МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ’Я УКРАЇНИ
ХАРКІВСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ

OVERVIEW OF THE BIOGENIC ELEMENTS. COMPLEX FORMATION IN BIOLOGICAL SYSTEMS

Methodical instructions for 1st year students’ self-work
in Medical Chemistry

ЗАГАЛЬНІ ВІДОМОСТІ ПРО БІОГЕННІ ЕЛЕМЕНТИ. КОМПЛЕКСОУТВОРЕННЯ У БІОЛОГІЧНИХ СИСТЕМАХ

Методичні вказівки для самостійної роботи студентів 1-го курсу
з медичної хімії

Затверджено
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Загальні відомості про біогенні елементи. Комплексоутворення у біологічних системах; методичні вказівки для самостійної роботи студентів 1-го курсу з медичної хімії / уклад. Г. О. Сирова, Т.С. Тішакова, О.В. Савельєва та ін. – Харків: ХНМУ, 2017 – 38 с.

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Subject «OVERVIEW OF THE BIOGENIC ELEMENTS. COMPLEX FORMATION IN BIOLOGICAL SYSTEMS»

1. **Number of hours** 4
2. **Material and methodological support.**

Tables:

1. Scheme of structure of the subject.
2. Mendeleyev's Periodic table.
3. Iron-containing proteins.
4. Ions of metals in the metal enzymes.
5. Properties d-block elements in the organism.
6. Heme.
7. Chlorophyll.
8. Vitamin B_{12}.
9. Carbonic anhydrase.

Educational literature

1. Medical chemistry / V.A. Kalibabchuk, V.I. Halynska, V.I. Hryshchenko et al.; – Kyiv:AUS Medicine Publishing, 2010, - 224 p.
2. Fundamentals of medical chemistry: manual for students' self-work / A.O. Syrovaya, E.R. Grabovetskaya, L.G. Shapoval. – Kharkiv: KhNMU, 2015.–196 p.
3. Medical chemistry. Adapted concise course: manual for students' self-work / A.O. Syrovaya, E.R. Grabovetskaya, L.G. Shapoval. - Kharkiv: KhNMU, 2013. – 160 p.
4. Medical chemistry: workbook for self-work of first-year students of medical and dentistry faculties / compiled by A. O. Syrovaya, V. N. Petunina, V. A. Makarov et al. – Kharkiv : KhNMU, 2017. – 72 p.
5. Overview of the biogenic elements. Complex formation in biological systems; methodical instructions for 1st year students' self-work in Medical Chemistry / compiled by A.O. Syrovaya, T.S. Tishakova, E.V. Savelieva et al. – Kharkiv: KhNMU, 2017. – 38 p.
6. Individual tasks for students' self-control of knowledge in Medical Chemistry / A.O. Syrovaya, L.G. Shapoval, V.N. Petiunina et al. – Kharkiv: KhNMU, 2014. – 50 p.
7. Text of Lecture.

2. **Substantiation for the subject**. All living organisms, their tissues and organs contain different quantities of all known chemical elements. The role of chemical elements in the organism is many-sided. 96% of the human body is made up of four *p*-block elements – organogens: carbon, oxygen, hydrogen, and nitrogen. There is a great content of sodium, potassium, calcium, phosphorus, sulfur, etc. in the human organism. Microelements represented by *d*-block elements are in the composition of enzymes, hormones, vitamins and other biologically active substances which participate in reproduction, growth, and metabolism processes. Studying of properties of chemical elements, their role in vital activity is necessary for a future physician for

better understanding the normal and pathological processes taking place in the human organism.

Coordination compounds (complexes) are widely present in the minerals, plants and animals and play many important functions. Many biologically important compounds are coordination compounds in which complicated organic species are bound to metal ions. The common examples are: hemoglobin which is coordination compound of iron, chlorophyll which is coordination compound of magnesium, etc.

3. **The purpose of the subject**:

- general:

to explain the common physical and chemical properties of s-, p-, d-block elements in the living organism.

to explain the common physical and chemical properties of complexing agent, show an example.

- specific:

to be able to analyze the relationship between concentration of ionic form of elements and disease caused by change in their content in the organism; to study the methods of treatments.

to be able to analyze the relationship between complex compounds and other reactants in the living organism.

a) **to know:**

content in the organism; day requirements; the role of s-, p-, d-block elements in the metabolism of the living organism; peculiarities of influence of hypo- and hyper-content of different elements on the enzymatic processes and other biological processes in the organism.

the role of complex compounds in the metabolism of the organism, characteristic of the common enzymatic reactions with participation of complex compounds in the processes of life; to know the application of complexons in medicine.

b) **to be able to**:

use norms of content of s-, p-, d-block elements for the evaluation of states of biological processes; predict states of the organism in case of hypo- and hyper-content of elements.

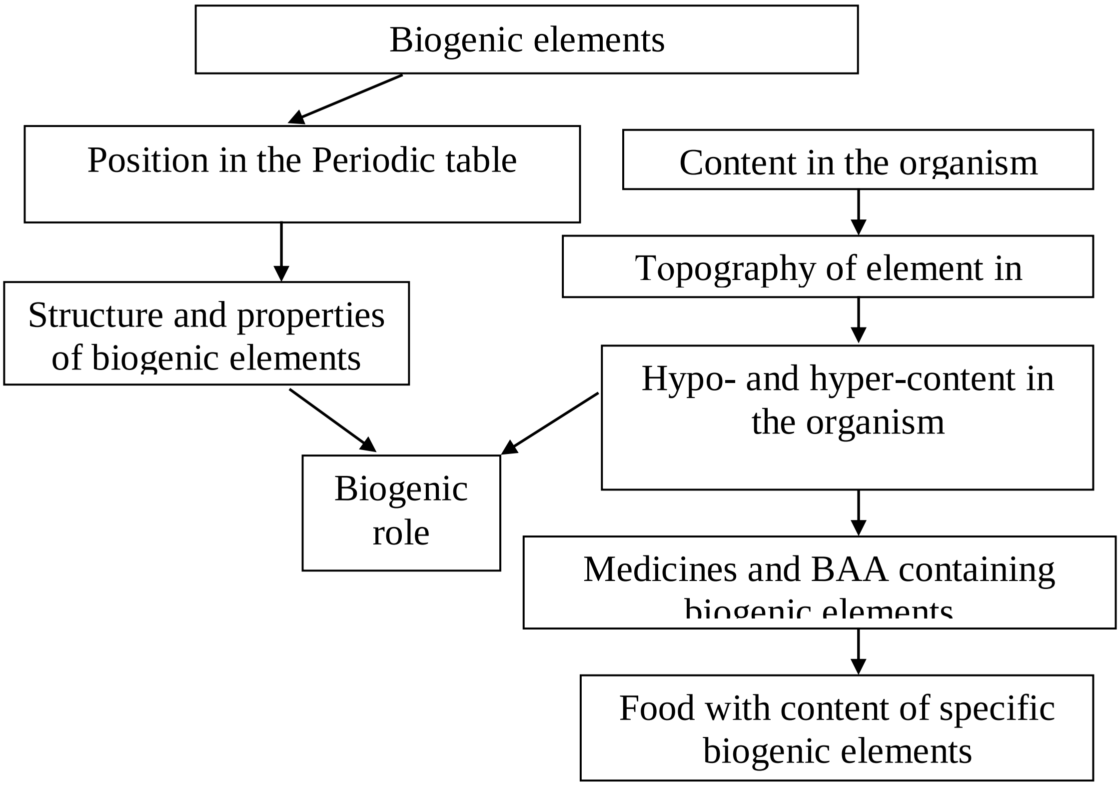
determine the type of the complex compound; name the complex compound; write the equation of the complex ion dissociation; write the equation of the constant of instability of the complex ion; determine oxidation state of the complexing agent (central ion), the charge of complex ion, coordination number.

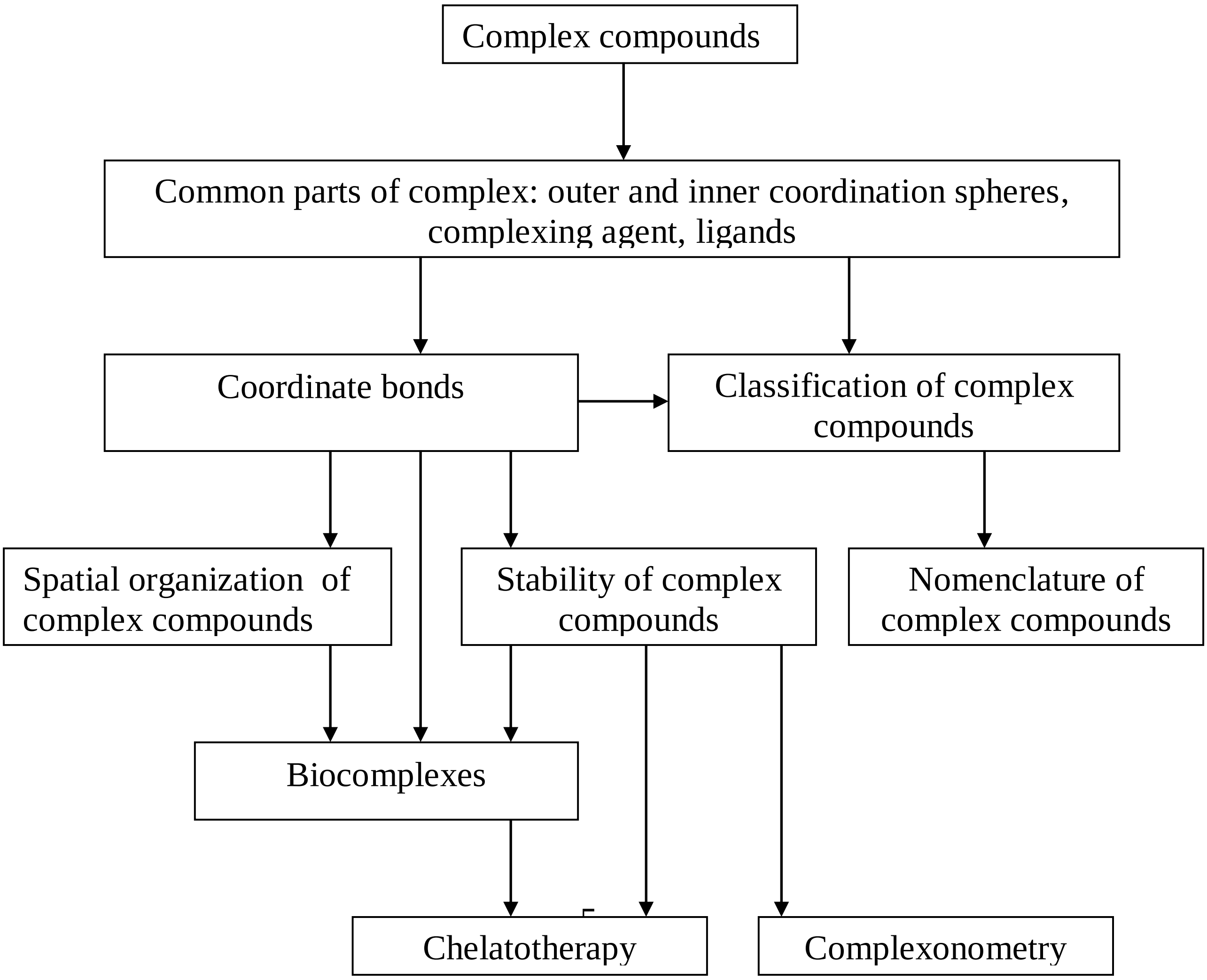
4. **Practical skills**

- To be able to characterize elements from the point of view of their electronic structure and their position in Mendeleyev's Periodic table.
- To have the idea about biogenic role of the most important *s*- and *p*-block elements.
- To be able to characterize electronic structure of *d*-block elements atoms and to predict their properties;

4. To have the idea about biogenic role of *d*-block elements.

5. **Scheme of structure of the subject.**





6. Plan of students' work.

№	Stages	Time (min.)	Training and visual aids	Location
1.	Motivation description and plan of topics. Questions and answers	25	Manual	Class room
2.	Incoming control	20		
3.	Independent work of students with methodical literature, the solution of educational problems, filling of work-book	70	Methodical instructions for students, text of lecture, manual for students' self-work, work-book, reference data, tables	
4.	Laboratory work	25	Methodical instructions for students, text of lecture, manual for students' self-work, work-book, reference data	
5.	Final control	25		
6.	Analysis and conclusions Home work	10 5		

7. **Tasks for self-work:**

- List of questions to be studied:

1. Chemical elements: common data.
2. Biogenic elements: general aspects.
   – V. I. Vernadsky's theory;
   – content of elements in the human organism and environment;
   – pollution of environment;
   – endemic diseases
3. Biological role of chemical elements, application in medicine. Toxicity of compounds.
4. Laboratory work on biogenic elements.
5. Complexes: general aspects, fundamentals of the Alfred Werner's coordination theory.
6. Structure of complex compounds.
7. Bonding in Coordination Compounds.
8. Spatial Structure and Isomerism in Coordination Compounds.
9. Classification of Complex Compounds.
10. Nomenclature of Coordination Compounds (given by IUPAC).
11. Equilibria in the solutions of Complexes. Stability of Complex Compounds
12. Biologically important complexes. Chelation.
13. Complexometric analysis.

