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ODESA NATIONAL MEDICAL UNIVERSITY
Department of Medical Biology and Chemistry

CONFIRMED by
Vice-rector for scientific and
pedagogical work
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**METHODOLOGICAL DEVELOPMENT
TO THE LECTURES ON EDUCATIONAL DISCIPLINE
"MEDICAL CHEMISTRY"**

Department, course **International faculty, 1st course**
Specialty: **221 "Dentistry"**
Discipline **Medical chemistry**

The program was approved:
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Medical chemistry

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Lecture № 1

Topic: «Chemistry and dentistry. Biogenic elements and their biological role.»

Actuality of theme: Medicinal chemistry studies the structure and reactivity of the most important biologically active molecules, the theory of chemical bonding in complex compounds of biometals with bioligands, and the role of biogenic elements in the vital activity of the body. It investigates the processes that take place at the molecular and submolecular levels, and it is precisely here that the causes of the occurrence of various forms of diseases and the specificity of hereditary characteristics should be sought.

Aims: show the value of chemistry for the development of modern medicine, the interrelationship of the biological action of elements depending on their location in the periodic table in accordance with the electronic classification of s -, p-, d -, f- blocks of elements. To acquaint students with the structure and content of the "Medical Chemistry" course. Pay attention to safety rules when working in a chemical laboratory. Trace the relationship between the biological activity of chemical elements and the electronic structure of their atoms. Consider different types of classifications of biogenic elements.

Basic concepts: atomic structure, biogenic elements, s-, p-, d-elements, classification of biogenic elements.

Plan and organizational structure of the lecture:

1. relationship between chemistry and medicine.
2. Classification of biogenic elements.
3. Biogenic s-elements. Biological role.
4. Biogenic p-elements. Biological role.
5. Biogenic d-elements. Biological role.

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Content of lecture material (lecture text)

For modern physicians and pharmacists, the study of inorganic chemistry is of great importance because many drugs are inorganic in nature. Therefore, physicians must clearly know their properties: solubility, mechanical strength, reactivity, impact on humans and the environment.

Modern medicine has extensively studied the relationship between the content of chemical elements in the body and the occurrence and development of various diseases. It turned out that the body is particularly sensitive to changes in its concentration of trace elements, i.e. elements present in the body in an amount less than 1 g per 70 kg of human body weight. Such elements include copper, zinc, manganese, molybdenum, cobalt, iron and nickel.

Of the non-metalloids, atoms of hydrogen, oxygen, nitrogen, carbon, phosphorus and sulfur in organic compounds and atoms of halogens and boron both as ions and as part of organic particles can almost always be found in living systems. Deviations in the content of most of these elements in living organisms often lead to quite severe metabolic disorders.

Most diseases are caused by a deviation of concentrations of any substance from the norm. This is due to the fact that a huge number of chemical transformations within the living cell occurs in several stages, and many substances are important to the cell not by themselves, they are only intermediaries in a chain of complex reactions, but if any link is broken, then the whole chain as a result often ceases to perform its transfer function; stops the normal work of the cell for the synthesis of necessary substances.

Changes in zinc concentrations have been proven to be associated with the course of cancer, cobalt and manganese with heart muscle diseases, and nickel with blood clotting processes. Determination of the concentration of these elements in the blood can sometimes detect early stages of various diseases. Thus, changes in zinc concentrations in blood serum are associated with the course of liver and spleen

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diseases, and concentrations of cobalt and chromium - with some cardiovascular diseases.

The role of organic molecules in maintaining the normal vital functions of the body is very great. They can be divided into three groups according to the principles inherent in their design: biological macromolecules (proteins, nucleic acids and their complexes), oligomers (nucleotides, lipids, peptides, etc.) and monomers (hormones, antibiotics, vitamins and many other substances).

It is especially important for chemistry to establish the connection between the structure of a substance and its properties, in particular its biological action. For this purpose, many modern methods from the arsenal of physics, organic chemistry, mathematics, and biology are used.

