be titrated with sodium hydroxide in the presence of phenolphthalein with sufficient precision:



The quantitative determination is carried out in a mixture (1:4) of freshly boiled purified water (released from CO_2) and glycerin (neutralized after phenolphthalein) at ambient temperature. To avoid the hydrolysis of the complex sodium salt, glycerin is added before the end of the titration. The pink color must not disappear. If it disappears, glycerin will be added and the titration will be extended. Boric acid can also be titrated in the presence of some saccharides (mannite, dulcit, sorbet, etc.).

Boric acid has weak disinfectant properties, it is used in ointments, powders, for gargle (1-2% solution), as a weak antiseptic, for nasal washes, in diseases of the external auditory canal, skin infections.

Store in tightly closed containers.

Sodium tetraborate can be obtained by treating borocalcite or boric acid with hot sodium carbonate solution. The filtrate is cooled and the precipitate that settles is recrystallized from water.

Identification. Sodium tetraborate gives all the reactions for boric acid (see above). Sodium tetraborate also colors the flame yellow (Na^+). By treating the hot sodium tetraborate solution with hydrochloric acid and cooling, boric acid precipitate is formed.

The assay of Sodium tetraborate is done by the acid-base titration method. Titrate with 0.1 mol/l hydrochloric acid solution in the presence of the methyl orange indicator, until a pink-orange coloration:

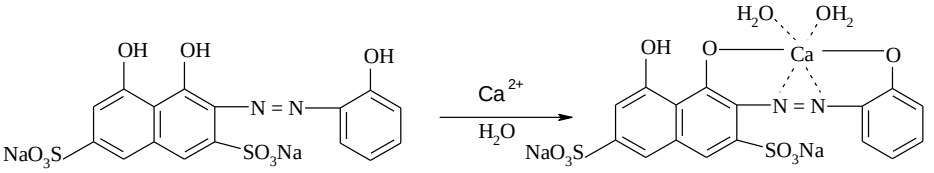
$$Na_2B_4O_7 \cdot 10H_2O + 2HCl \rightarrow 4H_3BO_3\downarrow + 2NaCl + 5H_2O$$

Sodium tetraborate is used for gargling, as a weak antiseptic, for nasal washes. Store in tightly closed containers in a cool place.

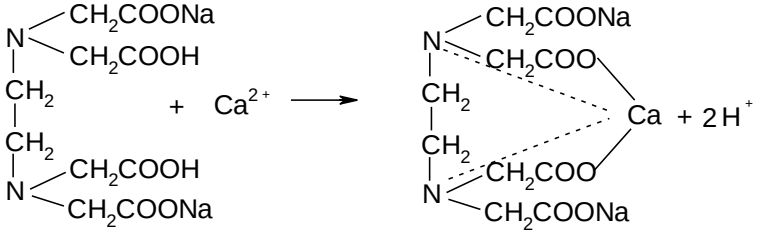
Calcium compounds. ***Calcium chloride*** it is obtained when processing chalk or marble with hydrochloric acid. For the purification of iron and magnesium salts (after oxidation to Fe^{3+}), iron and magnesium are precipitated with the help of calcium hydroxide. The heated solution is filtered, neutralized with hydrochloric acid and evaporated until $CaCl_2 \cdot 6H_2O$ crystallizes.

To identify calcium chloride, the presence of calcium and chlorine ions is determined.

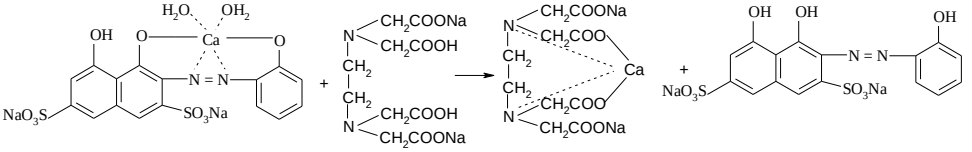
The quantitative determination of calcium chloride is done by the complexonometric method. The chromium indicator - blue - dark acid in the presence of the buffer ammonia solution forms a complex compound, colored pink, with the calcium ion:



When titrating with trilon B, the calcium ions from the solution enter the reaction first:



Next, trilon B binds the calcium ion from the calcium-indicator complex, a fact that contributes to the coloring of the solution at the equivalence point in the color of the free indicator (blue - violet).



Also, calcium chloride can be determined quantitatively by the Mohr argentometric method:

$$CaCl_2 + 2AgNO_3 \rightarrow 2AgCl\downarrow + Ca(NO_3)_2$$

$$2\ AgNO_3 + K_2CrO_4 \rightarrow Ag_2CrO_4\downarrow + 2KNO_3$$

In medicine, calcium chloride is widely used as a medicinal substance with anti-allergic, anti-inflammatory, diuretic and hemostatic

action. It is administered orally (5-10% solutions) or intravenously in 5, 10, 15 ml of 10% solution.

Calcium chloride is stored in well-closed glass containers, paraffined, in a dry place, taking into account the high hygroscopicity of the preparation. Depending on this property of the preparation, a 50% aqueous solution of calcium chloride is prepared in the pharmacy, from which different medicinal forms are then prepared.

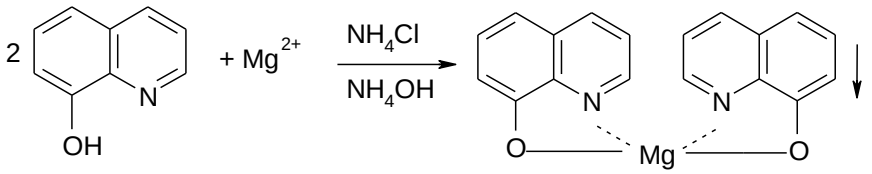
Magnesium compounds. ***Magnesium sulphate*** is obtained by heating magnesite with dilute sulfuric acid in excess. The obtained solution is concentrated until crystallization begins. Since magnesium sulfate is administered internally in large quantities, a high degree of purity is expected, which must not contain iron impurities, chlorides, heavy metals and especially traces of arsenic.