1. Chemical elements: common data.

All matter in the Universe occurs in the form of atoms of a small number of elements. An atom is the fundamental unit of an element. For each element, it consists of a unique (fixed) number of positively charged protons in a central nucleus – the atomic number for that element – surrounded by a cloud of an equal number of negatively charged electrons. Electrons exist in principal energy levels known as ***shells***. Each successive level out from the nucleus is higher in energy and has a progressive higher capacity for electrons. The electron capacity of a shell is determined from the formula $2n^2$ where n is an integer that designates each energy level and is referred to as the ***principal quantum number.*** For the first energy level, n=1, for the second energy level, n=2; and so forth. The electron capacity for the first shell is 2, for the second shell is 8, for the third is 18, for the fourth is 32.

Shells contain one or more ***subshells***. For each shell, the number of subshells is equal to the value of its quantum number n. The first shell (n=1) has an *s* subshell. The second shell (n=2) has two subshells, an *s* and a *p*. The third shell (n=3) has three (*s, p* and *d*) and the fourth shell (n=4) has four (*s, p, d* and *f*). Each subshell is composed of one or more ***orbitals***. *An orbital is the region of space where there is the highest probability of finding a particular electron.* An orbital can contain one or two electrons. An *s* subshell is composed of one orbital and has a capacity of two electrons. A *p* subshell is composed of three orbitals, so it has a capacity of six electrons (two per orbital). A *d* subshell is composed of five orbitals (maximum is 10 electrons), and *f* subshell is composed of seven orbitals (14 electrons). The different types of orbitals are differentiated by their shape.

There are 92 naturally occurring chemical elements in the Universe. All substances in the Universe are formed through chemical reactions among combinations of atoms of these elements. In the Universe, the chemical elements differ greatly in their relative abundance. Hydrogen and helium are the most common elements. In the Earth System, the chemical elements also differ greatly in their relative abundance. There are about 25 biogenic elements which play major roles in the living systems.

The Periodic Table is a two-dimensional tabular arrangement portraying the elements in terms of similarities and differences in chemical properties. This method makes use of the ***periodicity***, or repeating nature, of properties of the elements. The periodicity results from the way in which electrons fill in *s, p, d,* and *f* orbitals.

In the table, the elements are arranged in rows in increasing order of atomic number, running from left to right across the table. The horizontal rows are called ***periods***. The periods are numbered from one to seven using Arabic numerals, corresponding to the seven energy levels of an atom that can contain electrons. This means that any element in, say, period 3 has its outermost electrons assigned to the third energy level. Across each period, going from left to right, there is a progression from metals to non-metals.

The columns are termed ***groups*** or ***chemical families*** and are usually denoted with roman numerals. There are eight groups (I to VIII). In each group, the outermost electron shell contains the same number of electrons for each member. The number of electrons in this outermost shell is the group number. The number of electrons in the outermost energy level (***valance electrons)*** determines the chemical characteristics of the element. In the periodic classification of elements, the elements have been broadly divided into four blocks namely *s, p, d,* and *f*-blocks. The division is based on the type of atomic orbital which receives the last electron in the atom.

The groups are numbered from left to right by Roman numerals I through VIII and the letters A and B. The elements belonging to ***s*- and *p*- blocks** in the periodic table are called **representative elements** or **the main groups elements.** They belongs to groups I – VIII A. The main elements of life – **macroelements** (**macrominerals)** – C, H, O, N, P, S, Na, Ca, K, Mg, Cl – are in this category. All ***s*-block** elements are metals possessing pronounced reducing properties. They locate in groups IA and IIA. Highly reactive metals – **alkali metals** are in group IA. Another group of metals that are also chemically reactive is found in group IIA and are known as the **alkaline earth metals**. The elements belonging to groups IIIA to VIIIA belong to ***p*-block**. Some of them are metals and others are non-metals. Five out of thirty p-block elements (C, O, N, P, S) are organogens. Group VIIA are all nonmetals and are known as the **halogens**. Atoms of these non-metals contain seven electrons in their outer electron shell. All form univalent anions, *e.g.*, Cl^{-}. They are oxidizing agents, decreasing in oxidizing power (and chemical reactivity) with increasing period, so that fluorine is the most reactive and iodine the least.

The elements in group VIIIA are collectively termed ***noble*** or ***inert gases***. Their electronic configurations are very stable as the outer shell of electrons is complete. They gain or lose electrons only in extreme conditions and so do not normally enter into chemical reactions. They exist as monatomic gases.

The **B** group elements consist of three rows of 10 elements in the middle of the table and are called the ***transition elements***, o***r transition metals***. They are ***d*-block** elements. These elements have very similar chemical properties not only within the group, but also along periods. This similarity in chemical behavior results from the fact that across the transition elements, electrons are being added to the *d*-subshell of next-to-outermost level. The outermost level of each transition element contains only one or two electrons in its *s*-orbital. The elements of this block have general characteristic properties intermediate between the elements of *s*-block and *p*-block. In other words, *d*-block elements represent change (or transition) in properties from most electropositive *s*-block elements to least electropositive *p*-block elements. All the transition elements are metals. In contrast to representative elements, the transition elements form a large number of coordination complexes. The transition metal ions bind to a number of anions or neutral molecules in these complexes. The common examples are $[Ni(NH_3)_6]^{2+}$, $[Fe(CN)_6]^{3-}$, $[Co(NH_3)_6]^{3+,}$ $[Fe(CN)_6]^{4-}$, etc. Such vitally important biological compounds as hemoglobin, myoglobin, vit B_{12}, cytochromes, catalase, peroxidase, chlorophyll, etc are also complexes. The high tendency of transition metal ions to form complexes is due to small size of the atoms and ions of transition metals, high nuclear charge, and availability of vacant *d*-

orbitals of suitable energy to accept lone pairs of electrons donated by other groups (called ligands).

The elements in which the last electron enters the *f*-orbital of their atom are called ***f*-block elements**. In these elements, the last electron is added to the *f*-orbital of the third to the outermost (called antepenultimate) energy level. These elements are also called ***inner transition elements.*** Elements 58 to 71 are the ***Lanthanide*** or ***Rare Earth*** elements. Elements 90 to 102 (to 103 if the elements that have been created artificially are counted) are termed the ***Actinide*** elements. Lanthanide and Actinide form two rows of 14 elements at the bottom of the table.

2. Biogenic elements: general aspects.

Living organisms, like all other matter on earth, are composed of atoms of the naturally occurring elements. Fifteen elements – oxygen, silicon, aluminum, iron, calcium, sodium, potassium, magnesium, hydrogen, titanium, chlorine, phosphorus, carbon, sulfur, nitrogen – constitute 99.68% of Earth's mass. All other elements make up less than 1%. 82 out of 92 of naturally occurring elements are found in living organisms, and there are about 25 elements that have so far been shown to be essential to life.

V. I. Vernadsky (1863-1945), Academician, an outstanding mineralogist and geochemist, was one of the founders of geochemistry and its branch – biogeochemistry – studying the part played by living organisms in geochemical processes. He introduced the term "biosphere" – the portion of the earth which is occupied and changed by living organisms. Biosphere contains 100 billion tons of live substance. Living organisms participate in continuous redistribution of chemical elements in the Earth's crust, that's why almost all elements of the crust and sea water can be found in the human body.

The main book of V.I. Vernadsky is *The Living Substance* in which he described all the spheres of the Earth, such as atmosphere, hydrosphere, lithosphere and biosphere and described their evolution. He wrote, "Between inert and live substance in biosphere there is, however, a never interrupted, constant link which can be expressed as incessant biogenic flow of live substance atoms into inert substance and back". This biogenic atomic flow is expressed in never stopping breathing, nourishment, propagation, etc.

Some elements widely present in nature are seldom detected in human and vice versa. Peculiarities of elemental accumulation are displayed in this fact – active and selective use of outer elements to support homeostasis and construct organism independently of changing environmental parameters.

Hydrogen, carbon, nitrogen, and oxygen make up 96% of the mass of human body. Calcium, phosphorus, potassium and sulfur constitute 3% of the mass of human body. Iodine, iron, sodium, chlorine, magnesium, copper, manganese, cobalt, zinc and other elements make up 1%.

The biogenic elements can be classified as **macroelements (macro-minerals)** – the content in the organism is **more than 10^{-2}%** and **microelements (trace elements)** – the content in the organism is $10^{-3} – 10^{-5}$% .

Macroelements are elements found in almost all of Earth's living systems. There are 11 of them. Six are called ***organogens*** or ***major biogenic elements***. Organogens are: **C, O, H, N, P, S.** The content of them is 97% in the organism. These elements have not very large atomic radii and intermediate values of electronegativity. These facts are favorable for strong covalent bonds formation.

Remaining five macrominerals or ***minor biogenic elements*** (elements found in living systems in relatively small quantities), are **Ca, Cl, Mg, K, Na**.

Microelements are essential elements necessary only in very small quantities to maintain the chemical reactions on which life depends. These are: **Cu, Fe, Mo, Zn, Co, F, I, B, Mn, Se, As, Si, Cr, Ni, Sn, V.**

The main organogen is carbon. It is capable to form strong covalent bonds. Carbon, hydrogen, oxygen, nitrogen, sulfur, phosphorus constitute proteins, nucleic acids, carbohydrates, lipids. In the proteins the content of carbon is 51–55%, oxygen – 22–24%, nitrogen – 15–18%, hydrogen – 5– 7%, sulfur – 0.3–2.5%. Besides, organogens make up many inorganic molecules (carbon dioxide, nitrogen (II) oxide (important bioregulator) and anions (carbonate, phosphate, sulfate, etc) which are important for body functions. In the past the necessity of microelements to good nutrition was largely overlooked, with most emphasis focused on the importance of vitamins. Today it is recognized that the microelements play an equally important nutritional role. Many microelements form important parts of enzymes. Because enzymes can be used over and over again, the microelements can be effective even when present in only very low concentrations in the cells of the body. Having considered biological role of microelements and its participation practically in all the biochemical processes in human organism, questions of environmental pollution alarm not only ecologists but physicians of all specialties. Conception of ***microelementoses*** has been introduced to mark all pathological processes provoked by deficiency, surplus or misbalance of microelements. Nowadays, the problem of human metabolism disturbances provoked by environmental pollution and effects of negative ecological factors is very actual.

For each microelement within the body a specific range of concentration allows the body to function normally. If the minimum concentration is not present, signs of a deficiency begin to appear. As a concentration of a microelement continues to decrease, a deficiency disease develops and death can result. Each of the microelements is also potentially toxic if the range of safe and adequate concentration for that element is exceeded. Physicians long ago paid attention to interrelation of many diseases with intake deficiency and content in organism of definite elements. For example, connection between iron deficiency status of organism and anemia development was determined.

The role of iodine deficiency in endemic pathogenesis had been proved at the close of XIX century.