In modern science, many new sciences have emerged on the boundary of chemistry and biology, which differ in their methods, goals, and objects of study. All these sciences are commonly grouped under the term "physicochemical biology". This field includes:

- a) Chemistry of natural compounds (bioorganic and bioinorganic chemistry, bioorganic chemistry and inorganic biochemistry, respectively);
- b) biochemistry;
- c) biophysics;
- d) molecular biology;
- e) molecular genetics;
- f) pharmacology and molecular pharmacology and many related disciplines.

The scientific substantiation of the doctrine of chemical elements was obtained in academic Vladimir Vernadsky works, who showed a close relationship between the chemical composition of the Earth's crust, oceans and living organisms. He believed that living organisms and the Earth's crust form a single system, and living organisms are involved in the geochemical processes of the distribution of chemical elements in the Earth's crust.

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The shell of the Earth, within the boundaries of which organisms live, is called the *biosphere*.

The most important studies of the biosphere were carried out by the first president of the Ukrainian Academy of Sciences V.I. Vernadsky (1863-1945). Studying geochemical transformations in the Earth's crust, V.I. Vernadsky established that the changes occurring in its upper layers in a certain way affect the chemical composition of living organisms. Studies of the chemical composition of the Earth's crust, soil, sea water, plants, animals, and humans have shown that living organisms, including the human one, contain almost all the elements that exist in the Earth's crust and sea water. V.I. Vernadsky believed that living organisms and the earth's crust make up one system.

Studying the movement (migration) of elements, V.I. Vernadsky established that migration, dispersion and concentration of elements depend on the atomic mass of the chemical element, the atomic and ionic radius, and also on the ability of the elements to form chemical compounds.

All chemical elements that take part in the biological processes of living organisms are called *biogenic elements*.

The quantitative content of chemical elements in living matter (living matter is the totality of all living organisms) is inversely proportional to their numbers in the periodic system of elements, i.e. the quantitative chemical composition of living matter is a periodic function of the element number. However, this regularity is violated for elements of the main subgroups of I, II, and VII groups.

Violation of this pattern depends on the nature of the chemical bond between the atom of the element in question and other atoms included in the molecules of bioorganic compounds.

The quantitative content of covalently bound atomic elements decreases with increasing charge of atoms in the group (for example, N, P, As, Sb), and the elements that are in the body in the form of ions (S-elements of I and II groups, p-elements of group VII) - increases (to the optimum ionic radius), and then decreases. For example, when switching from beryllium to calcium, the content of an element in a living

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organism increases, and then decreases; during the transition from fluorine to chlorine, it also increases, and then decreases (table 1).

Table 1. The dependence of the quantitative content of chemical elements on the nuclear charge

Element	Content, mass fraction, %	Element	Content, mass fraction, %
${}^4\text{Be}$	$10^{-7}-10^{-4}$	${}^9\text{F}$	10^{-5}
${}^{12}\text{Mg}$	$2,7 \cdot 10^{-2}$	${}^{17}\text{Cl}$	$1 \cdot 10^{-1}$
${}^{20}\text{Ca}$	2,0	${}^{35}\text{Br}$	$10^{-4}-10^{-3}$
${}^{38}\text{Sr}$	$10^{-3}-10^{-2}$	${}^{53}\text{I}$	$10^{-5}-10^{-3}$
${}^{56}\text{Ba}$	$10^{-5}-10^{-4}$		

There are several classifications of chemical elements contained in the human body.

So, V.I.Vernadsky, depending on the average content in living organisms, divided the elements into three groups:

1. Macroelements. These are elements which content in the body is above $10^{-2}\%$. These include C, H, O, N, P, S, Ca, Mg, Na, and Cl.
2. Microelements. These are elements whose content in the body ranges from 10^{-2} to $10^{-12}\%$. These include I, Cu, As, F, Br, Sr, Ba, Co.
3. Ultramicroelements. These are elements whose content in the body is below $10^{-12}\%$. These include Hg, Au, U, Ra, etc.