The identity of the preparation is determined by the magnesium cation and the sulfate anion:

- ✓ the formation reaction of double ammonium and magnesium phosphate - white crystalline precipitate, insoluble in water and soluble in acetic acid:

$$MgSO_4 + Na_2HPO_4 + NH_4OH \rightarrow MgNH_4PO_4\downarrow + Na_2SO_4 + H_2O$$

- ✓ the reaction with 8-oxyquinoline in the presence of ammonia and ammonium chloride. A yellow-green crystalline precipitate is observed:



Assay is done by the complexonometric method. The preparation is dissolved in dilute hydrochloric acid, ammonia buffer solution is added and the magnesium ion is titrated with 0.05 M trilon B solution (Na_2 - EDTA), in the presence of chrome black, a special acid, as an indicator, until the color changes from red-violet to blue (see $CaCl_2$).

In medicine, magnesium sulfate is used differently:

• in doses of 2-5 g it has a laxative effect;

• in doses of 20-30 g, dissolved in warm water, has a purgative action.

It is also indicated in states where the need for magnesium is increased (pregnancy, stress), in mercury, arsenic, tetraethyl lead poisoning. Magnesium sulfate is released in powder form and in ampoules containing 2, 5, 10 and 20 ml of 25% solution.

Magnesium sulfate should be kept in well-closed containers, because by exposure to air, after some time, it loses a molecule of crystallized water and becomes powdery.

4. Drug substances from the group of derivatives of silver, calcium, magnesium, zinc, iron (II), aluminum and bismuth

Zinc compounds. Zinc is frequently found in nature in the form of ores, most often in sphalerite ZnS. Zinc is found in plant and animal organisms in the tissues of muscles and teeth (table 4).

Silver compounds. Silver is found in nature in the form of compounds with sulfur (Ag_2S) and halogens (AgCl, AgI, AgBr). Silver nitrate and silver colloidal preparations are used in medicine: collargol and protargol (table 4).

Iron (II) compounds. Iron has been known since ancient times. After aluminum, iron is the most widespread metal in nature. It represents 5.1% of the earth's crust. It is found in the form of various compounds, ores, as well as in its native state. Iron compounds with oxygen and sulfur are widely distributed in nature: magnetite (Fe_3O_4), hematite (Fe_2O_3), limonite ($2Fe_2O_3 \cdot 3H2O$), siderite (FeCO3), pyrite (FeS_2), etc. Pure iron is obtained by reducing iron oxide with hydrogen or by electrolysis of some iron salts (table 4).

Bismuth compounds. Bismuth is found both in its native state and in the form of minerals, the most important of which are bismuth (Bi) and bismuth oxide (Bi_2O_3). Bismuth as a chemical element as such has no uses in pharmacy, but it is an important raw material for obtaining basic salts or oxides with therapeutic uses (table 4).

Aluminum compounds. In clinical practice, aluminum hydroxide, aluminum sulfate, aluminum alums and aluminum acetate solution (Licorea Burovi - Liquor Burovi) are used.

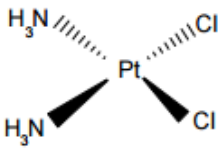
Platinum compounds. The antitumor activity of coordination combinations of Pt(II) seems to be limited to those of the type $[PtA_2X_2]$ and electrically neutral characteristic of cis isomers. The coordination combinations of Pt(II) with electric charge are inactive, even if the ligands are easily exchangeable.

The antitumor activity of Pt(II) complexes, of the $[PtA_2X_2]$ type, depends on the nature of the ligands. The best results were obtained with chlorine and bromine ions, monodentate anionic ligands with intermediate exchange capacity and with oxalate, malonate anions, bidentate carboxylate ligands.

Therefore, cis-dichlorodiaminoplatinum (II), cis $[Pt(NH_3)_2Cl_2]$ also known as Peyrone's Salt, introduced in therapeutics by Rosenberg and Van Camp, shows the highest antitumor activity (table 4).

Table 4. **Compounds of zinc, silver, iron (II), bismuth, aluminum, platinui**

The name in Latin, Romanian. Chemical formula	**Physical properties. Solubility**
Zinc sulfate ***Zinci sulfas*** $ZnSO_4 \cdot 6H_2O$	Colorless, transparent prismatic crystals or fine powder, with an astringent metallic taste, efflorescent in dry air, odorless. It dissolves very easily in water, soluble in glycerin (1:10), insoluble in alcohol. M_r = 269,5 g/mol
Silver nitrate ***Argenti nitras*** $AgNO_3$	Crystalline blades or cylindrical sticks, white or, translucent or white-gray, with a crystalline structure without odor, with an unpleasant metallic taste. It dissolves easily in water, forming transparent solutions with a neutral reaction; hardly soluble in alcohol and ether. M_r = 169,9 g/mol
Iron sulfate ***Ferri sulfas*** $FeSO_4 \cdot 7H_2O$	Prismatic, transparent, blue-green crystals, efflorescent in air. It dissolves in two parts of water, it does not dissolve in alcohol. M_r = 278,0 g/mol
Bismuth oxide ***Bismuthi oxydum*** Bi_2O_3	White, amorphous or microcrystalline powder. Practically insoluble in water and alcohol, slightly soluble in nitric and hydrochloric acid. M_r = 465,96 g/mol

The name in Latin, Romanian. Chemical formula	**Physical properties. Solubility**
Aluminum hydroxide ***Aluminii hydroxydatum*** $Al(OH)_3$	White, amorphous, fine powder, odorless and tasteless. Practically insoluble in water and alcohol. It dissolves, by heating to about 500C in dilute mineral acids and in alkaline hydroxide solutions, forming transparent or cloudy solutions. The aqueous suspension has a slightly alkaline reaction. M_r = 78,0 g/mol
Cisplatin ***Cisplatinum***  $[Pt(NH_3)_2Cl_2]$ *cis-diclorodiaminoplatină (II)*	Yellow to yellow-orange crystalline powder. Slightly soluble in 0.9% isotonic sodium chloride solution and 0.1 mol/l hydrochloric acid solution, very slightly soluble in water, practically insoluble in 95% ethyl alcohol. Table A M_r = 300,01 g/mol

Zinc compounds. ***Zinc sulfate*** is obtained by dissolving zinc or zinc oxide in dilute sulfuric acid.