In a region of China where food was grown on selenium – deficient soils, people suffered from a disease of the heart muscle called Keshan disease. This heart disease largely disappeared when the people in the area were treated with selenium salts. The death rate from heart disease is higher in regions of the USA where soils are deficient in selenium. By way of contrast, if selenium is present in large amounts in soil it causes disease called "blind staggers". This disease affects grazing animals. Symptoms include impaired vision, muscle weakness, loss of hair, and sometimes necrosis of the liver and death from respiratory failure. The minimum daily requirement for selenium in adult men is 0.07μg, but intake of 1 mg daily can cause toxic effects.

In New Zealand where the content of cobalt in the grass is low, animals died because of anemia.

In Australia, in regions rich in manganese, aborigines suffered from illness which is similar to Parkinson's disease – a brain disease that causes a tremor and makes muscles become rigid.

3. Biological role of chemical elements, application in medicine. Toxicity of compounds.

Hydrogen is one of six elements – organogens (C, H, O, N, P, S), which constitute 97.4% of human body mass. Hydrogen makes up about 10 % of human body mass. Hydrogen is included into composition of most important organic and inorganic substances which play great biological role in the human organism. For example, the content of the hydrogen in the proteins is from 6.5 to 7.3%, molecules of nucleic acids are connected by hydrogen bonds. Hydrogen also is a component of such biologically important compounds as vitamins, hormones, enzymes, water, etc. The water content in the body of the adult person is about 70 %. Water is the necessary metabolite; it participates in hydrolysis reactions, hydration and swelling processes. Water maintains acid-base, osmotic, hemodynamic, and thermal equilibria, and also provides turgor of tissues. The natural mineral water possessing physical influence on an organism is applied in medicine. Hydrogen peroxide H_2O_2 in the form of 3% solution is used as disinfectant and hemostatic substance.

Lithium is a microelement (10^{-4}%). It is included in the composition of blood, tissues and organs of human and animals. Especially there is a lot of Li in muscles. Lithium being antagonist of sodium and potassium displaces them out of tissues when gets into the organism. Lithium ions influence the transport of sodium ions in neurons and myocytes. Lithium takes part in regulation of higher nervous activity and also affects immunity and water-salt metabolism. Lithium carbonate Li_2CO_3 is used in psychiatric practice and when treating immune deficiency states. Lithium salts possess antistress action – they suppress pathological emotional lability and exaltation, aggression at mental diseases.

Higher concentration of lithium in hair may be detected in patients with disturbances of kidneys excretive function, sodium metabolism, overdose of lithium preparations. Low level of lithium is detected in patients with psychic disorders, kidneys diseases as well as in offspring of dipsomaniacs, in patients with immune deficiency diseases including neoplasm risk.

Sodium is a macroelement (0.25 %). It is the main extracellular ion. It is contained in the plasma, lymph, digestive juice. Daily requirement for human is 4–7 g. Among the blood plasma cations, sodium heads the list and accounts for 93% (mass) of their total amount. Sodium is a major osmotically active ion in extracellular space. Sodium plays the most important role in water-and-salt balance, regulation of nervous-muscle activity, kidneys function. Na^+ ion participates in the maintenance of pH in the organism. Sodium and potassium ions provide generation and sustenance of bioelectric potentials – the so-called resting potential and action potential in the nerve cell and myocytes (sodium pump). These ions maintain transmission of nervous impulses through membranes of nervous cells and sustain a normal excitability of cells.

The change of sodium ions content in an organism disturbs functions of nervous, cardiovascular systems, smooth and skeletal muscles. Sodium influences the function of enzymes and participates in the regulation of water metabolism. Sodium is able to increase the swelling of proteins (fixing of water by proteins).

Isotonic solution of sodium chloride (0.9% (mass)) is used to help cure poisonings, toxic dyspepsia, vomiting, cholera, acute hemorrhage, shock. It is also used for dissolution of different medicines. The hypertonic solution is administered intravenously for treatment of pulmonary, gastric, intestinal and other internal bleedings. Externally it is applied as compresses to cure purulent wounds.

Sodium sulfate is used as purgative, cholagogue agent, diuretic. Sodium bicarbonate neutralizes hydrochloric acid of the gastric juice, increases buffer capacity of the blood and reduces acidosis. Sodium bicarbonate is administered orally for cure of hyperacid gastritis, peptic ulcer of a stomach and duodenal intestine. The source of sodium for the organism is common salt (NaCl).

Potassium is a macroelement (0.22%). It is in composition of organs and tissues of the organism. It is contained in liver, kidneys, heart, brain, muscles, blood, etc. Potassium is the main intracellular ion, so the potassium level in the cells is much higher as compared to the extracellular space. Potassium ions along with sodium ions are responsible for the generation and sustenance of bioelectric potentials. Potassium ions participate in the protein synthesis, carbohydrates metabolism, they influence activity of some enzymes. Potassium is especially essential for muscle activity, including myocardium, supporting of water-salt balance, and function of endocrine system.

The increased content of potassium in the organism is accompanied by decreasing of nerve and muscles excitability and conductibility, large doses of potassium suppress cardiac contraction (bradycardia). Toxic doses cause appearing of small intestine ulcers and cardiac standstill.

The decreased content of potassium leads to grave disturbances of cardiac performance (tachycardia). Potassium chloride helps cure serious intoxications, persistent vomiting, muscular dystrophy, disturbances of cardiac rhythm; it is used for restoration of potassium level in the organism. Potassium acetate CH_3COOK is applied for edemas reducing. Potassium bromide and potassium iodide are administered for nervous system and myocytes regulation. Potassium orotate is antiarrhythmic substance.

Vegetables (e.g. Brussels sprouts) and meat are the source of potassium for the organism. Potassium surplus may lead to calcium deficiency.

Magnesium is a macroelement (0.04%). The bivalent magnesium ion, Mg^{2+}, is found mostly within the cells. Topography of magnesium in the organism is the following: dentine, enamel of teeth, bones, pancreas, skeletal muscles, kidneys, brain, liver, heart. The daily requirement is 10 mg per 1kg of body weight. In biological fluids magnesium is present in the free state as well as being bonded with proteins. There is a lot of magnesium in plants. It is in composition of chlorophyll molecules $C_{55}H_{72}O_5N_4Mg$ (up to 2% (mass)), Mg^{2+} ions are complexing agents in these molecules. Magnesium is of great importance for the organism. Ions Mg^{2+}, depending upon the concentration, block or provide nervous – muscular transmission, they suppress the respiratory center, decrease the arterial pressure. Magnesium is a component and activator of some enzymes, (e.g. carboxypeptidase, cholinesterase, etc.) Magnesium forms complex compounds with proteins of some enzymes (e.g. enolase, phosphorylase, etc). Mg^{2+} ions inhibit acetylcholine secretion, promote cholesterine excretion, and stimulate peristalsis of the intestine and bile secretion. They also influence carbohydrate metabolism, stimulate protein formation, regulate energy storage and redemption in ATP, decrease excitation in nervous cells, and relax cardiac muscle.

Magnesium compounds are widely used in medicine. Magnesium sulfate $MgSO_4 \cdot 7H_2O$, or Epsom salt, is recommended for the treatment of cramps, hypertension, gallbladder disease, for anesthesia of labor. If administered internally it provides laxative, cholagogue, diuretic actions. White clay (ammonium silicate with calcium and magnesium silicates impurity) possesses adsorbing properties. In dermatology it is used externally in the composition of powders, ointments, pastes, internally – in case of intoxication. Magnesium thiosulfate MgS_2O_3 is prescribed internally in case of hypertension, atherosclerosis, chronic coronary failure, alimentary canal disorders. Magnesium carbonate (magnesia alba) $3MgCO_3 \cdot Mg(OH)_2 \cdot 3H_2O$, magnesium oxide (magnesia usta) and magnesium trisilicate $Mg_2Si_2O_8 \cdot H_2O$ have antacid action, they are used in case of hyperacid gastritis, peptic ulcer of stomach and duodenum, poisonings with acids. Magnesium peroxide ($MgO_2 \cdot MgO$) is antimicrobic and astringent substance. It is used in case of dyspepsia, meteorism, and diarrhea. Asparcam consisting of potassium aspartate and magnesium aspartate is used to compensate the deficiency of potassium and magnesium in the organism and is prescribed as antiarrhytmic drug.

Vegetables with green leaves (containing chlorophyll) are the source of magnesium for the organism. Surplus of magnesium may lead to calcium deficiency.

Calcium is one of the most widespread elements in nature. Calcium is present in every cell of human body. It is a macroelement (1.4 %). The daily requirement for calcium is 0.8–0.9g. Concentration of calcium ions in the organism is regulated by hormones of parathyroid gland. Calcium absorption in the organism depends upon many factors and is controlled by vitamin D. In the case of vitamin D deficiency the absorption of calcium decreases. Calcium being in the form of salts $CaCO_3$ and $Ca_3(PO_4)_2$ is the major structural component of osseous tissue and teeth. The content of calcium in bones closely relates with the presence of phosphoric acid salts. Hardness and growth of skeleton, bones mineralization depend upon the content of calcium. Calcium is actively involved in the processes of neuromuscular excitation (as an antagonist to K^0 ions), muscular contraction, and blood clotting; calcium affects the permeability of cell membranes. Ca^{2+} ions promote acetylcholine secretion (magnesium antagonist). Calcium is present in the composition of some enzymes (e.g. lecithinase) and influences their activity. Calcium ions influence acid-base equilibrium; thyroid glands function, possess anti-inflammatory and desensitized actions. Calcium ions are antagonists for the sodium, potassium and magnesium ions.

Calcium chloride decreases vessels permeability, causes antiallergic and anti-inflammatory action. It is used in case of allergy, radiation sickness, bleeding, bones fractures, dermal diseases, and poisonings with magnesium salts, oxalic acid, hydrofluoric acid, lead, mercury, and phosgene. Calcium carbonate deposited $CaCO_3$ has antacid and absorptive properties. It is administered internally to treat disorders of alimentary canal. Calcium sulfate (dried gypsum) $2CaSO_4 \cdot H_2O$ is applied for gypsum bandages in case of fractures. Calcium hydroxide and calcium oxide find their use in stomatology. Soluble calcium salts are used in medicine for electrophoresis.

Milk food, vegetables, cereals are the source of calcium for the organism.

Strontium is a microelement (10^{-3} %). Strontium is accumulated chiefly in bones, it partially substitutes calcium. Strontium is important for strength of teeth enamel. It participates in osteogenesis. Radioactivity of ^{90}Sr isotope formed in atomic explosion causes radiation sickness, sarcoma, leukosis. Accumulation of ^{90}Sr nuclide in the atmosphere is very dangerous for human, at the same time, radioactive nuclides ^{89}Sr and ^{90}Sr are applied for bones tumors cure.

Barium is a microelement (10^{-5} %). Barium is accumulated in the eyes, e.g. its amount in retina is 1.5% (mass), but its biological function is not clear yet. Barium sulfate finds its use in medicine. It is applied in X-ray diagnostic of alimentary canal diseases. In case of poisoning with barium salts soluble salts of sulfuric acid have to be administered in order to produce hardly soluble barium sulfate. Chemically pure barium sulfate is administered in case of peptic ulcer of stomach and duodenum.

Boron is a microelement (10^{-5} %). It is contained in lungs, thyroid gland, spleen, liver, brain, kidneys, myocardium. Biological role of boron is not found out. It is known that boron participates in carbohydrate – phosphorus metabolism, interacts with some biologically active compounds, e.g. carbohydrates, enzymes, vitamins, hormones. Boron enhances parathormone action and the metabolism of $Ca^{2+,}$ P, and $Mg^{2+.}$ Excess intake of boron leads to disorder of the carbohydrate and protein metabolism. Compounds containing boron possess antiseptic and anti-inflammatory properties. If taken internally show antiepileptic action. Boric acid H_3BO_3 is a mild disinfectant and is used in ophthalmology, otolaryngology and dermatology being in the form of solution, ear and eye drops, powders, ointments, etc. Boric acid along with potassium iodide, copper sulfate and vitamins is prescribed for the treatment of oligotrophy. Borax ($Na_2B_4O_7$) is antiseptic substance. It is used externally as antimicrobic and anti-inflammatory agent for syringing, gargles etc.