Biogeochemistry was further studied in the Academician A.P. Vinogradov works.

In the process of evolution from inorganic substances to bioorganic basis for the use of certain chemical elements in the creation of biosystems is natural selection. As a result of this selection, only six elements form the basis of all living systems: C, H, O, N, P, S, called organogens. Their content in the body reaches 97.4%.

From the point of view of chemistry, the natural selection of organogen elements can be explained by their ability to form chemical bonds: on the one hand,

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they are strong enough, that is, energy-intensive, and on the other hand, quite labile, which could easily give in to hemolysis, heterolysis, and cyclic redistribution.

The number one organogen is undoubtedly carbon. Its atoms form strong covalent bonds between themselves or with atoms of other elements. These bonds can be ordinary or multiple, thanks to such bonds, carbon can form conjugate or cumulated systems in the form of open or closed chains, cycles. Unlike carbon, organogen elements do not form hydrogen and oxygen labile bonds, but their presence in an organic, including bioorganic, molecule determines its ability to interact with a bio-solvent - water. In addition, hydrogen and oxygen are carriers of the redox properties of living systems, they ensure the unity of redox processes. The remaining three organogens - N, P and S, as well as some other elements - Fe, Mg, which make up the active centers of enzymes, like carbon, are able to form labile bonds. A positive property of organogens is that they, as a rule, form compounds that are readily soluble in water and therefore are concentrated in the body.

Of all the biogenic elements, eleven (O, H, N, S, Ca, Mg, K, Na, Cl, P, C) make up 99.5% of the body mass. The content of all other elements is less than 0.5%.

The natural selection of elements was due to such factors:

- the ability to form strong (energy-intensive) bonds;
- the ability to form chains;
- lability of bonds;
- “lability” of atoms, for example, S, P, Fe /according to J. Bernal /;
- the formation of compounds readily soluble in water, which contributed to their concentration in the body;
- the tendency to form stable coordination compounds with biological molecules.

Human organs differently concentrate various chemical elements in themselves, that is, micro and macro elements are unevenly distributed between different organs and tissues. Most trace elements accumulate in the liver, bone and muscle tissue. These tissues are the main depot (reserve) for many trace elements.

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It is known that Cu is concentrated in the liver, Zn - in the pancreas; I - in the thyroid gland; F - in tooth enamel; Al, As accumulate in the hair and nails; Cd, Hg, Mn - in the kidneys; Sr - in the prostate gland; Ba - in the retina.

Developing the ideas of V.I. Vernadsky on the role of the elemental composition of the soil in the evolution of organisms, A.P. Vinogradov developed the doctrine of biogeochemical provinces - areas with an increased or decreased content of an element in them - and endemic diseases caused by the associated content of elements in the human body.

Diseases associated with a deficiency or excess of elements in the human body have been identified. So, with rickets, there is a violation of phosphorus-calcium metabolism, which leads to a decrease in calcium content. With jade, due to a violation of electrolyte metabolism, the content of calcium, sodium, chlorine decreases and the content of magnesium and potassium in the body increases. Cuprum deficiency is one of the causes of cancer. In some cases, doctors associate lung cancer with elderly people with an age-related decrease in the content of cuprum in the body. However, an excess of cuprum in the body leads to mental disorders and paralysis of some organs (Wilson's disease). Only relatively large amounts of cuprum compounds are harmed. Such patterns are due to the fact that in the human body a balance of optimal concentrations of nutrients is maintained - chemical homeostasis. Violation of this balance can lead to various diseases.

Nowadays it has been firmly established that the lack of certain chemical elements in the soil leads, respectively, to a lower level of these elements in the body of people living in a given area, and to certain diseases.

So, in Ukraine, the Carpathians and Crimea there are geochemical provinces with a low iodine content, and the Kropyvnytskyi region – there is a high content of uranium.

Information on the content of one or another chemical element in the human body is important both for the diagnosis of the disease and for the direction of its treatment. Deficiency of chemical elements in the human body is characterized by certain symptoms (table 2).