The identity of zinc sulfate is established by reactions for zinc and sulfate ions:

- ✓ reaction with sodium sulfide – pharmacopoeial reaction. Sodium sulfide in a neutral environment precipitates zinc sulfide from zinc salts – a weak amorphous precipitate, soluble in mineral acids:

$$ZnCl_2 + Na_2S \rightarrow ZnS\downarrow + 2NaCl$$

$$ZnS + 2HCl \rightarrow ZnCl_2 + H_2S$$

- ✓ the zinc cation forms with the potassium ferrocyanide solution a white precipitate of zinc and potassium ferrocyanide, insoluble in dilute acids and soluble in alkaline solutions:

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

Assay of Zinc sulfate is done by the complexonometric method (*see* Calcium Chloride).

Another method of quantitative determination is the iodometric method, based on the reduction of potassium ferricyanide with potassium

iodide to potassium ferrocyanide, which reacts with the zinc ion to form the insoluble complex salt. The presence of the sulfate ion prevents the reversibility of the reaction:

$$2K_3[Fe(CN)_6] + 2KI \rightarrow 2K_4[Fe(CN)_6] + I_2$$

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

$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$$

Zinc sulfate is used externally as an astringent and disinfectant in ophthalmological practice in the form of 0.1 solutions; 0.25; 0.5%.

It is released in powder form and will be stored with caution (table B) in well-closed containers.

Silver compounds. Silver nitrate is obtained by dissolving the silver and copper alloy in nitric acid when heated. In order to purify the silver nitrate obtained from impurities, it is precipitated with hydrochloric acid in the form of silver chloride, being then reduced to metallic silver freed from impurities, which again transforms into silver nitrate. The obtained solution is concentrated until crystallization begins. The crystals are washed with water and dried in the dark.

The identity of the preparation is determined by the silver ion and the nitrate ion.

Identification of the silver ion:

- ✓ when hydrochloric acid is added, silver chloride salt is precipitated, insoluble in nitric acid and easily soluble in ammonia:

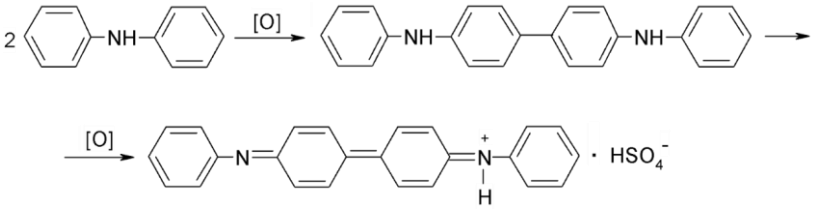
$$AgNO_3 + HCl \rightarrow AgCl\downarrow + HNO_3$$

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

- ✓ eduction of silver from the ammonia solution of silver nitrate when heated with formic aldehyde solution:

$$Ag^+ + CH_2O + 3NH_3 + H_2O \rightarrow Ag\downarrow + 3NH_4^+ + HCOO^-$$

Identification of the nitrate ion. The reaction with diphenylamine and the formation of the brown ring under the action of silver nitrate in the presence



The quantitative determination of silver nitrate is done by the thiocyanometric method*:*

$$AgNO_3 + NH_4NCS \rightarrow AgNCS\downarrow + NH_4NO_3$$

The excess ammonium rhodanide titrant reacts with the indicator - ferroammoniacal alum solution, coloring the mixture at the end of the titration in pink yellow:

$$3NH_4NCS + FeNH_4(SO_4)_2 \rightarrow Fe(NCS)_3 + 2(NH4)_2SO_4$$

Silver nitrate is used in medicine as an astringent and cautery in eye diseases, urethral and urinary bladder diseases. It is administered prophylactically in eye diseases in newborns in the form of a 1-2% solution.

Silver nitrate is stored with caution (table A) in well-closed dark glass containers.

Iron (II) compounds. ***Iron (II) sulfate*** it is obtained by dissolving reduced iron taken in excess in 25-30% sulfuric acid solution when heated to 80^0C.

The solution is evaporated until crystallization begins and the obtained preparation is dried at a temperature of 30^0C.

The drug substance is identified by the ion of Fe^{2+} and SO_4^{2-}:

- ✓ the reaction with the alcoholic solution of dimethylglyoxime. A complex compound is obtained - a red precipitate, insoluble in ammonia.
- ✓ reaction with potassium ferricyanide. An intense blue precipitate (Turnbull's blue) is formed:

$$FeSO_4 + K_3[Fe(CN)_6] \rightarrow KFe[Fe(CN)_6] + K_2SO_4$$

Dosing is permanganateometrically. For the dosage of iron, the property of Fe^{2+} to oxidize to Fe^{3+} is used, therefore the sample of the

preparation is dissolved in sulfuric acid when heated and after cooling it is titrated with a 0.1 mol/l potassium permanganate solution until a stable pink coloration.

It is administered in the form of gelatin capsules 0.3-0.5 g 3-4 times a day.

Store in well-closed containers, better in waxed or paraffined containers (to avoid the transition of Fe^{2+} to $Fe3^{+}$).

Bismuth compounds. ***Bismuth oxide.*** Chemical methods are used to identify bismuth:

- ✓ the reaction with alkaline solutions or ammonia, after which a white precipitate of bismuth hydroxide is formed, insoluble in excess reagent, but soluble in mineral acids:

$$Bi^{3+} + 3OH^{-} \rightarrow Bi(OH)_3\downarrow$$

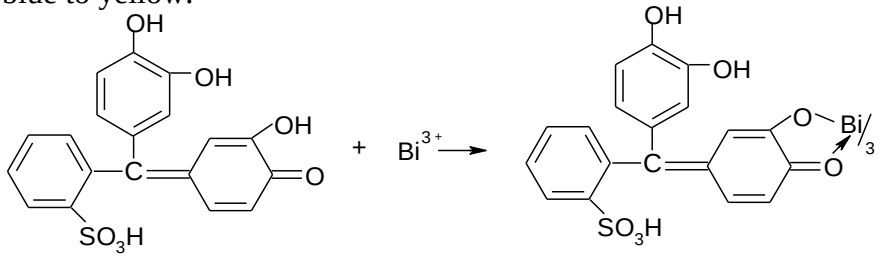
- ✓ the reaction with the sulfide ion: the bismuth ion in the medium of dilute hydrochloric acid forms a brown-black precipitate with the sulfide ion:

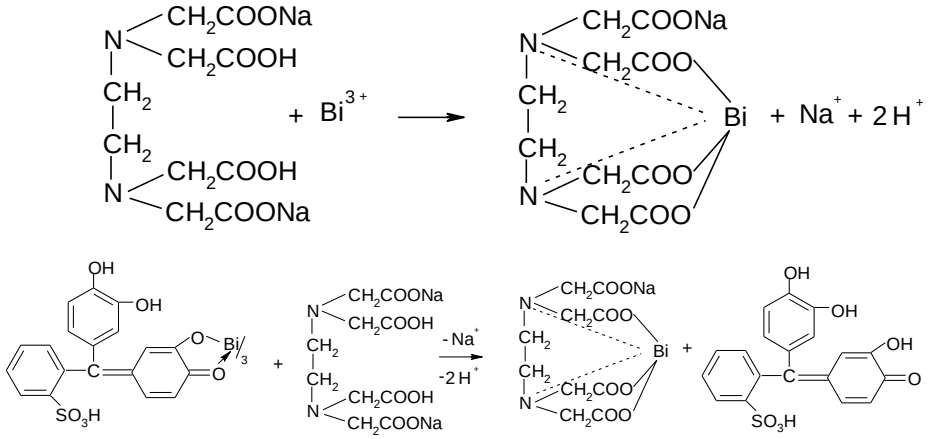
$$Bi^{3+} + S^{2-} \rightarrow Bi_2S_3\downarrow$$

- ✓ the reaction to form complex compounds with potassium iodide, as a result of which a black precipitate is obtained, soluble in excess reagent with the formation of the yellow-orange bismuth tetraiodide ion (III):

$$Bi^{3+} + 3I^{-} \rightarrow BiI_3\downarrow$$
$$BiI_3 + I^{-} \rightarrow [BiI_4]^{-}$$

The complexonometric method of quantitative analysis of bismuth preparations. Trilon B 0.05 mol/l solution serves as the titrant solution. The titration is done in the presence of pyrocatechin violet indicator or xylene orange. The equivalence point is determined by the color change from blue to yellow.





Aluminum compounds. ***Aluminum hydroxide*** is obtained by boiling the 10% aluminum sulfate solution with ammonia solution. The precipitate obtained from aluminum hydroxide is washed well until the sulfate ions are removed and dried at 40^0C, then the temperature is increased to 100^0C:

$$Al_2(SO_4)_3 + 6NH_4OH \rightarrow 2Al(OH)_3\downarrow + 3(NH_4)_2SO_4$$

Identification methods of aluminum hydroxide:

- ✓ when aluminum hydroxide is calcined with cobalt nitrate a blue color appears:

$$Al^{3+} + Co(NO_3)_2 \rightarrow Co(AlO_2)_2\downarrow + 2NO_2\uparrow + O\uparrow$$

- ✓ following reactions with sodium hydroxide and ammonium chloride, a white, gelatinous precipitate is obtained:

$$Al(OH)_3 + NaOH \rightarrow Na[Al(OH)_4]$$

$$2\ Al(OH)_4^- + NH_4^+ \rightarrow Al_2O_3 \cdot nH_2O\downarrow + NH_3\uparrow$$

Assay of aluminum hydroxide by the complexonometric method. Trilon B 0.05 mol/l solution serves as the titrant solution. The titration is done in the presence of the pyrocatechin violet indicator. The equivalence point is determined by the color change from red to yellow.

Conservation and use in medical practice of aluminum hydroxide. Aluminum hydroxide is used internally as an antacid and externally to treat burns, eczema and other ailments.

Aluminum hydroxide is stored in tightly closed containers.

Platinum compounds. *Cisplatin* can be identified by:

- ✓ the presence of platinum in cisplatin: following the reaction with formic acid, platinum is reduced to metallic platinum, which is deposited as a black sediment:

$$[Pt(NH_3)2Cl_2)] + HCOOH \rightarrow Pt\downarrow + 2\ NH_4Cl + CO_2\uparrow + N_2\uparrow$$

- ✓ the presence of chlorine ion in cisplatin is determined by the reaction with silver nitrate. A white precipitate of silver chloride will form.
- ✓ the presence of ammonia in cisplatin: when boiling the preparation with sodium hydroxide solution in the presence of zinc powder, ammonia will be released, detected by the specific smell and the yellowing of the litmus paper:

$$Pt(NH3)2Cl2)] + 4NaOH + Zn + 2H2O \rightarrow$$
$$\rightarrow 2NH3\uparrow + Na2[Pt(OH)2Cl2 + H2\uparrow + Na2[Zn(OH)4]$$

- ✓ comparing the infrared spectrum of the cisplatin sample to be analyzed with that of the standard cisplatin solution.

Assay:

- ✓ gravimetric method;
- ✓ the Kjeldahl method (after nitrogen);
- ✓ HPLC.

Use in medical practice. Since 1978, cisplatin as a single preparation or combined with other cytostatics (vinblastine, bleomycin, adriamycin, cyclophosphamide) has been used in the treatment of ovarian, lung, bladder and head-neck carcinomas (figure 1).

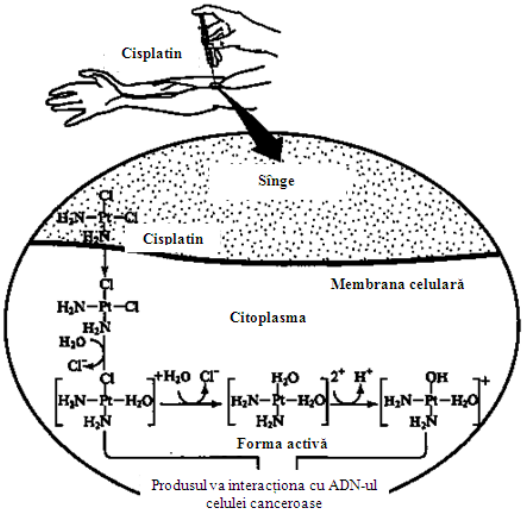


Figure 1. **Mechanisms of molecular transformation of Cisplatin into the active form in the body**

Cisplatin is administered intravenously as a 0.01% injectable solution. It is stored according to table A, at a temperature of $+40^0$C, in a place protected from light.