Aluminum is essential microelement (10^{-5}%). Basically it accumulates in blood serum, lungs, liver, bones, and kidneys. It is also contained in the nerve cells membranes. Daily requirement in human organism is 49 mg. Biological function is not investigated well. In the organism aluminum participates in the formation of epithelial and connective tissues which make up about 50% (mass) of body mass, in the process of bones regeneration, in the phosphorus metabolism.

High Al ability to complex formation determines its role in reduction of many enzymes activity.

Aluminum ions Al^{3+} possess astringent, anti-inflammatory, and antimicrobic action. Aluminum foil is used for treatment and protection of wound, burn, and ulcer surfaces because aluminum normalizes oxidation-reduction processes. Aluminum hydroxide is used externally in the form of powders, pastes, ointments as absorptive and enveloping substance in dermatology. It is administered internally as antacid preparation. Alum $KAl(SO_4)_2 \cdot 12H_2O$ is employed in the form of water solutions as astringent and anti-inflammatory agent (in dermatology, stomatology, ophthalmology, etc.).

Carbon The total content of the carbon in human organism make up 21.15%(mass). Carbon – is a base of all organic compounds. Carbon is characterized by the ability to form covalent bonds. From the biochemical point of view is very important that all chemical bonds formed by the carbon are strong and labile at the same time, which means that they can be broken easily in the course of biochemical reactions. That’s why carbon is considered to be organogen number one. Carbon is in composition of all tissues, cells and biologically important compounds: proteins (from 50.6 to 54.5% (mass)), vitamins, hormones, enzymes, etc.

Carbon dioxide (3–5–7 %) in mixture with oxygen is used in medicine for inhalations. It stimulates and excites respiratory center. Mixture of carbon dioxide and oxygen is administered in case of shock, depressing of respiratory center, asphyxia in newborns, poisonings, etc. Beverages containing CO_2 increase secretion and absorption in alimentary canal. Dry ice is used for freezing of tissues in histology, in dermatology it applied for cure neurodermite, leprosy, warts, etc.

Potassium and sodium bicarbonates along with carbonic acid form buffer system in the organism. Activated carbon (pharmaceutical compound) adsorbs gases, alkaloids, toxins. It is administered in case of meteorism, alimentary intoxications, poisonings with alkaloids and salts of heavy metals. Sodium bicarbonate (pharmaceutical compound) neutralizes hydrochloric acid of the gastric juice, i.e. possesses antacid properties, increases alkaline buffer capacity of the blood and takes out acidosis. It is administered in case of hyperacid gastritis, peptic ulcer of a stomach and duodenal intestine, acidosis. It is prescribed externally in otolaryngology, stomatology and ophthalmology. It may be used for neutralization of acids got on the mucosas and integuments.

Silicon is a microelement (10^{-3}%). It chiefly accumulates in liver, adrenal glands, hairs, and lens. Silicon and its compounds influence formation and function of epithelial and connective tissues giving them strength, elasticity, and impermeability. It is required for bone growth. Silicon compounds prevent penetration of lipids into the blood plasma and deposition of them in vascular walls. Many pathological processes in the organism are related to disturbance of silicone metabolism (hypertension, rheumatism, peptic ulcer, hepatitis, anemia, some diseases of skin, bones, etc.). The content of silicon in blood plasma increases in case of infectious hepatitis and may serve as diagnostic test. Silicon compounds are used in orthopedics and stomatology.

Tin and **Lead** are microelements. The total content of tin and lead, in the organism is 10^{-4}, and 10^{-6}% respectively. Biological function of these elements is not found out. **Lead and its compounds are poisonous** and cause chronic poisonings. Lead strenuously accumulates in case of Ca and Zn deficiency. Lead is one of the basic anthropogenic elements from the group of heavy metals that is related to high industrial pollution and dischargers of transport using ethylated petroleum. In case of lead poisoning organs of cardiovascular system and hemopoiesis (early development of arterial hypertension and arteriosclerosis, anemia), nervous system (encephalopathy and neuropathy), kidneys (nephropathy) are affected first of all. Lead dioxide and some salts of lead, e.g. lead (II) acetate known as lead sugar, are used in medicine for syringing and lotions as astringent, anti-inflammatory and antimicrobic agents.

Metal taste in the mouth, stomach pains, diarrhea, and nausea may be related to tin surplus.

Nitrogen is one of six elements – organogens (C, H, O, N, P, S) which form the majority of human body mass (97.4%). The total amount of nitrogen in the organism is 3.1% mass. Nitrogen is the obligatory component of aminoacids, proteins (15 to 17.6%), vitamins, hormones, phospholipids, nucleic acids, etc. Nitrogen forms rather strong polar covalent bonds which can be broken easily under the action of enzymes. This fact favors to biochemical reactions.

Free nitrogen is the main component of the air, which contains 78.2% of it. Liquid nitrogen is affective agent in treatment of some skin and mucosas diseases (warts, vascular birthmarks, papillomas, etc.). Nitrous oxide (N_2O) is a safe anaestetic with very few side effects. It is widely used to induce surgical anaesthesis. Spirit of ammonia is widely used in medicine. If taken orally or inhaled it stimulates central nervous system. It is used in case of faints, alcoholic intoxications. A number of inorganic and organic nitrites (sodium nitrite, ethyl nitrite, glyceryl trinitrate (nitroglycerine), etc. have been reported as useful coronary dilators. Nitroglycerine is taken sublingually and is useful for both relief of heart attacks and long term management of angina patient. It produces vasodilation in several minutes. Ammonium chloride is used as diuretic in case of edemas caused by heart failure.

Besides, NH_4Cl is used as expectorant. Nitric acid is employed in laboratory researches for quantitative determination of proteins in the urine and other biological fluids. The source of nitrogen is meat, fish and milk (protein containing products).

Phosphorus is one of organogens. The total content of phosphorus in the human organism is 0.95%. It is needed by all living beings because it enters the composition of some proteins of both a vegetable and an animal origin (0.5–0.6%), nucleic acids, nucleotides, phospholipids, enzymes, etc. Phosphorus is contained in proteins of milk, blood, brain, and nerve tissues. A large amount of phosphorus (85% of total amount) is also contained in the bones and teeth, mainly in the form of the compounds $3Ca_3(PO_4)_2 \cdot Ca(OH)_2$ and $3Ca_3(PO4)_2 \cdot CaCO_3 \cdot H_2O$. The daily requirement for phosphorus in human is 1.3 g. Carbohydrates and fatty acids can be utilized in the organism only being phosphorylated. Phosphorus metabolism is closely bound with calcium one. Calcium can not be assimilated well in the lack of phosphorous and vitamin D which results in rickets developing. Phosphorus plays an especially important role in activity of brain, skeletal and cardiac muscle. Phosphorus takes part in ionic transmembrane transport. Phosphoric acid and its salts form buffer systems which maintain the pH level in the organism. Significant energy portion evolved in metabolism of carbohydrates and other compounds accumulates in the organic compounds of phosphoric acid rich in energy. Phosphate groups joining ADP form ATP which is the universal energy source and supports physiological activity of organism cells. Phosphorus metabolism is regulated by parathyroid glands.

Some phosphorus containing compounds are used in medicine. ATP is prescribed in case of muscle dystrophy, muscle atrophy, myocardial dystrophy, stenocardia, hypertension, etc. Calcium glycerophosphate enhances anabolic processes, normalize the nerve system function. It is prescribed in neurasthenia, overfatigue, dystrophy, etc. Phosphorus compounds are also employed in stomatology.

Milk and fish can serve as the source of phosphorus.

Arsenic is a microelement (10^{-6}%). It accumulates in liver, kidneys, spleen, lungs, hairs, bones. The maximum concentration is observed in brain and muscles. Arsenic stimulates hemopoiesis, take part in hemoglobine synthesis, oxidation-reduction processes and nucleic acids metabolism. It is required for adequate growth and reproduction. But in large doses **arsenic and its compounds are strong poisons.** Arsenic suppresses enzymes activity. Intravascular hemolysis, acute renal insufficiency, disorders of nervous system – toxic encephalopathy – (dysphrasia, disorders of coordination of movements, epileptiform convulsions, psychoses) are the main complications of acute intoxication.

Diarsenic trioxide (arsenous anhydride or white arsenic) finds its use in medicine. If used externally it necrotizes pathologically changed tissues (integuments, pulp) and is employed in dermatology and stomatology in the pasta form. If used internally it stimulates hemopoiesis, increases anabolic processes, normalizes nerve system function, and improves trophic processes in integuments. It is prescribed in case of anemia, neurasthenia, attrition. Sodium arsenate 1% solution in small doses stimulates erythrogenesis, increase anabolic processes, improve skin trophicity, in large doses suppress leucopoiesis. It is administered in case of neurosis, anemia, attrition, in large doses – in case of leukosis.

Oxygen is organogen. The total content of oxygen in the human organism is 62.43%. The organism of adult men consumes 264 cm^3 of oxygen per minute in the rest state. Oxygen plays an exceedingly important role in nature. It takes part in all types of metabolism. It participates in one of the most important vital processes – respiration. Another important process which oxygen participates in is the decomposition and decay of dead animals and plants. Here complex organic compounds transform into simpler ones (in the long run into CO_2, water and nitrogen), and the latter again return to the general cycle of substances in nature. Plants produce oxygen in the course of photosynthesis. All oxidation-reduction reactions proceed in the presence of oxygen. Oxygen enters the composition of proteins (21.5–23.5%), carbohydrates, lipids, nucleic acids, vitamins, hormones, enzymes, etc. The lowering of the oxygen content in the organism decreases its protective activity. When oxygen is used along with carbonic acid, it stimulates respiratory and vasomotor centers. Oxygen introduced in stomach suppresses some helminthes (ascarides). Oxygen and its compounds help cure cardiovascular, infectious diseases, malignant tumors, etc. Oxygenotherapy finds its use in many branches of medicine. Oxygen is used in case of hypoxia, pneumonia, poisoning with carbon monoxide, hydrocyanic acid. In anesthesiology it is employed along with inhalation narcotics. Radioactive isotope ^{15}O is used for the determination of oxygen content in the organs.

Ozone O_3 is of great biological importance. Being a strong oxidizing agent, ozone kills bacteria, fungi, viruses and is therefore used for disinfecting water and air. If inhaled along with air it stimulates metabolism, kidneys function, increases protective functions of the organism, and improves sleep and state of health. That is why it is used in treatment of heart, kidneys, alimentary canal, skin diseases, helps cure tuberculosis, etc.

Ozone is poisonous. Its maximum allowable content in air is 10^{-5}%. Its odour is well discerned at this concentration. At higher concentrations it causes headache, nausea, nasal bleeding, and eyes inflammation. Ozone layer protects the Earth from the harmful solar ultraviolet radiation.

Sulfur is organogen (0.16%). The daily requirement in adult men is about 4–5g. Sulfur enters the composition of many organic substances including aminoacids (cystine, cysteine, methionine), proteins, hormones (insulin), vitamins (vit B_1). There is a lot of sulfur in the hair keratin, wool, bones, and nerve tissue. In the organism sulfur gets oxidized with formation of sulfuric acid, which participates in detoxication of poisonous compounds formed in intestine from aminoacids (phenol, cresol, skatole, indole), and alien substances, e.g. drugs, etc.

Purified sulfur has antimicrobic and antiparasitic action. It is used externally in dermatology. Sulfur dioxide SO_2 serves as a disinfectant for destroying mould fungi in basements, cellars, fermentation tanks, etc. Sulfozinum (1% solution of sulfur in peach-kernel oil) is administered for treatment of schizophrenia, general paralysis, dipsomania.

If used internally along with organic substances, precipitated sulfur (pharmaceutical compound) forms sulfides and pentathionic acid which possess antimicrobic and antiparasitic action. It is used in dermatology.

Sodium thiosulfate ($Na_2S_2O_3$) and its 30% solution for injections are used for detoxication, as anti-inflammatory, antiallergic and antiparasitic agents. Sodium thiosulfate is also administered as antidote in poisonings with heavy metals, hydrocyanic acid, halogens, arsenic, and mercury. Lean, fish and milk provide sulfur for the organism.