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Table 2. Characteristic symptoms of chemical elements deficiency in the human body

Element deficiency	Typical symptom
Ca	Skeletal growth retardation
Mg	Muscle cramps
Fe	Anemia, a violation of the immune system
Zn	Skin damage, growth retardation, sexual maturation retardation
Cu	Arterial weakness, impaired liver function, secondary anemia
Mn	Infertility, skeletal growth impairment
Mo	Slowing down cell growth, caries tendency
Co	Pernicious anemia
Ni	Increased depression, dermatitis
Cr	Diabetes Symptoms
Si	Skeletal growth impairment
F	Tooth decay
I	Disruption of the thyroid gland, slowing down metabolism
Se	Muscular (particularly heart) weakness

The rapid technical development of civilization has led not only to the creation of modern technologies, but also to the appearance of environmental problems.

The environment is polluted in two ways: natural or man-made, i.e. due to human activity. Natural disasters - earthquakes, volcanic eruptions, etc. - strongly pollute the environment. But nature over many years has adapted to most natural pollution and learned to neutralize it.

Over the years of technological progress, man-made disasters have become more frequent. For example, on April 26, 1986, the largest nuclear accident occurred.

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Radioactive substances from the reactor entered the atmosphere and formed a radioactive cloud, which was 30 km wide and 100 km long. Ukraine experiences the consequences of this disaster even after 30 years.

Significant amounts of SO₂, NO, CO, CO₂ accumulate in the atmosphere as a result of human industrial activity and, together with the air we breathe, enter our body, which negatively affects our health. In recent years, the CO₂ content in the atmosphere has increased dramatically, which, according to scientists, has led to a 1 degree increase in temperature on the planet over the past 100 years. In 1997, in Kyoto at the International Conference, the developed countries of the world signed an agreement, according to which a limit was set for emissions of industrial gases into the atmosphere.

In the practice of sanitary-hygienic, biochemical, clinical and analytical laboratories for the study of the quality of drinking and wastewater, food, air, soil, methods of qualitative analysis occupy a leading place. In clinical and biochemical laboratories, these methods are used to study the chemical composition of individual organs and tissues, metabolism in humans and animals in normal and pathological conditions. A chemical analysis of blood, urine, gastric juice and other biological fluids facilitates the diagnosis of the disease and makes it possible to monitor the course of the disease in dynamics.

V.V. Kowalski created the doctrine of geochemical ecology - biochemical and physiological adaptations of the body to the chemical elements of this environment. According to Kowalski, most organisms adapt to the unusual content of certain elements and develop normally. And only 5 to 20% of organisms in these conditions suffer from endemic diseases. He, based on the degree of importance of chemical elements for human life, divided them into three groups:

Irreplaceable elements. They are constantly in the human body, are part of its inorganic and organic compounds. These are H, O, Ca, N, K, P, Na, S, Mg, Cl, C, I, Mn, Cu, Co, Zn, Fe, Mo, V. A deficiency in the content of these elements leads to a disruption in the normal functioning of the body.

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Impurity elements. These elements are constantly found in the human body, but their biological role has not always been clarified or little studied. These are Ga, Sb, Sr, Br, F, B, Be, Li, Si, Sn, Cs, As, Ba, Ge, Rb, Pb, Ra, Bi, Cd, Cr, Ni, Ti, Ag, Th, Hg, Ce, Se.

Microimpurity elements. They are found in the human body, but there is no information about the quantitative content or the biological role. These are Sc, Tl, In, La, Sm, Pr, W, Re, Tb, etc.