TASKS FOR INDIVIDUAL WORK

I. Oxygen compounds

1. Indicate the pharmacopoeial preparations of hydrogen peroxide.
2. Write the chemical reaction that can be used to demonstrate the identity of hydrogen peroxide. State the conditions for the reaction to occur.
3. Explain how the acidity of hydrogen peroxide can be confirmed.
4. Quantitative determination of hydrogen peroxide. Write the chemistry of the reaction and indicate the principle and essence of the method.
5. Indicate the use of hydrogen peroxide in medical practice and the storage conditions.
6. Name the factors that contribute to the degradation of hydrogen peroxide following improper storage. Indicate the possibilities of increasing the stability of hydrogen peroxide.
7. Write the chemistry of the reactions, in which hydrogen peroxide has reducing and oxidizing properties.

II. Compounds of halogens with alkali metals

1. Indicate the chemical properties characteristic of the elements of group VII, the main subgroup of the periodic table.
2. List the medicinal substances, derivatives of alkali metal halides used in medical practice.
3. Write the chemical reactions used for the qualitative determination of medicinal substances, derivatives of alkali metal halides. State the conditions under which chemical reactions take place.
4. Indicate the impurities provided in the pharmacopoeia for medicinal substances, derivatives of alkali metal halides.
5. Indicate the methods used for the quantitative determination of medicinal substances, derivatives of alkali metal halides. Write the

chemical reactions and explain the principle and essence of the methods.

6. Indicate the varieties of the argentometric method of quantitative analysis of medicinal substances, derivatives of alkali metal halides. State the advantages and disadvantages of each method.

7. Indicate the medicinal substance that is presented in the form of a potassium salt of a halide, which, when stored improperly: in a humid place, became wet.

8. The sodium salts of chloride, bromide and iodide were stored improperly: at high humidity, 2 of them being moistened, and 1 turning yellow. Indicate the medicinal substances that have degraded.

9. Explain how sodium chloride, sodium bromide and sodium iodide can be distinguished from each other by the reaction with silver nitrate. Write the chemistry of the reactions. Indicate the conditions for carrying out the reactions.

10. The quantitative analysis of 2 medicinal substances was carried out: sodium chloride and potassium iodide in the presence of two indicators: potassium chromate and sodium eosinate. Indicate which indicator was used to determine each medicinal substance.

11. Following the dosing of sodium chloride, the reaction medium was acidic. Select from the following indicators: sodium eosinate, bromphenol blue, potassium chromate, and ammonium ferric alum which can be used in this situation and explain the choice.

12. When titrating 0.2972 g of potassium iodide (Mr = 166), 17.6 ml of 0.1 mol/l silver nitrate solution (K=1.01) was consumed. Write the chemical reactions, explain the cause of the change in the color of the indicator and calculate the content (%) of potassium iodide in the preparation.

13. Check if the potassium bromide (Mr = 119) corresponds to the pharmacopoeial requirements: at least 99.5% and at most 100.5%, if 18.0 ml of silver nitrate solution was consumed during the titration of 0.2145 g of sample 0 .1 mol/l (K=0.99).
14. When titrating the sample of sodium iodide (Mr = 149.89) with a mass of 0.3165 g, 20.2 ml of 0.1 mol/l silver nitrate solution was consumed. Check if the sodium iodide corresponds to the pharmacopoeial requirements, if the mass loss on drying was 5%, and in the dry preparation it must be not less than 99.0% and not more than 100.5%.
15. In the sample of potassium chloride, the presence of sulfate ions is allowed in an amount no greater than 0.005%. To determine this impurity, 2.0 g of sample was dissolved in 10 ml of purified water. Calculate the maximum allowed content (%) of sulfate ions in the obtained solution and check if it corresponds to the content (%) of sulfate ions in the standard solution.

III. Compounds of carbonates, hydrocarbons, boron, calcium and magnesium

1. Write the chemical reactions by which the identity of boric acid and sodium tetraborate can be demonstrated. Indicate the conditions for the reaction.
2. List the allowed impurities and indicate their permissible limits in boric acid and sodium tertraborate according to the pharmacopoeial regulations.
3. List the impurities that must be absent in boric acid and sodium tertraborate according to pharmacopoeial regulations. Write the chemistry of chemical reactions.
4. Indicate possible sources of impurities in boric acid and sodium tetraborate.

5. Write the chemistry of the reactions for the quantitative determination of boric acid. Explain the principle and essence of the method.
6. Write the chemistry of the reactions for the quantitative determination of sodium tetraborate. Explain the principle and essence of the method.
7. Explain the purpose of adding glycerine to the quantitative determination of boric acid.
8. Indicate the medical use of boric acid and sodium tertaborate.
9. Indicate what explains the fact that aqueous solutions of sodium tertarborate have a basic environment, and glycerine solutions - acid.
10. Explain how medicinal substances can be distinguished: sodium tetraborate from boric acid by solubility in different solvents.
11. Alcoholic solutions of boric acid when burning color the flame with green edges. Explain what chemical processes are taking place. Argue under which conditions the analogous chemical reaction can also be performed for sodium tetraborate.
12. When determining the impurity of arsenic in boric acid, cotton wool soaked in lead acetate solution was not inserted into the apparatus. Can the result be wrong because of this? Explain for what purpose the cotton wool is inserted for the determination of arsenic.
13. For the quantitative determination of boric acid, the titration ended without the repeated addition of glycerin. Argue whether the determination was made correctly. Indicate what mistake is possible under these conditions.
14. For the quantitative determination of sodium tetraborate, 20 ml of 0.1 mol/l hydrochloric acid solution was consumed. The sodium tetraborate content was 102.5%. Calculate what sample mass was taken for analysis.

15. Explain how the impurities of manganese salts in magnesium sulfate are determined.
16. Calcium chloride is recommended to be kept in pharmacies in the form of a 50% aqueous solution. Argue how this fact is explained.
17. Explain how calcium chloride can be distinguished from magnesium sulfate by solubility in water and ethanol.
18. Following some quantitative determinations, the content of calcium chloride was obtained as 101.1%, and the content of magnesium sulfate – 102.0%. Check that the medicinal substances correspond to the Dosage index according to the pharmacopoeial requirements.
19. In the sample of magnesium sulfate, the presence of iron ions is allowed in a quantity no greater than 0.002%. To determine this impurity, a 15% magnesium sulfate solution was prepared. Calculate what is the maximum allowed content (%) of iron ions in the obtained solution and check if it corresponds to the content (%) of iron ions in the standard solution.
20. For the quantitative determination of a sample of magnesium sulfate, 15 ml of trilon B solution 0.05 mol/l was consumed. The magnesium sulfate content was 99.0%. Calculate what sample mass was taken for analysis.