Selenium is a microelement. The minimum daily requirement for selenium in adult men is 0.07µg. Selenium accumulates in organs and tissues of high functional activity (liver, kidneys, heart, hypophysis, skeletal muscles). There is a lot of selenium in retina (about 7 µg). Selenium is important for vision. It also influences genital glands functions, e.g. it is necessary for normal pregnancy and has the expressed protective action on spermatozoids and provides their mobility. Selenium is part of the enzyme glutathione peroxidase, which protects cellular membranes. The enzyme prevents the accumulation of hydrogen peroxide and organic peroxides in cells. Such organic peroxides are thought to play a role in cancer development.

Selenium is a mercury (Hg) and arsenic (As) antagonist; it acts as antioxidant in synergism with vitamin E, can protect the body against the toxicity of heavy metals (Hg, Cd). **Selenium compounds are toxic** and their action is similar to that of arsenic. But in microdoses selenium is used in medicine, e.g. to prevent diseases of necrotic character, to cure some diseases of eyes, liver, pancreatic gland, dystrophic processes in different tissues. Sulsenum (contains sulfur and selenium) is used in dermatology for skin diseases treatment.

Fluorine is a microelement (10^{-5}%). It is found in all organs and tissues of the organism, but most of it is in hairs, bones, teeth. It is present in the organism being in the form of CaF_2. The daily requirement for fluorine is 1.5–4 mg. The main biological function of fluorine is its participation in osteogenesis, teeth enamel and dentine formation. Fluorine is important in prevention of dental caries. However, F^- ion paralyses some enzymes, suppresses carbohydrates and lipids metabolisms, and inhibits thyroid gland function and tissue respiration. Fluorine excess in the organism may cause dental disease – fluorosis. The source of fluorine is milk and drink water. The normal content of F^- in drink water is 1.5 mg/L. Compounds of fluorine (NaF, KF, etc.) are used for treatment of thyrotoxicosis, endemic goiter, and also applied in stomatology.

Chlorine is a macroelement (10^{-2}%). Mainly it is present in extracellular liquid. The daily requirement for chlorine is 4–6 g. Chlorine ions promote deposition of glycogen in the liver, participate in the blood buffer system formation, osmotic pressure and water-and-salt balance regulation. Chlorine enters the composition of many enzymes, activates amylase secreted by salivary glands. Chlorine ion Cl^- is in composition of hydrochloric acid which is very important for digestion. A concentration of hydrochloric acid in the gastric juice of healthy men is 0.5%. The content of hydrochloric acid in the gastric juice may vary in different pathological conditions. That’s why determination of hydrochloric acid content in gastric juice is of great diagnostic and clinical significance. Chlorine is used for disinfection because it destroys microorganisms by interacting with amino groups of amino acids in microbe cells. Chlorine enters the composition of many organic compounds which possess narcotic and anesthetic properties. These compounds are widely used in medicine.

Hydrochloric acid diluted (8.2–8.4%) – pharmaceutical compound – stimulates pancreatic gland and liver secretion, activates stomach and intestine function, promotes iron absorption in alimentary tract, has antimicrobic action. It is used in case of anacid and hypoacid gastritis, dyspepsia.

Sodium chloride is used for isotonic solution preparation, for bathes and showers. Sodium hypochlorite NaClO (0.5% solution) is used for spraying of wounds. Lime chloride $CaOCl_2$ is employed for disinfection. Many chlorine containing compounds (chloroform, pantocidum, chloraminum) are used as solvents and medicines. Chlorine deficiency in the organism may be caused by vomiting, treatment with diuretics, kidneys diseases. The main source of chlorine for the organism is a table salt.

Bromine is a microelement (10^{-4}%). It is encountered in all organs and tissues. The most of bromine is in kidneys, thyroid gland, hypophysis, blood, and urine. The daily requirement for bromine is 0.821 g. Bromine salutary influences the nervous system because it is able to increase the inhibition of central nervous system. Small doses of bromine preparations (salts of sodium, potassium, and ammonium) concentrate and enhance inhibition in cerebral cortex. In case of increased excitability of central nervous system they recover the equilibrium between excitement and inhibition. Large doses of bromides suppress excitement in the brain. Bromine participates in sex hormones (testosterone) biosynthesis and regulates genital glands function. Many bromine compounds (salts of sodium, potassium, and ammonium) are used in case of neuro-psychic activity disorder, including epilepsy, neurasthenia, hysteria, insomnia, delirium tremens, and mental overfatigue. It is also used to cure hypertension, peptic ulcer, etc. Radioactive isotope ^{82}Br finds its use in scientific and clinical researches.

Iodine is a microelement (10^{-4}%). Iodine is essential for life and as constantly present in the organism. 15 mg of the total amount is contained in thyroid gland, the rest – in muscles, skin, bones, kidneys, brain, blood, etc. The concentration of iodine in blood is constant – 10^{-6}%–10^{-5}%. Iodine gets into the body in the composition of food and water. The daily requirement for iodine is 0.2 g. Iodine is required for normal thyroid function. It is found in thyroid hormones (thyroxine, triiodothyronine). In children the iodine deficiency results in cretinism. In the adult age it leads to the compensatory enlargement of the thyroidal tissue – endemic goiter. The therapy of this pathologic state is dietary intake of iodine-enriched nutrients, in particular, table salt with inorganic iodine additives. Iodine participates in water-and-salt balance, influences concentration of potassium and sodium ions in the organism. Iodine stimulates immunity. Iodine and its compounds increase activity of some sex hormones.

Tincture of iodine (5 and 10% solution) is used externally as antiseptic and anti-inflammatory agent. It is administered internally in case of hypothyroidism and hyperthyroidism, endemic goiter, atherosclerosis, bronchitis, asthma, rheumatism, poisoning with mercury, lead, etc. Microiodum (iodine – 0.0005 g, potassium iodide – 0.005 g, valeriana – 0.05 g) is a tranquilizer. Iodine compounds are employed as radiopaque substances (cardiotrastum, bilignostum) due to the ability of iodine to retain x-rays. Radioactive isotope ^{131}I is used to cure thyrotoxicosis, thyroid gland cancer. The source of iodine is table salt with inorganic iodine additives, seafood.

Chromium is a microelement (10^{-5} %). The daily requirement for chromium in adults is 0.05–0.2 mg. Biological activity of chromium is due to its ability to form coordination complexes. Chromium stimulates hemopoiesis and several enzymes. It is a component of digestive enzyme trypsin (one chromium atom for each enzyme molecule). Chromium participates in stabilizing of nucleic acids structure. Chromium participates in the processes of carbohydrates metabolism. It lowers blood sugar level by increasing the effectiveness of insulin. Chromium deficiency is a cause of glucose tolerance decrease. Chromium has been reported to disturb thyroid gland function. Chromium, especially hexavalent one, surplus intake may induce carcinogenic and allergenic effects, predisposes to more frequent development of gastritis, hepatitis, asthenoneurotic disorders. Some chromium compounds are known to cause antitumoral action. Metallic chromium in the composition of alloys is used in prosthetic dentistry and orthopedics. Radioactive isotope ^{51}Cr is used for diagnostic of different blood diseases and gastro-intestinal bleedings. Soluble chromium compounds are poisonous.

Molybdenum is a microelement (10^{-5} %). The daily requirement for molybdenum in adults is 0.075–0.25 mg. It accumulates in liver, kidneys, and endocrine glands. Molybdenum stimulates hemoglobin synthesis. Molybdenum is essential component and activator of several enzymes, e.g. hydrogenase, xanthine oxidase, and some enzymes of flavine group. Enzymes containing molybdenum participate in nucleic acids (purines) metabolism and nitrogen assimilation. This metal promotes xanthine and purine oxidation in milk and liver. Endemic gout develops in case of continuous surplus intake of molybdenum. This is because high molybdenum level in the organism promotes the rate of uric acid formation and insoluble salts of this acid are deposited in joints. In case of excess content in food, molybdenum displaces copper from the liver and phosphorus from the bones. Molybdenum in the composition of enzyme participates in assimilating of atmospheric nitrogen.

Sodium molybdate Na_2MoO_4 increases the phagocytal activity of the blood, i.e. molybdenum stimulates immunity. Ammonium molybdate $(NH_4)_2MoO_4$ has antimicrobic action and is used as disinfectant.

Manganese is a microelement (10^{-5} %). The daily requirement for manganese in adults is 2.0–5.0 mg. Most of this element is present in lungs, muscles, liver, brain, kidneys, spleen, bones, etc. It is essential for several enzymes, bone and cartilage growth, and brain and thyroid function. It influences fat, protein and carbohydrate metabolisms, participates in the ascorbic acid synthesis in the animal organisms. It also influences reproduction and cell division. It stimulates growth and development. Manganese increases the rate of proteins decay. Manganese decreases the fat deposition in the organism, e.g. pathological obesity caused by the manganese deficiency can be treated by means of additional intake of this element.

Manganese has a great influence on the mineral metabolism: manganese salts promote phosphorus and calcium assimilation. Manganese has insulin-like effect; it decreases the glucose content in the blood and stimulates synthesis of glycogen. Manganese salts influence the status of central nerve system. Manganese stimulates immunity by increasing the rate of phagocytosis. Manganese participates in iodine assimilation and synthesis of parathyroid gland hormones, i.e. its deficiency may cause development of endemic goiter. Manganese enters the composition of several enzymes (arginase, phosphotransferase).

$MnCl_2$ and $MnSO_4$ are used to cure anemia caused by pregnancy and labor. Manganese compounds are used to cure obesity, atherosclerosis, avitaminosis, etc. Potassium permanganate solutions are used for gargles, syringes, lavage of stomach (0.01–0.1 %), lavage of wounds (0.1–0.5 %), etc. The major source of manganese for the organism is vegetable food.

Iron is essential microelement (10^{-5} %). The daily requirement for iron is 10 mg for men and 15 mg for women. Major part of iron is contained in erythrocytes (60–73% enter the composition of hemoglobin) and in cytochromes which are enzymes of electron transport chain in mitochondria. Iron participates in oxidation-reduction reactions, taking place in the organism. Iron ions Fe^{2+} and Fe^{3+} enter the composition of many enzymes, e.g. catalase, cytochrome oxidase, peroxidase, etc. Four ions Fe^{2+} are in composition of hemoglobin. The hem iron always retains its oxidation state unchanged. The deficiency of iron in the organism develops into an anemia.

Iron containing compounds are widely used in medicine as antianemic agents.

Cobalt is a microelement (10^{-5} %). It accumulates in liver, kidneys, pancreatic gland. The daily requirement for cobalt is 0.05–0.1 mg. Cobalt is related to enzymes, vitamins, hormones. It influences protein, fat, carbohydrate and mineral metabolisms. It is also relates to growth and reproduction functions. It stimulates hemogenesis by increasing the number of erythrocytes and hemoglobin quantity in the blood. In case of cobalt deficiency the quantity of hemoglobin in the blood decreases. But if cobalt is taken in surplus immunobiological reactivity of the organism decreases, conditioned-reflex activity is disturbed; hemopoietic organs are affected, etc.

Cobalt stimulates vitamins metabolism, e.g. metabolism of ascorbic acid, nicotinic acid (vitamin PP) synthesis, and especially cyanocobalamin (Vitamin B_{12} $C_{63}H_{90}N_{14}PCo$) synthesis. Its content in this vitamin is 4.5 %. Cyanocobalamin plays important role in hemopoiesis and other processes. Micro doses of cobalt salts stimulate protein metabolism, e.g. promote deposition of proteins in tissues, increase muscle proteins synthesis. Cobalt stimulates formation of glycogen. Cobalt salts in dose 1–5 mg cause hypoglycemia, in higher doses – hyperglycemia. Cobalt sulfate $CoSO_4$ stimulates calcium and phosphorus assimilation. Cobalt ions, depending on concentration, can act either as activator or inhibitor of enzymes, especially of oxidizing enzymes. Cobalt suppresses excitability of central nerve system. Cobalt chloride $CoCl_2$ stimulates immunity by increasing the rate of phagocytosis.