A.I. Venchikov believed that chemical elements, regardless of their quantitative content, should be given the name of biotic elements if their physiological activity is proven. By A.I. Venchikov, biotics are chemical elements of exogenous origin that are part of the biochemical structures and systems of the body, participating in biochemical and physiological processes and capable of increasing the body's resistance to the action of harmful agents on it. It follows from this definition that both macro- and microelements that are part of vitamins, enzymes and other substances that are necessarily involved in metabolic processes can be classified as biotics. In accordance with this classification, elements playing the role of plastic material in the body, as well as creating physical and chemical conditions for physiological processes (pH of the medium, osmotic pressure, etc.) to this group, except C, N, O, H can be attributed macroelements Na, Ca, K, Mg, Cl, P. The next group includes elements involved in metabolic processes. These are biocatalytic elements (Fe, Cu, Mn, etc.). They activate the enzymatic processes of the body or enter the structure of enzymes (Zn), vitamins (Co), hormones (I).

The third group includes the so-called reticuloendothelial elements (As, Hg, Sb, etc.), which contribute to the reticuloendothelial system of the formation of substances that inhibit the vital activity of microbes.

A.P. Vinogradov proposed a fundamentally new classification, based on which the biological role of elements was made dependent on the electronic structure of their atoms, i.e. it was depended on the position in the periodic system of elements D.I. Mendeleev.

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Based on the electronic structure of atoms, elements of s, p, d - blocks are referred to biogenic elements. The electronic structure of an atom determines the features of its behavior in chemical reactions, and affects the types of chemical bonds formed by it in compounds.

S-BLOCK BIOGENIC ELEMENTS

S-ELEMENTS OF GROUP I

In the periodic system of chemical elements of D.I. Mendeleev, biogenic s-elements are included in the main subgroups of I and II groups. They are located at the beginning of periods and are typical metals.

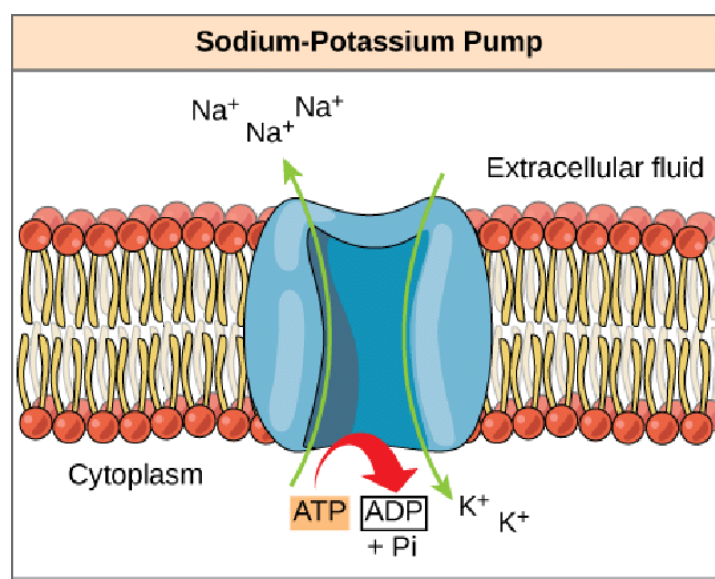
s-Elements are characterized by small values of ionization potentials at sufficiently large values of the radii of atoms and ions. Group I s-elements, as a rule, form compounds with an ionic type of bond, group II s-elements in this respect are somewhat inferior to them. These properties make them physiologically active, and such elements as K, Na, Ca, Mg are vital and exhibit unique properties in the body. Most biogenic s-elements are macroelements. Their high concentration in the body is associated with the formation of compounds that are readily soluble in biological fluids (s-elements of group I), and hardly soluble salts involved in the formation of bone tissue (s-elements of group II). The biogenic elements of group I are necessary for the normal living organism functions. First of all, these are macroelements - hydrogen, potassium and sodium.

Macroelements potassium and sodium are distributed throughout the body. According to A. Webb, in all organs except the kidneys, the potassium content is greater than sodium. By chemical properties, potassium differs markedly from sodium. This is largely due to the presence of free d-orbitals in potassium and its analogues, which have energy close to the energy of ns - sublevels. The difference in properties possibly determines their different behavior in living organisms. The main difference is that sodium ions are part of intercellular fluids, and potassium ions are intracellular; sodium cations suppress the activity of muscle functions and are therefore necessary for

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their contraction; potassium cations help to relax the heart muscles between contractions.