IV. Compounds of zinc, silver, iron (II), bismuth, aluminum and platinum

1. Indicate the medicinal substances, derivatives of zinc, silver, iron (II), bismuth, aluminum and platinum that are included in the pharmacopoeia.
2. Write the identification reactions of medicinal substances, derivatives of silver and zinc.
3. Explain the principle and essence of the quantitative determination by the complexonometric method of bi- and trivalent metal salts.

4. Explain for what purpose the ammonia buffer solution is added to the quantitative analysis by the complexonometric method.
5. Indicate which indicators are used in the complexonometric method. Explain which fact is due to the change in the color of the titration solutions at the equivalence point.
6. Indicate the methods by which the quantitative determination of zinc sulphate can be carried out.
7. Write the chemical reactions that are used to determine the impurities of iron, copper, aluminum salts in zinc sulfate.
8. Explain how acidity and basicity are determined in solutions of medicinal substances derived from zinc.
9. Write the chemical reactions used to identify the silver ion. Indicate the conditions of their party.
10. State the method by which the quantitative analysis of iron (II) sulfate can be carried out. Write the chemistry of the reactions
11. Write the chemical reactions used for the quantitative determination of silver nitrate. Explain the principle and essence of the method.
12. Indicate the use of silver compounds in medical practice.
13. Explain why silver nitrate belongs to list A.
14. As a result of long storage in the light, the silver nitrate turned black. What explains this fact? Argue through chemical reactions.
15. Calculate the content (%) of silver nitrate, if 12.2 ml of ammonium thiocyanate solution 0.1 mol/l was consumed during the titration of a sample weighing 0.2100 g, K=1, Mr (silver nitrate)= 169.9 g/mol. Conclude whether the sample to be analyzed corresponds to the requirements of the pharmacopoeial monograph (at least 99.5% and at most 100.5%).

PRACTICAL WORK OF STUDENTS

I. Analysis of drugsubstances from the oxygen group

Task 1. ***To assess the quality of medicinal substances according to the indications: "Description" and "Solubility".***

The obtained results are noted and the conclusion is made about the quality of medicinal substances. Solvents are chosen according to the provisions of DAN.

Task 2. To determine the quality of drug substances.

1. Hydrogen peroxide

1.1. Identification.

1.1.A. Formation of perchromic acids. To 1 ml of hydrogen peroxide solution, add 0.2 ml of dilute sulfuric acid, 2 ml of ether, then add 0.2 ml of potassium dichromate solution and stir, the ether layer turns blue.

1.1.B. Oxidizing properties of hydrogen peroxide. To 2 ml of diluted hydrogen peroxide solution, add 1 ml of sulfuric acid, 1 ml of potassium iodide solution, 5 ml of chloroform, stir, the chloroform layer turns purple.

1.1.C. The reducing properties of hydrogen peroxide. To 5 ml of diluted hydrogen peroxide solution, add 1 ml of sulfuric acid, 0.5 ml of 1% potassium permanganate solution; the potassium permanganate solution discolors.

1.2. Assay.

1.2.A. Permanganometric method. Take an exact volume of 10 ml sample and add it to a volumetric flask with a capacity of 100 ml, bring it up to the level with purified water (solution A). Add 5 ml of sulfuric acid to 10 ml of solution A and titrate with potassium permanganate solution until a faint pink coloration.

1 ml of potassium permanganate solution 0.1 mol/l corresponds to 0.001701 g of hydrogen peroxide, which in the preparation must be 2.7-3.3%.

II. Analysis of drug substances from the halogen group

Task 1. To assess the quality of medicinal substances according to the indications: "Description" and "Solubility".

The obtained results are noted and the conclusion is made about the quality of medicinal substances. Solvents are chosen according to the provisions of DAN.

Task 2. To perform the identification reactions of medicinal substances.

1. Identification of the sodium ion

1.1. Flame coloring. Sodium salt, introduced into the flame, colors it yellow.

1.2. Reaction with zinc uranyl acetate. 1 ml of 10% sodium chloride solution is acidified with diluted acetic acid, filtered if necessary, then 0.5 ml of zinc uranyl acetate solution is added, a yellow crystalline precipitate is formed.

2. Identification of the potassium ion

2.1. Reaction with tartaric acid. To 1 ml of 10% potassium iodide solution, add 1 ml of tartaric acid solution, 1 ml of sodium acetate solution, 0.5 ml of ethanol and stir, cooling the walls of the test tube. A white crystalline precipitate is deposited, which dissolves in mineral acids.

2.2. Reaction with sodium cobalt nitrite. To 1 ml of 10% potassium iodide solution, previously calcined to remove ammonium salts, add 0.5 ml of diluted acetic acid solution, 0.5 ml of sodium cobalt nitrite solution; a yellow, crystalline precipitate is formed.

2.3. Flame coloring. Potassium salt, introduced into the flame, colors it purple.

3. Identification of the potassium ion

3.1. Silver nitrate reaction. To 2 ml of sodium chloride (potassium chloride) 0.5% solution, add 0.5 ml of dilute nitric acid solution and 0.5 ml of silver nitrate solution. A white casey precipitate, soluble in ammonia, is obtained.

4. Identification of the bromine ion

4.1. Silver nitrate reaction. To 1 ml of 1% potassium bromide (sodium bromide) solution, acidulated with nitric acid, add a few drops of silver nitrate solution. A caseous yellow precipitate is obtained, hardly soluble in ammonia solution.

4.2. Oxidation reaction with chloramine. To 1 ml of 1% potassium bromide (sodium bromide) solution, add 1 ml of diluted hydrochloric acid solution, 0.5 ml of chloramine solution, 1 ml of chloroform and stir. The chloroform layer turns yellow-brown.

5. Identification of the iodine ion

5.1. Silver nitrate reaction. To 2 ml of 1% potassium iodide (sodium iodide) solution, add 0.5 ml of nitric acid solution and 0.5 ml of silver nitrate solution. A caseous yellow precipitate is obtained, insoluble in ammonia solution.