Several preparations of cobalt are used in medicine. Cyanocobalamin (Vit B_{12}), coamidum (complex preparation of Co with nicotinic acid amide) along with iron preparations are used to cure anemias, liver and nerve diseases, etc. Cobalt sulfate $CoSO_4$ is administered in case of anemias related to pregnancy and labor. Cobalt preparations along with manganese preparations are used in inflammations of vessels, liver, in case of epilepsy, hypertension. Radiocobalt-60 (^{60}Co) is used to cure cancer. Products of animal origin are the source of cobalt for the organism.

Copper is essential microelement (10^{-4} %). Most copper of the organism is contained in liver, the least – in bones. The daily requirement for copper in adults is 2–3 mg. Copper of the blood plasma makes part of ceruloplasmin. Copper is the part of enzymes essential for the formation of hemoglobin, blood vessels, bones, tendons, and the myelin sheath. Copper relates to enzymes, vitamins, hormones, and other biologically active substances. It enhances the action of insulin and hypophyseal hormones, which stimulate development and function of genital glands. Copper salts stimulate growth and development of the organism; it gives the basis to assume that copper promotes protein synthesis and influences protein metabolism. Copper has specific action on hemoglobin synthesis and erythrocytes formation. Copper participates in carbohydrate metabolism regulation. It possesses insulin-like activity and promotes glycogen formation in liver. Copper influences water and mineral metabolisms.

Copper makes part of the active site of the enzymes oxidases: cytochrome-c-oxidase, ferroxidase, etc. Copper can act either as activator or inhibitor of enzymes. Copper sulfate CuSO4 (0.003–0.25 mg %) increases immunobiological reactivity of the organism.

Copper sulfate $CuSO_4$ is applied as antiseptic, astringent and caustic substance. It is used as antidote in poisoning with white phosphorus. Micro doses of copper are administered for treatment of anemias, including those related to pregnancy and labor. Copper preparations are used in psychiatry as they decrease excitation in psychopaths. Copper containing compounds along with iodine are prescribed for prophylaxis and treatment of endemic goiter.

Silver is a microelement (10^{-6} %). It accumulates in liver, kidneys, bones, and endocrine glands. Physiological and biological role of silver is not completely found out. It is poisonous for enzymes: high concentrations of silver inactivate definite sites of enzymes molecules. Depending upon concentration, silver causes astringent, anti-inflammatory and antibacterial action.

Silver nitrate $AgNO_3$ is applied for disinfection of mucosas in ophthalmology, urology, dermatology. Colloidal solutions of silver stabilized by special additives (silver albuminates) – protargolum (complex compound of protein with silver), colloid silver and others – are used for lavage of urinary tract, in ophthalmology, surgery and dermatology as astringent and antiseptic agents.

Zinc is essential microelement (10^{-3} %). Most zinc of the organism is contained in retina, prostate gland, sperm, mammary gland, liver, muscles. The daily requirement for zinc in adults is 10–15 mg. It increases in the period of growth, sexual maturation, and pregnancy. Zinc relates to endocrine glands function. Zinc influences reproduction processes. It stimulates growth and development, which means that it participates in protein metabolism. Zinc ions take part in fat metabolism, e.g. they decrease the content of fat in organs, in particular in liver. Zinc also influences the level of glucose in the blood. Zinc is the component of insulin and stimulates insulin secretion. Zinc influences mineral metabolism: when added to food it increases phosphorus excretion and decreases that of calcium.

Zinc is an essential component of more than 40 enzyme systems, e.g. carboanhydrase, aldolase, lactate dehydrogenase, malate dehydrogenase, carboxypeptidase. Zinc activates several enzymes (peroxidase, aminopeptidase, enolase, arginase), and inhibits others (phosphoglucomutase, protease, alkaline phosphatase, ribonuclease, etc.). Zinc chloride increases the phagocytal activity of leucocytes, i.e. zinc stimulates immunity. Zinc participates in respiration, particularly in the electrons transfer.

Zinc sulfate $ZnSO_4$ has antimicrobic action, causes astringent and anti-inflammatory effect. Diluted solutions of zinc sulfate (0.1–0.25 %) are used in ophthalmology. Zinc chloride has astringent and antiseptic effect and is used to heal ulcers, fistulas, etc. Zinc oxide is applied in dermatology in the form of ointments and powders as astringent and antimicrobic agent. Radioactive isotope ^{65}Zn is used to cure cancers. Several zinc compounds are employed in stomatology.

In high concentrations zinc compounds are poisonous.

Cadmium is a microelement (10^{-4} %). It accumulates mostly in liver and kidneys. Biological role of this element is not found out. Cadmium inhibits activity of most enzymes, especially those containing HS-groups, because it has high affinity to this group. Cadmium salts decrease the content of ascorbic acid in the organs and tissues, glucose and cholesterol in the blood. It has been reported about cadmium influence on the carbohydrate metabolism.

Small doses of cadmium cause prolonged hypoglycemia. Solutions of cadmium salts depending upon the concentrations have astringent, irritant and antiseptic action. Cadmium is toxic and possesses cumulative properties. Cadmium and zinc are antagonists.

Mercury is a microelement (10^{-6} %). Mercury accumulates in kidneys and liver. Biological role of this metal is not completely found out. Mercury stimulates phagocytal activity of leukocytes. It has been reported that mercury influences hemopoiesis.

If used externally mercury causes antibacterial and mild irritant action. Antibacterial action is explained by the reaction of mercury with proteins of microbic cells which results in formation of friable albumins. Mercury ions are capable to block sulfhydryl groups (–SH groups) of enzymes and thus inhibit enzymatic activity. Mercury and its soluble salts are highly toxic.

Mercury containing compounds are used in medicine as antiseptic, antiparasitic, antisyphilitic, diuretic and laxative agents. Mercury(II) chloride $HgCl_2$ (poison!) (concentration 1:1000) is used as antiseptic. Mercury (II) iodide is used for syphilis treatment. Mercury amidochloride $HgNH_2Cl$ in the ointment form is applied in dermatology. Mercury oxide HgO is used in dermatology (2% ointment) and ophthalmology. Mercury (I) chloride Hg_2Cl_2 (calomel) is used as laxative, and sometimes as diuretic and cholagogue agent.

LABORATORY WORK

Experiment 1. Test for carbonate ions (CO_3^{2-})

Place 2—3 drops of 1% calcium chloride in a test tube and add 2—3 drops of 1% sodium carbonate solution. White precipitate forms. This precipitate is soluble in acetic and hydrochloric acids. Write the formation reaction equations and dissolution of this precipitate.

Experiment 2. Test for thiosulfate ions ($S_2O_3^{2-}$)

Place 2—3 drops of 1% sodium thiosulfate in a test tube, add 2—3 drops of diluted sulfuric acid. Turbidity of solution can be observed. Write the reaction equation.

Experiment 3. Test for permanganate ions (MnO_4^-)

Place 2−3 drops of 1% potassium permanganate in a test tube, acidify test solution with 2 drops of diluted sulfuric acid and add 2−3 drops of 1% oxalic acid. Potassium permanganate solution is **decolorized**. Write the reaction equations.

Experiment 4. Test for iron (III) cations (Fe^{3+})

Place 2−3 drops of 1% iron(III) sulfate solution in a test tube. Add 2−3 drops of 1% potassium hexacyanoferrate (II). **Observe** the formation of dark-blue precipitate of Prussian blue (iron hexacyanoferrate(II)). Write the reaction equations.

Write observations and make conclusions.

3. **Tasks for knowledge control**

1. Which of the following is *p*-block element?
   a.sodium;

b. calcium;
c.phosphorus;
d. manganese.

2. How does electronegativity of *s*- and *p*-block elements change while going down the group?
   a. decreases;
   b. increases;
   c. does not change;
   e. there is no such property.
3. All living organisms are ___ water.
   a. less than 10%
   b. 10 – 30%
   c. 40 – 60%
   d. 70 – 90%.
4. Calcium is needed for:
   a.formation of nucleic acids;
   b. formation of bones and teeth;
   c.hypertension treatment;
   d. atherosclerosis treatment.
5. Which of the following is an inert (non-reactive) atom?
   a. hydrogen; atomic number = 1
   b. oxygen; atomic number = 8
   c. neon; atomic number = 10.

Ans. 1– c; 2 – a; 3 – d; 4 – b; 5 – c.

4. **Recommendations for the work results design**

Algorithms for solving educational problems of class work and self-work should be recorded in the workbook. Make a protocol of laboratory work, conclusions about content and properties of biogenic block elements, hypo- and hyper-content in the organism and removal their states.

5. Complexes: general aspects, fundamentals of the Alfred Werner's coordination theory

Complexes (coordination compounds, complex compounds) are a special class of compounds in which the central metal atom or ion is surrounded by oppositely charged ions or neutral molecules more than its normal valence. These compounds are widely present in the minerals, plants and animals and play many important functions. Many biologically important compounds are coordination compounds in which complicated organic species are bound to metal ions. The common examples are: hemoglobin which is coordination compound of iron, vitamin B_{12} which is coordination compound of cobalt, chlorophyll which is coordination compound of magnesium, etc.

The properties and structure of complex compounds are explained most successfully by the ***coordination theory*** proposed by Alfred Werner (1866–1919), a Swiss chemist, Nobel Prize winner, in 1893. According to the coordination theory, one of the ions in a molecule of any complex compound, generally a positively charged one occupies a central position and is called a ***complexing agent*** or ***central ion.*** Around it in direct proximity are arranged, or as we say, coordinated, a certain number of oppositely charged ions or electrically neutral molecules called ***ligands***. They form the ***inner coordination sphere*** of the compound. The remaining ions not accommodated in the inner sphere are farther from the central ion and form the ***outer coordination sphere***. The number of ligands surrounding the central ion is called the ***coordination number***.

The inner sphere of a complex retains its stability when dissolved. Its boundaries are shown in formulas by brackets. The ions in the outer sphere are readily detached in solutions. For this reason, the ions in the inner sphere are said to have a ***non-ionizable*** bond, and those in the outer sphere, an ***ionizable*** one. Let's consider the structure of complex compound in detail.

6. Structure of complex compounds

Complex ion

As it was mentioned above a coordination compound contains a central metal atom or ion surrounded by a number of oppositely charged ions or neutral molecules. For example, $[Co(NH_3)_3Cl_3]$ is a coordination compound in which the cobalt (+3) ion is surrounded by three ammonia molecules and three negatively charged chloride ions. Other examples are $[Ni(NH_3)_6]Cl_2$, $K[Ag(CN)_2]$, $[Cu(NH_3)_4]SO_4$, etc. As you can see, a coordination compound contains a complex ion. For example, $[Ni(NH_3)_6]Cl_2$ contains complex ion $[Ni(NH_3)_6]^{2+,}$ $[Cu(NH_3)_4]SO_4$ contains complex ion $[Cu(NH_3)_4]^{2+,}$ $K[Ag(CN)_2]$ contains complex ion $[Ag(CN)_2]^{-}$ and so on. ***A complex ion*** may be defined as an electrically charged species which consists of a central metal atom or ion surrounded by a group of ions or neutral molecules. For example, $[Ni(NH_3)_6]^{2+}$ is a complex ion in which the central nickel ion, $Ni^{2+,}$ is surrounded by six ammonia molecules. It may be noted that the complex ion may be positively charged or negatively charged or a neutral species.

Cationic complex is a complex ion which has a net positive charge. For example, $[Co(NH_3)_6]^{3+,}$ $[Ni(NH_3)_6]^{2+}$

Anionic complex is a complex ion which has a net negative charge. For example, $[Ag(CN)_2]^-$, $[Fe(CN)_6]^{4-}$.

Neutral complex is a complex ion which has no net charge. For example, $[Co(NH_3)_3Cl_3]$, $[Ni(CO)_4]$, $[Pt(NH_3)_2Cl_2]$.