A different concentration of potassium and sodium cations inside and outside the nerve cell and its axon and the greater ease of passage of K^+ ions through the membrane than Na^+ leads to the appearance of a potential difference in the cell body of the order of 60-90 mV, while the inner surface of the cell membrane is negatively charged with respect to the outside. A peculiar - Na^+ - K^+ - pump is formed. When excited, biochemical processes occur that lead to a change in the permeability of the cell membrane. As a result, sodium ions penetrate into the cell, causing local damping of the negative charge and its change to a positive one. The so-called action potential arises. The restoration of the initial potential occurs not as a result of the reverse movement of sodium ions, but as a result of the release of an equivalent amount of potassium ions from the cell.



S - Elements of group II

The biogenic S-elements of group II include macrocells magnesium and calcium, which, according to the classification of A.I. Venchikova belong to the group of biotics, playing the role of plastic material, as well as creating physico-chemical conditions for physiological processes, and trace elements of beryllium and strontium; the role of the

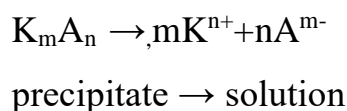
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remaining micro- and ultramicroelements (barium and radium) in the body is not well understood.

Magnesium and calcium are vital elements. Calcium is the main structural element of living organisms; Magnesium is a part of a large number of enzymes and is an activator of many biochemical processes.

The calcium atom is larger in size than the magnesium atom; therefore, its ability to form hydrates, as well as the solubility of its carbonates and phosphates in water, is significantly lower compared to magnesium compounds. Calcium carbonates and phosphates are the main material that forms bone and dental tissue.

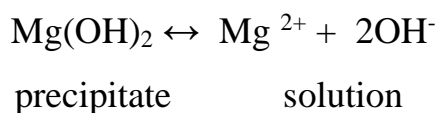
A quantitative characteristic of the solubility of compounds is the solubility product (SP). Its meaning becomes clear if we consider the equilibrium processes that occur in heterogeneous systems. In such systems — saturated solutions of sparingly soluble substances — the solid phase is in equilibrium with the hydrated ions in solution. In general:



This state is characterized by the equilibrium constant, which is obtained using the law of mass action, and is called the solubility product:

$$SP = [K_p^{n+}]^m \cdot [A_p^{m-}]^n \quad (1)$$

For a saturated solution of $Mg(OH)_2$ in equilibrium with the precipitate:



the expression for the solubility product is:

$$SP (Mg(OH)_2) = [Mg^{2+}] \cdot [OH^-]^2$$

Thus, in a saturated solution of a sparingly soluble compound, the product of the concentrations of its ions in degrees of stoichiometric coefficients at a given temperature is a constant value (table 3).

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Table 3. The solubility product of some sparingly soluble electrolytes in water, $t = 25^{\circ}\text{C}$.

Compound	SP	$p\text{SP} = -\lg \text{SP}$
CaCO_3	$4,8 \times 10^{-9}$	8,32
$\text{Ca}_3(\text{PO}_4)_2$	$2,0 \times 10^{-29}$	28,70
CaF_2 ,	$4,0 \times 10^{-11}$	10,40
$\text{Mg}(\text{OH})_2$	$5,5 \times 10^{-12}$	11,26
BaSO_4	$1,8 \times 10^{-10}$	9,75

It is likely that the elements involved in the formation of bone tissue should satisfy the basic requirements: to be macroelements, have high energy for the formation of chemical bonds, form poorly soluble compounds; easily absorbed by a living organism. Calcium phosphate and calcium carbonate meet these requirements. Calcium, phosphorus, carbon and oxygen are macrocells; the binding energy of oxygen with phosphorus and carbon, through which calcium binds to them, is quite high; calcium phosphate and calcium carbonate sparingly soluble compounds; all these elements are easily absorbed by the body, since in nature they exist in easily accessible forms for assimilation. Magnesium, which is also a macronutrient, forms poorly soluble phosphates and basic carbonates, but they are more soluble than calcium.