5.2. Oxidation reaction. To 2 ml of 1% potassium iodide (sodium iodide) solution, add 0.2 ml of dilute sulfuric acid solution, 0.2 ml of sodium nitrite solution or iron (III) chloride solution and 2 ml of chloroform. Upon stirring, the chloroform layer turns purple.

Task 3. Assay of medicinal substances from the group of halogen compounds.

3.1. Assay of potassium bromide by Mohr's argentometric method. Take an exact amount of 0.2 g of the sample, previously dried at 1100C for 4 hours, dissolve in 20 ml of purified water and titrate with a 0.1 mol/l solution of silver nitrate until a color is obtained yellow-orange (potassium chromate indicator).

1 ml of 1 mol/l silver nitrate solution corresponds to 0.01190 g of potassium bromide, which in the dry preparation must be no less than 99.0% and no more than 100.6%.

3.2. Assay of potassium iodide by the Fajans argentometric method. Take an exact amount of 0.3 g of the sample, previously dried at 1100C for 4 hours, dissolve in 30 ml of purified water, add 1.5 ml of diluted acetic acid, 5 drops of sodium eosinate. Titrate with the

0.1 mol/l silver nitrate titrant solution until the color of the precipitate changes from yellow to pink. In this case, an adsorption indicator is used.

1 ml of 1 mol/l silver nitrate solution corresponds to 0.01660 g of potassium iodide, which in the dry preparation must be no less than 99.5%.

3.3. Assay of potassium chloride by Mohr's argentometric method. Take an exact amount of 1 g of the sample, dissolve it with purified water in a graduated flask with a volume of 50 ml and bring the volume of the solution to the mark with purified water. Take 5 ml of the obtained solution and dilute it with purified water to a volume of 40 ml and titrate with a solution of 0.1 mol/l silver nitrate until a yellow-orange color is obtained (indicator - potassium chromate).

1 ml of 1 mol/l silver nitrate solution corresponds to 0.007456 g of potassium chloride, which in the dry preparation must be no less than 99.5%.

3.4. Assay of sodium bromide. The quantitative determination is carried out analogously to potassium bromide.

1 ml of 1 mol/l silver nitrate solution corresponds to 0.01029 g of sodium bromide, which in the dry preparation must be no less than 99.0% and no more than 100.6%.

3.5. Assay of sodium iodide. The quantitative determination is carried out analogously to potassium iodide.

1 ml of 1 mol/l silver nitrate solution corresponds to 0.01499 g of sodium iodide, which in the dry preparation must be no less than

III. Analysis of drugsubstances from the group of boron, calcium, magnesium, carbonates and hydrocarbons

Task 1. To assess the quality of medicinal substances according to the indications: "Description" and "Solubility".

The obtained results are noted and the conclusion is made about the quality of medicinal substances. Solvents are chosen according to the provisions of DAN.

Task 2. To determine the quality of medicinal substances.

1. Acid boric

1.1.A. The reaction with curcumin paper. The curcumin paper, soaked with the aqueous solution of the preparation (1:10) and a few drops of hydrochloric acid, turns pink or red-brown after drying, which turns green-black when soaked with ammonium hydroxide solution.

1.1.B. Boroethyl ester formation reaction. When the boric acid sample is dissolved in ethyl alcohol, boroethyl ester is formed, which burns with a green flame.

1.2. Dosage.

1.2.A. Alkalimetric method. About 0.2 g of sample (exact mass) is dissolved in 10 ml of freshly boiled and cooled water, 40 ml of glycerin, previously neutralized after phenolphthalein, is added. Mix the solution, add 15 drops of phenolphthalein solution and titrate with 0.1 mol/l sodium hydroxide solution until pink. Then add another 10 ml of neutralized glycerin to the titrated solution, and if the pink color disappears, titrate again until the pink color of the solution appears. Add glycerin and titrate with sodium hydroxide until the last 10 drops of neutralized glycerin disappear.

10 ml of sodium hydroxide solution 0.1 mol/l corresponds to 0.006183 g of boric acid, which in the preparation must be no less than 99.5%.

2. Sodium tetraborate

2.1. Identification.

2.1.A. The reaction with curcumin paper. See 1.1.A.

***2.1.B. Boroethyl ester formation reaction*.** Take 0.2 g of the preparation in a porcelain crucible, dissolve in one ml of concentrated sulfuric acid, add 3 ml of ethanol. The mixture burns with a green flame (see 1.1.B.).

2.1.C. Reaction with zinc uranyl acetate. 1 ml of 10% sodium tetraborate solution is acidified with diluted acetic acid, filtered if necessary, then 0.5 ml of zinc uranyl acetate solution is added, a yellow crystalline precipitate is formed.

2.1.D. Flame coloring. Sodium salt, introduced into the flame, colors it yellow.

2.2. Assay.

2.2.A. The neutralization method. About 0.5 g of sample (exact mass) is dissolved in 30 ml of water and titrated with 0.1 mol/l hydrochloric acid solution until a pink-orange color (indicator: methyl orange).

1 ml of 0.1 mol/l hydrochloric acid solution corresponds to 0.01907 g of sodium tetraborate, which in the preparation must be no less than 99.5% and no more than 103.0%.

3. Calcium chloride

3.1. Identification.

3.1.A. Reaction with ammonium oxalate. To 1 ml of 5% calcium chloride solution, add 1 ml of ammonium oxalate solution. A white precipitate forms. The precipitate is insoluble in dilute acetic acid and ammonia solution, but is soluble in dilute mineral acids.

3.1.B. Flame coloring. Sodium salt soaked in hydrochloric acid colors the flame brick-red.

3.1.C. The reaction with silver nitrate. To 2 ml of 0.5% calcium chloride solution, add 0.5 ml of dilute nitric acid solution and 0.5 ml of

silver nitrate solution. A white casey precipitate, soluble in ammonia, is obtained.

3.2. Assay.

3.2.A. The complexonometric method. About 0.8 g of sample (exact mass) is dissolved in water, transferred to a volumetric flask with a volume of 100 ml, the volume of the solution is brought up to volume with purified water and mixed well. To 25 ml of the obtained solution, add 5 ml of ammonia buffer solution, 7 drops of eriochrome blue solution and titrate with trilon B solution 0.05 mol/l until blue-violet coloration.