Central ion and Ligands

The cation to which on or more neutral molecules or anions are attached is called ***central ion*** while the neutral molecules or ions are called ***ligands.*** In the complex ion

$[Ni(NH_3)_6]^{2+}$, Ni^{2+} ion is the central ion and the molecules of ammonia are the ligands. Similarly, in the complex ion $[Co(NH_3)_5Cl]^{2+}$, Co^{2+} ion is the central ion while the ammonia molecules and the chloride ion are the ligands. The ligands are attached to the central metal atom or ion through ***coordinate bonds***. It means that while central ion should have vacant orbitals, the ligands should have lone pairs of electrons in the outermost orbitals which can be donated to the central ion. The atom in the ligand which can donate the electron pairs is called ***donor atom***. For example, in ammonia nitrogen is the donor atom and in water oxygen is the donor atom.

Types of Ligands

The ligands may contain one or more than one donor atoms for coordination with the central atom. Accordingly, the ligands are classified as follows:

1. ***Unidentate or monodentate ligands*** are ligands which can coordinate to the central ion through only one donor atom. For example, NH_3, H_2O, Cl^-, CN^-, OH^-, etc.

2. ***Bidentate ligands*** are ligands which have two donor atoms and therefore, can coordinate to the central ion at two positions. For example, oxalate ion $C_2O_4^{2-}$, Ethylenediamine $H_2N–CH_2–CH_2–NH_2$ (abbreviated as **en**).

3. ***Polydentate ligands*** are those having more than two donor atoms present in the molecule. Theses may be called ***tridentate, tetradentate*** ligands etc**.** depending upon the number of donor atoms present in their molecules.

Coordination Number

The ligands in a coordination compound are attached to the central metal ion through coordination bonds. The total number of ligands attached to a central metal ion is called the ***coordination number*** (C.N.) of that ion. In other words, coordination number is the number of ligands in the coordination sphere of the complex compound. For example, the coordination number of central metal ion in different complexes is:

$[Ag(CN)_2]^-$	C.N. of $Ag^+ = 2$
$[Cu(NH_3)_4]^{2+}$	C.N. of $Cu^{2+} = 4$
$[Co(NH_3)_3Cl_3]$	C.N. of $Co^{3+} = 6$

Charge of a Complex ion

The charge carried by a complex ion is the algebraic sum of charges carried by the central ion and the ligands coordinated to it. For example, $[Ni(NH_3)_6]^{2+}$ carries a charge of +2 because Ni^{2+} ion carries a charge of +2 and ammonia molecule is neutral.

$$[Ni(NH_3)_6]^{2+}: \text{Charge} = +2 + 6(0) = +2.$$

A coordination compound sometimes may not have any charge. For example, $[Co(NH_3)_3Cl_3]$ carries no charge because Co^{3+} ion carries a charge of +3, three ammonia molecule are neutral and three Cl^{-} ions carry together a charge of -3.

$[Co(NH_3)_3Cl_3]$: Charge = +3 +3(0)–3 =0.

Oxidation number or oxidation state of the central metal atom

It is the number which represents the charge which an atom actually has when combined with the other ions or molecules. For example, the oxidation number (O.N.) of Co in the complex $[Co(NH_3)_6]^{3+}$ is +3. Oxidation number of the central atom is the main factor affecting the coordination number. A comparison of the most characteristic coordination numbers in solutions and the charge of the central ion is given below:

Charge of the central ion	+1	+2	+3	+4
Coordination number	2	4,6	6,4	8

The coordination numbers encountered more often when two different kinds of coordination are possible are set here in boldface type. The coordination number 6 is encountered in the complex compounds of Pt^{4+}, Cr^{3+}, Co^{3+}, and Fe^{3+}, the coordination number 4 – in the complexes of Cu^{2+}, Zn^{2+}, Pd^{2+} and Pt^{2+}, the coordination number 2 – in the complexes of Ag^{+} and Cu^{+}.

Knowing the charge of the complex ion, we can calculate the oxidation number of the central metal atom. For this, the oxidation number of the central metal atom is assumed to be x and the oxidation number of all other species are substituted. The sum of the oxidation numbers is equated to the total charge of the complex and the value of x is calculated.

$[Ni(NH_3)_6]^{2+}$: $x+6(0)= +2$ or $x = +2$

O.N. of Ni = +2

These calculations will be used while writing the names of compounds. The different terms in a complex $[Co(NH_3)_4Cl_2]Cl$ are illustrated below:

7. Bonding in Coordination Compounds

The main assumptions of **Valence Bond Theory** for bonding in coordination compounds are listed below:

1. The central metal ion in the complex makes available a number of empty orbitals for the formation of coordinate bonds with suitable ligands. The number of empty orbitals made available for this purpose is equal to coordination number of the central metal ion. For example, if coordination number is 6, six empty orbitals are made available in the central metal ion.

2. The appropriate atomic orbitals (*s*, *p* and *d*) of the metal hybridize to give a set of equivalent orbitals of definite geometry such as square planar, tetrahedral, octahedral and so on. The following types of hybridization are involved for different geometries of the complexes.

Coordination number	Hybridisation	Geometry
4	sp^3	Tetrahedral
4	dsp^2	Square planar
6	sp^3d^2 or d^2sp^3	Octahedral

3. The *d*-orbitals involved in the hybridization may be either inner *d*-orbitals i.e. (n–1)d or outer *d*-orbitals i.e. For example, in case of octahedral hybridization, the orbitals may be two 3*d*, one 4*s* and three 4*p* (d^2sp^3) or one 4*s*, three 4*p* and two 4*d* (sp^3d^2 hybridization).

4. Each ligand has at least one orbital (of donor atom) containing a lone pair of electrons.

5. The empty hybrid orbitals of metal ion overlap with filled orbitals of the ligand to form metal-ligand coordinate covalent bonds.

Be^{2+} + 4:F^- → $[BeF_4]^{2-}$

acceptor donor tetrahedral geometry (sp^3 hybridization)

Cr^{3+} + 6:H_2O → $[Cr(H_2O)_6]^{3+}$

acceptor donor octahedral geometry (d^2sp^3 hybridization).

8. Spatial Structure and Isomerism in Coordination Compounds

Identical ligands are symmetrically arranged in the space around the central atom.

The even coordination numbers 2, 4 and 6 are encountered more often.

For the coordination number 4 and tetrahedral configuration, all the positions of the ligands relative to the central atom are equivalent. Consequently, tetrahedral complexes of the $[MA_2B_2]$ type (where M is the central atom and A and B are ligands) have no isomers. For square-planar configuration two isomers are possible.

For example, the complex $[Pt(NH_3)_2Cl_2]$ have two isomeric forms differing in colour, solubility, reactivity, and the way of preparation. In one of the isomers, the chlorine atoms are diagonally opposite (trans-isomer), and in the other one they adjacent to each other (cis-isomer).

Compound $[Pt(NH_3)_2Cl_4]$ (where the coordination number of the platinum is 6) exists in two isomeric forms differing from each other in their colour and in other properties. In one case, the NH_3 molecules are at diagonally opposite corners of the octahedron (trans-isomer), and in the other at adjacent corners (cis-isomer).

9. Classification of Complex Compounds

The basic types of complex compounds include the following.

Ammines – complexes in which ammonia molecules are the ligands, for instance $[Cu(NH_3)_4]SO_4$, $[Co(NH_3)_6]Cl_3$. Complexes similar to the ammines are known in which the role of the ligands is played by amine molecules: CH_3NH_2 (methylamine),

$C_2H_5NH_2$ (ethylamine), $H_2NCH_2CH_2NH_2$ (ethylenediamine), etc. Such complexes are known as ***aminates***.

Aquacomplexes contain water as the ligand: $[Co(H_2O)_6]Cl_2$, $[Al(H_2O)_6]Cl_3$, etc.

Acidocomplexes. In these complexes, anions are the ligands. For example, $K_2[PtCl_4]$, $K_4[Fe(CN)_6]$, $Na_2[Sn(OH)_4]$, $Na_2[Sn(OH)_6]$.

Transition series exist between these classes, which include complexes with different ligands. Below is given the transition series between the ammines and Acidocomplexes of platinum (II): $[Pt(NH_3)_4]Cl_2$, $[Pt(NH_3)_3Cl]Cl$, $[Pt(NH_3)_2Cl_2]$, $[Pt(NH_3)Cl_3]$, and $K_2[PtCl_4]$.

Cyclic or ***chelate*** (from the Greek word «chele» – claw) complex compounds contain a bi- or polydentate ligand that grips the central atom, as it were, like the claws of a crab. Chelating ligand is attached by two or more donor atoms to the same central metal ion forming a ring structure. For example, when a bidentate ligand such as ethylenediamine attaches to Cu^{2+} ion through amino groups and forms a ring structure, it is called chelating ligand. The resulting complex ion $[Cu(en)_2]^{2+}$ is called a chelate.

Similarly, $[Fe(C_2O_4)_3]^{3-}$ is a chelate in which oxalate ion acts as chelating ligand. The group of chelates also includes ***intracomplex compounds*** in which the central atom is part of a ring, forming covalent bonds with ligands in various ways – donor-acceptor bonds and bonds at the expense of unpaired atomic electrons. Complexes of this kind are very characteristic of the aminocarboxylic acids. Their simplest representative is aminoacetic acid (glycine) NH_2CH_2COOH – it forms chelates with Cu^{2+}, Pt^{2+} ions, for example:

Complexes are also known with more complicated aminocarboxylic acids and their analogues. Such ligands are known as ***complexons.*** The doubly charged anion of ethylenediaminetetraacetic acid in the form of its bisodium salt is called ***complexon III*** or ***B trilon***.

Chelate compounds are extremely stable because their central atom is "blocked", as it were, by the cyclic ligand. Complexons bond metal cations very strongly. That's why they are used for softening water, in medicine as antidotes in poisonings with metals. Chelate compounds play a great role in nature. For instance, hemoglobin consists of a complex – heme – bonded to a protein – globin. The central ion in heme is the Fe^{2+} ion around which four nitrogen atoms are coordinated that belong to a complex ligand with cyclic groups. Hemoglobin reversibly attaches oxygen and carries it from lungs via the blood vessels to all the tissues. Chlorophyll, which participates in photosynthesis processes in plants, has a similar structure, but its central ion is Mg^{2+}.

All the classes of complex compounds listed above contain one central atom, i.e. they are ***mononuclear***. Complexes are also encountered with a more complicated structure that contain two or more central atoms of the same or different elements. These complexes are known as ***polynuclear*** ones.

10. Nomenclature of Coordination Compounds (given by IUPAC)

1. Order of naming ions. In ionic complexes, the cation is named first and then the anion (as in NaCl: sodium chloride). Non-ionic complexes are given a one word name.

2. Naming the coordination sphere. In naming the coordination sphere, the ligands are named first and then the central metal ion.

3. Names of ligands. The names of negative ligands end in ***–o*** and names of positive ligands end in ***–ium.*** The neutral ligands are named as such. For example:

a) negative ligands end in *–o*:

b) positive ligands end in –ium:

NO^+ – nitrosonium, NO_2^+ – nitronium, etc;

c) neutral ligands are named as such

$NH_2CH_2CH_2NH_2$ – ethylenediamine, C_6H_5N pyridine, etc.

However, there are a few exceptions in naming neutral ligands, for example: H_2O aquo (aqua), NO nitrosyl, NH_3 ammine, CO carbonyl.

4. Order of naming ligands. When more than one type of ligands are present, they are named in **alphabetical order** of preference without separation by hyphen. For example, in the complex $[Co(NH_3)_4Cl(NO_2)]^+$, the ligands are named in the order: ammine, chloro and nitro.

5. Numerical prefixes to indicate number of ligands. When more than one ligands of a particular kind are present in the complex, the prefixes di-, tri-, tetra, penta-, hexa-, etc. are used to indicate their number: two, three, four, five and six respectively.

6. Ending of names. When the complex is anionic, the name of the central metal atom ends in **–ate**. For cationic and neutral complexes, the name of the metal is written without any characteristic ending.

$[Co(NH_3)_6]Cl_3$ Hexaamminecobalt (III) chloride (cationic complex – no characteristic ending).

$K[Pt(NH_3)Cl_5]$ Potassium amminepentachloroplatinate (IV) (anionic complex is named with ending of the name of the metal as –ate).

$Ca_2[Fe(CN)_6]$ Calcium hexacyanoferrate (II).