Precipitation formation and dissolution conditions

As is known, the solubility product at constant temperature is a constant value. According to the rule of the solubility product, at the moment when the product of the ion concentration (ion product) of the sparingly soluble electrolyte reaches the value of its solubility product at a given temperature, the solution becomes saturated relative to this electrolyte.

If the product of the molar concentration of ions in the solution is greater than the product of solubility, then such a solution is supersaturated. From a supersaturated solution, sooner or later, a part of the dissolved substance will be released in the form

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of a solid phase (precipitate). Thus, denoting the product of molar concentrations of ions in solution through PC, the condition for the possible formation of a precipitate can be written as the inequality $pK > SP$.

If the ionic product is less than the solubility product ($pK < SP$), then the solution is unsaturated and no precipitate is formed.

For example, for $CaCO_3$, the following ratios of pK and SP are observed:



$$SP = [Ca^{2+}][CO_3^{2-}]$$

- a) in unsaturated solution: $C(Ca^{2+}) \cdot C(CO_3^{2-}) < SP (CaCO_3)$;
- b) in saturated solution: $C(Ca^{2+}) \cdot C(CO_3^{2-}) = SP (CaCO_3)$;
- c) in a supersaturated solution: $C(Ca^{2+}) \cdot C(CO_3^{2-}) > SP (CaCO_3)$.

Alkaline earth metals often compete with each other. For example, Ca^{+2} ions inhibit the activity of enzymes activated by Mg^{+2} ions (magnesium is an activator of more than 15 enzymes). Mg^{2+} in turn inhibits the action of myosin adenosine triphosphatase, which is activated by Ca^{2+} ions. Mg^{2+} ions are necessary for the transmission of nerve impulses, muscle contraction and carbohydrate metabolism. Together with calcium ions, magnesium ions are part of many cellular structures. Magnesium is more of an intracellular ion, while the calcium inside the cell is much less than outside it. Based on this, one can expect the presence of a magnesium - calcium pump between the intracellular and intercellular fluid. Moreover, in all cells, the separation of Ca^{2+} , Mg^{2+} , Na^+ , K^+ is strictly controlled.

BIOGENIC ELEMENTS OF THE D-BLOCK

More than 30 d-elements are known, which in the periodic system form three complete insert decades (Sc - Zn, Y - Cd, La - Hg) and several elements of the fourth decade. The electron filling of the d sublevel occurs in accordance with the Gurd rule, i.e. the total value of spin numbers should be maximum. At the external level of d-element atoms, there are one or two electrons of the s-state (with the exception of

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palladium atoms for which there are no s-electrons of the external level), which can be explained on the basis of the principle of least energy. A decrease in the number of s-electrons at the external level to one or their absence in palladium atoms occurs due to the “dip” (or slip) of electrons from the s-external to the d-pre-sublevel, due to which a more stable state with a smaller energy reserve is achieved. For example, in the atoms of the elements of chromium, molybdenum, niobium, cuprum, argentum, aurum, etc. there is a “dip” of one external s-electron, and in the atoms of the element of palladium - two external s-electrons.

For atoms of transition metals, two especially stable states are characteristic: in the first, the orbitals of the anterior d-sublevel are half filled (nd^5); in the second, d-orbitals are completely filled (nd^{10}).

Due to the high charge of the nucleus and the presence of free electronic orbitals, they are part of biologically active compounds (enzymes, hormones, vitamins, pigments, etc.) and have a high specificity of action.

THE BIOLOGICAL ROLE OF D-ELEMENTS AND THEIR COMPOUNDS

Organisms selectively assimilate necessary chemical elements from the external environment, concentrating them in certain organs and tissues. The source of income is food and water, and for some chemical elements, and air. The mass fraction of various elements is not the same and varies widely.