1 ml of trilon B solution 0.05 mol/l corresponds to 0.01095 g of calcium chloride, which in the preparation must be no less than 98.0%.

4. Magnesium sulphate

4.1. Identification.

4.1.A *The formation reaction of the double salt of ammonia solution of magnesium phosphate.* To 1 ml of 5% magnesium sulphate solution, add 1 ml of ammonium chloride solution; 0.5 ml sodium hydrogen phosphate solution and 1 ml ammonia solution. A white crystalline precipitate forms. The precipitate is soluble in acetic acid.

4.1.B. The reaction with barium chloride. To 2 ml of 5% magnesium sulphate solution, add 0.5 ml of diluted hydrochloric acid solution and 0.5 ml of barium chloride solution; a white precipitate is obtained. The precipitate is insoluble in dilute acids.

4.2. Assay.

4.2.A. The complexonometric method. About 0.15 g of sample (exact mass) is dissolved in 50 ml of purified water, 5 ml of ammonia buffer solution is added and titrated with vigorous stirring with trilon B solution 0.05 mol/l until the blue color (indicator – black of eriochrome). In parallel, the control test takes place.

1 ml of trilon B solution 0.05 mol/l corresponds to 0.01232 g of magnesium sulfate, which in the preparation must be no less than 99.0% and no more than 102.0%.

5. Sodium bicarbonate

5.1. Identification.

5.1.A. Reaction for the hydrocarbon ion. To 0.2 g of sodium carbonate (hydrocarbonate) or to 2 ml of 10% sodium bicarbonate solution, add 0.5 ml of dilute acid solution. Carbon dioxide bubbles are removed. When they pass through lime water, a white precipitate is formed.

5.1.B. The sodium ion. See 2.1.C.

5.2. Assay.

5.2.A. Acidimetric method. About 0.2 g of sample (exact mass) is dissolved in 30 ml of purified water and titrated with 0.1 mol/l hydrochloric acid solution until a pink-orange coloration (methyl orange indicator).

1 ml of 0.1 mol/l hydrochloric acid solution corresponds to 0.0084 g of sodium bicarbonate, which in the preparation must be no less than 99.5% and no more than 103.0%.

IV. Analysis of drug substances derivatives of silver, iron (II), bismuth, zinc, aluminum and platinum

Task 1. To assess the quality of medicinal substances according to the indications: "Description" and "Solubility".

The obtained results are noted and the conclusion is made about the quality of medicinal substances. Solvents are chosen according to the provisions of DAN.

Task 2. To determine the quality of medicinal substances.

1. Zinc sulfate

1.1. Identification.

1.1.A. Reaction with sodium sulfide. To 2 ml of 5% zinc sulfate solution, add 0.5 ml of sodium sulfide solution. A white precipitate forms. The precipitate is insoluble in dilute acetic acid and is slightly soluble in dilute hydrochloric acid.

1.1.B. Reaction with potassium hexacyanoferrate(II). To 2 ml of 5% zinc sulfate solution, add 0.5 ml of potassium hexacyanoferrate (II) solution (potassium ferrocyanide); a yellowish white precipitate is formed. The precipitate is insoluble in dilute hydrochloric acid.

1.1.C. Reaction with barium chloride. To 2 ml of 5% zinc sulfate solution, add 0.5 ml of dilute hydrochloric acid and 0.5 ml of barium chloride solution; a white precipitate is obtained. The precipitate is insoluble in dilute acids.

1.2. Assay.

1.2.A. The complexonometric method. Dissolve about 0.3 g of sample (exact mass) in 100 ml of purified water, add 5 ml of ammonia buffer solution and titrate with trilon B solution 0.05 mol/l until it turns blue (indicator – eriochrome black).

1 ml of trilon B solution 0.05 mol/l corresponds to 0.01438 g of zinc sulfate, which in the preparation must be no less than 99.5% and no more than 101.1%.

2. Silver nitrate

2.1. Identification.

2.1.A. Reaction with chloride ion. To 1 ml of 2% silver nitrate solution, add 2-3 drops of diluted hydrochloric acid solution or sodium chloride solution; a casey white precipitate is formed, insoluble in nitric acid, soluble in ammonia solution.

2.1B. The silver mirror forming reaction. Add ammonia solution to 1 ml of 2% silver nitrate solution until the precipitate formed at the beginning dissolves, then add 2-3 drops of formaldehyde and heat. A layer of metallic silver appears on the walls of the test tube.

2.1.C. The reaction for the nitrate ion. A few drops of diphenylamine solution are added to about 0.001 g of sodium nitrite; a blue color appears.

2.2. Assay.

2.2.A. Thiocyanometric method. Dissolve about 0.3 g of sample (exact mass) in 50 ml of purified water, add 5 ml of dilute nitric acid solution and titrate with 0.1 mol/l ammonium thiocyanide solution.

1 ml of 0.1 mol/l ammonium thiocyanide solution corresponds to 0.01699 g of silver nitrate, which in the preparation must be no less than 99.75%.

3. Iron (II) sulfate

3.1. Identification.

3.1.A. Reaction with potassium hexacyanoferrate (III). To 2 ml of 5% iron (II) sulfate solution, add 0.5 ml of diluted hydrochloric acid and 1 ml of potassium hexacyanoferrate (III) solution (potassium ferricyanide). A blue precipitate forms.

3.1.B. The reaction with sodium sulphide. A few drops of sodium sulfide or ammonium sulfide solution are added to 2 ml of 5% iron (II) sulfate solution. A black precipitate forms. The precipitate is soluble in dilute mineral acids.

3.1.C. The reaction for the sulfate ion. See 1.1.C.

Note. The results obtained when performing tasks 1-4 to be presented in table 5.

Table 5. The results obtained when performing tasks 1-4

Names of drug substances in Latin and Romanian; **chemical name; structure formula**	**Description (for analyzed substances), Identification of drug substancesc** - work technique (conditions, analytical effect); reaction chemistry (for analyzed substances)	**Quantitative determination** the working method, the chemistry of reactions for chemical methods of analysis or the basic principles for physico-chemical methods; calculation formula for determining the content of the active substance; the conclusion about the quality of the analyzed substance based on the results obtained.

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