It may be noted that for anionic complexes the Latin names of certain metals are commonly used. For example, ferrate for Fe, cuperate for Cu, argentate for Ag, aurate for Au, stannate for Sn, etc. However, if the complex is cationic the name of the metal ia given as such, e.g. iron for Fe, silver for Ag, gold for Au, copper for Cu, etc. For example: $K_3[Fe(CN)_6]$ – Potassium hexacyanoferrate (III), $[Fe(CO)_5]$ – Pentacarbonyl iron (0).

7. Oxidation state of central metal ion is designated by a Roman numeral in the brackets at the end of the name of the complex without a gap between the two. It may be noted that the gap should be only between cation and anion. The complex part should be written as one word.

$K^{+1}{}_4[Ni^0(CN)^{-1}{}_4]^{4-}$ – Potassium tetracyanonickelate (0)

$Cu^{+2}{}_2[Fe^{+2}(CN)^{-1}{}_6]^{4-}$ – Copper hexacyanoferrate (II)

$[Pt^{+4}(NH_3)^0{}_4Cl^{-1}(NO_2)^{-1}]^{2+}SO_4{}^{2-}$ – Tetraamminechloronitroplatinum (IV) sulfate

$K^{+1}[Ag^{+1}(CN)^{-1}{}_2]^{1-}$ – Potassium dicyanoargentate (I)

$[Ni^0 (CO)^0{}_4]^0$ – Tetracarbonylnickel (0).

11. Equilibria in the solutions of Complexes.

Stability of Complex Compounds

The inner and outer spheres of complex compounds differ greatly in their stability. The particles in the outer sphere are bonded to the complex ion mainly by electrostatic forces and are readily detached in an aqueous solution. This dissociation is called ***primary***. It proceeds almost to the end like dissociation of strong electrolytes. The ligands in the inner sphere are much more strongly bonded to the central atom and are detached only to a small degree. The reversible decomposition of the inner sphere of a complex compound is known as ***secondary dissociation.*** For example:

$$[Ag\,(NH_3)_2]\,Cl \rightarrow [Ag\,(NH_3)_2]^+ + Cl^-$$

primary dissociation

$$[Ag(NH_3)_2]^+ \rightarrow Ag^+ + 2NH_3$$

secondary dissociation

The dissociation of the $[Ag(NH_3)_2]^+$ ions obeys the law of mass action and can be characterized by the relevant equilibrium constant, known as the ***constant of instability*** of the complex ion:

The instability constants for various complex ions are quite diverse and can be a measure of stability of a complex. The above formula shows that the smaller the concentration of the decomposition products, i.e. the more stable is a complex, the smaller is its instability constant.

The complex particles that are the most stable in solutions have the lowest instability constants. For instance, among the following compounds of the same kind:

	$[Ag(NO_2)_2]^-$	$[Ag(NH_3)_2]^+$	$[Ag(S_2O_3)_2]^{3-}$	$[Ag(CN)_2]^-$
K_{inst}	$1.3 \cdot 10^{-3}$	$6.8 \cdot 10^{-8}$	$1 \cdot 10^{-13}$	$1 \cdot 10^{-21}$

the stability of the complex grows in going from $[Ag(NO_2)_2]^-$ to $[Ag(CN)_2]^-$.

Lately, it is preferable practice to use the reciprocal of the instability constant, called the **stability constant,** to characterize the stability of complex compounds. For the $[Ag(NH_3)_2]^+$, the stability constant is:

$$K_{inst} = \frac{[Ag^{+}][NH_3]^2}{[[Ag(NH_3)_2]^{+}]} = 6.8 \times 10^{-8}$$

The values of the instability and stability constants can be used to predict the course of reactions between complex compounds: a reaction will proceed in the direction of the formation of a complex with a greater stability constant or, which is the same, with a smaller instability constant.

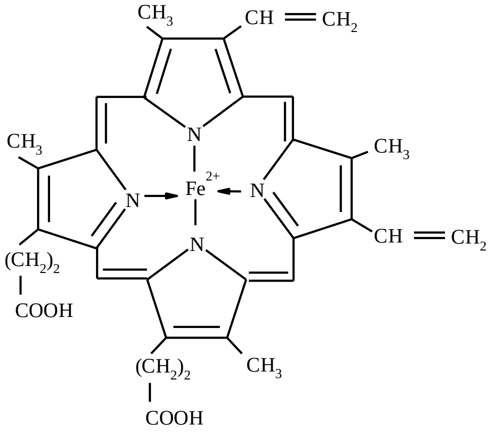
Complex compounds containing polydentate ligands are very stable. For example:

	$[Cu(NH_3)_4]^{2+}$	$[Co(NH_3)_4]^{2+}$	$Cu(Gly)_2$	$Co(Gly)_2$	Cu(EDTA)	Co(EDTA)
Kinst	$8 \cdot 10^{-13}$	$1 \cdot 10^{-5}$	$5 \cdot 10^{-16}$	$3.3 \cdot 10^{-9}$	$1.6 \cdot 10^{-19}$	$1 \cdot 10^{-16}$

12. Biologicaly important complexes. Chelation

Cations of d-block metals in the organism are tightly bonded with polydentate ligands, as a rule, with polypeptides or cyclic polydentate ligands – derivatives of porphyrins (e.g. in hemoglobin). In the free state these cations exist only in the blood plasma in negligible amounts.

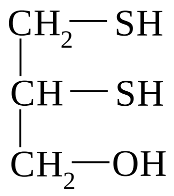
In the biological systems the amino acids, proteins and acids of Tricarboxylic acid cycle (Krebs cycle) are the main ligands and the metals involved are iron, magnesium, manganese, copper, cobalt, and zinc. Iron enters the composition of hemoglobin, myoglobin, oxidases, peroxidases, cytochromes. More than 60 biologically active substances contain zinc, e.g. enzymes carbonic anhydrase and carboxypeptidase. Cobalt is in composition of vitamin B_{12} (cyanocobalamin).



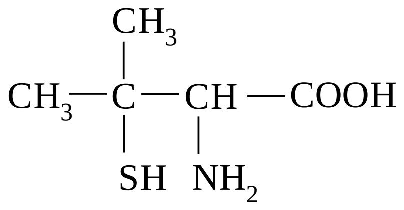
Formation and destruction of biological complexes occur constantly in the organism and metal-ligand homeostasis is maintained on the definite level. Metal-ligand homeostasis can be disturbed due to deficiency or excess of biometals cations, entering of toxic metals cations, entering or formation of alien ligands. For example, entering into the organism of such toxic ligand as carbon monoxide leads to the disturbance of hemoglobin function and hemoglobin loses its ability to transport oxygen. Toxicity of d-metals in many cases is explained by the stability of biological complexes formed by them.

Toxic metals and toxic ligands pollute the environment, enter into the human organisms and disturb metal-ligand homeostasis in the result of anthropogenous activity. Complexing agents are used for removal of metal poisoning. Antidote therapy of poisonings caused by heavy metals cations is based on the formation of stable complexes (chelation) between these metals and special ligands.

Dimercaprol is an effective antidote for the organic arsenical like lewisite, but can be used for poisoning due to antimony, gold and mercury.



2,3-dimercaptopropan-1-ol
(BAL, dimercaprol)



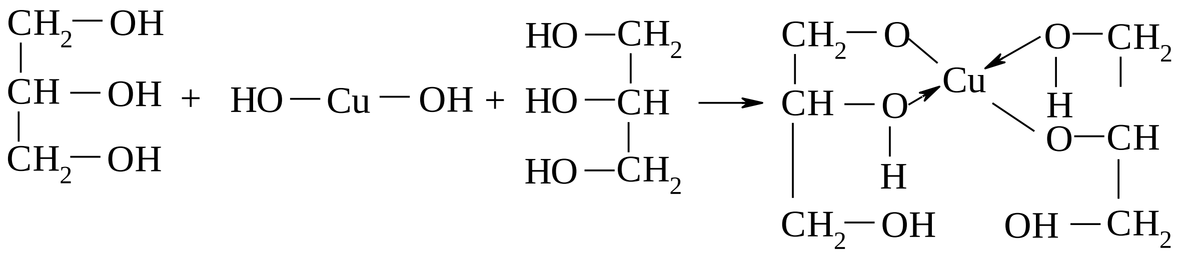
Penicillamine (dimethylcystein)

Penicillamine is an effective antidote for the treatment of poisonings by copper, mercury and lead. Trilon B (bisodium salt of EDTA) is used for treatment of hypercalcemia, poisoning by calcium compounds.

In general, chelation can be used for sequestration of metal ions, stabilization of drugs, elimination of toxic metals from intact organisms and also for the improvement of metal absorption. Recently, platinum complex cis $[Pt(NH_3)_2Cl_2]$ known as cisplatin has found use in cancer chemotherapy.

13. Complexometric analysis

Formation of complex compounds is widely used for qualitative and quantitative determination of different substances. Chelates are often coloured and chelation can serve as qualitative test for compounds capable for chelation, in particular for polyatomic alcohols and amino acids.



Glycerine (polyatomic alcohol) Copper glycerate (blue coloration)

The content of calcium and magnesium ions in water determines the total water hardness (H). The complexometric method of analysis is used to determine the quantity of these ions. It is based on the formation of complex compounds of various metals with the complexones.

Ethylenediaminetetraacetate should be referred to them and is used in the volumetric analysis as the operating solution. The ethylenediaminetetra-acetate is often called **B trilon**. The reaction takes place in the presence of indicator chromogen black or murexide. Ions of metals (Ca^{2+} and Mg^{2+}) form a complex with the indicator, which is less stable then a complex formed with B trilon. The complex of metal ion with the indicator is broken down in the process of titration, a new complex with B trilon is formed and the indicator is segregated in a free state. The indicator in the free state and the indicator combined with the metal ion are colored differently.

$$\underset{\text{blue}}{Me^{2+}+H_2Ind} \rightarrow \underset{\text{red}}{MeInd}+2H^+;\ \underset{\text{red}}{MeInd}+Na_2H_2Y \rightarrow Na_2MeY+\underset{\text{blue}}{H_2Ind}$$

As pH (pH = 8–10) influenced the equilibrium of the reaction, the process of titration should be carried out in the buffer solution of ammonia. The water used for everyday necessities of life is suitable if its hardness is not more than 8 mmoles per dm^3.

LABORATORY WORK

Experiment 5.

Study of instability constant's influence on the direction of complex formation.

Chromogen black and Trilon B form chelate complexes with calcium ions in accordance with the equations (see p.32). Chromogen black forms a less stable red complex with Ca^{2+}-ions (K_{inst} is high), which breaks after addition of Trilon B because Ca^{2+}-ions pass into more stable complex with Trilon B (K_{inst} is low). Solution turns blue due to the presence of free molecules of chromogen black.

Thus, complex formation reactions in the solution and in the human body proceed in the direction of stable complex formation with less instability constant.

Experimental technique

Place 20 drops of 0.1% calcium chloride in a test tube, add 10 drops of ammoniacal buffer solution and 1 drop of chromogen black. Observe appearance of colour in the solution. Add Trilon B drop by drop from the dropping bottle into the same tube until colour changes.

Write observations and make conclusions.

14. Tasks for knowledge control

Find the charge of complexing agent and coordination number in the following compound: $[Cr(H_2O)_4Cl_2]Cl$

1. Complexing agent is:
   a. Cr;
   b.H_2O;
   c. Cl.
2. The charge of the complexing agent is:
   a. +1;
   b.+2;
   c. +3.
3. The coordination number is:
   a. 2;
   b.4;
   c. 6.
4. The oxidation state of iron in $K_4\,[Fe\,(CN)_6]$ is
   a. 1
   b. 2
   c. 3
5. Which compound is zero valent metal complex?
   a. $[Cu(NH_3)_4]SO_4$
   b. $[Pt(NH_3)_2Cl_2]$
   c. $[Ni(CO)_4]$
   d. $K_3[Fe(CN)_6]$

Ans. 1– a; 2 – c; 3 – c; 4 – b; 5 – c.

Навчальне видання

Загальні відомості про біогенні елементи. Комплексоутворення у біологічних системах

Методичні вказівки для самостійної роботи студентів 1-го курсу з медичної хімії

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