The main factors determining the accumulation of chemical elements in the human body are the following: quantitative content in the external environment, properties of chemical elements, atomic mass and atomic nucleus charge, solubility of natural compounds, ability to complexation, etc. Complexation is a specific property of d-block elements. Most biogenic d-elements are trace elements. In the human body, as components of enzymes, hormones, vitamins and other biologically active substances, they participate in the processes of reproduction, growth, metabolism of proteins, lipids, carbohydrates, etc. Complex compounds in which the central ion is the elements of

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inserted decades, and the ligands are amino acids, proteins, etc., are easily soluble in water and well absorbed by living organisms. In the human body, proteins, amino acids and their derivatives, nucleic acids, nucleoproteins, nitrogen bases, peptides, fatty acids, carbohydrates, vitamins, enzymes, hormones, bile acids and other compounds are included in biological complexes as ligands. Among the numerous complex compounds in biosystems, biological complexes of metals with a porphyrin system should be distinguished: iron porphyrin complex (Fe ~ * ion is a complexing agent), cobaltoporphyrin complex (Co ion is a complexing agent). It is generally accepted that both living and non-living nature is more complex than other chemical compounds. In all of the above compounds, the molecules usually contain several functional groups of different types that can coordinate metal ions, including the transition, i.e. d-block elements.

General material and educational and methodological support of the lecture:

- Working program of the discipline
- Silabus
- Methodical recommendations for independent work of higher education applicants
- Multimedia presentations
- Situational tasks

Recommended literature

Basic literature:

1. Medical Chemistry: textbook / V.Y. Tsuber, A.A. Kotvytska, K.V. Tykhonovych et al. - - Kyiv, AUS Medicine Publishing, 2022. – 392 p.
2. Medical chemistry: a textbook for universities / V. O. Kalibabchuk, I. S. Chekman, V. I. Galynska and others; for ed. Prof. V. O. Kalibabchuk – 4th ed. – K. VSV "Medicine", 2019 – 336 p.
3. Medical chemistry / V.O. Kalibabchuk, V.I. Halynska, L.I. Hryshchenko et al. – Kyiv, AUS Medicine Publishing, 2020. – 224 p.

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4. General and Inorganic Chemistry: textbook / V.O. Kalibabchuk, V.V. Ohurtsov, V.I. Halynska et al. – Kyiv, AUS Medicine Publishing, 2019. – 456 p.

Additional literature:

1. Medical chemistry: a textbook / V. P. Muzychenko, D. D. Lutsevich, L. P. Yavorska; for order. B. S. Zimenkovsky. – 3rd ed., Ed. – K.: BCB «Medicine», 2018. – 496 p.

2. Mironovich L. M. Medical Chemistry: A Textbook. – Kyiv: Karavella, 2008. – 159 p.

3. Moroz A. S. Medical chemistry: a textbook / D. D. Lutsevich, L. P. Yavorska. – Vinnytsia: New book, 2006. – 776 p.

4. Gotsulyak L. O., Mardashko O. O., Yerigova S. G., Kuzmenko G. I., Kuzmina A. V., Zhilinskaya K. I. Bioinorganic, physicoloid and bioorganic chemistry. Teaching. manual. Odessa. Odessa State Medical University 1999. – 248 p.

5. Textbook of Medicinal Chemistry / [V. Alagarsamy](#) // CBS Publishers & Distributors Pvt Ltd, India; 3rd edition, 2018 – 584 p.

6. Richard Post. Chemistry: Concepts and Problems / Richard Post, Chad Snyder, Clifford C. Houk // A Self-Teaching Guide, Jossey-Bass, 2020. – 432 p.

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Lecture № 2

Topic: «Thermodynamic and kinetic laws of biochemical processes»

Actuality of theme: During biochemical processes, chemical and physical phenomena, which are studied by physical chemistry, are closely related. Studying the course of physical and colloidal chemistry will allow the future specialist to acquire knowledge in the field of manufacturing, quality control and storage of medicines, as well as their biotransformation in the human body. The laws of chemical kinetics are used to explain the mechanisms of biochemical reactions (normal and malignant tissue growth), kinetic assessment of treatment effectiveness, achieving the maximum yield of reaction products, studying the distribution of drugs introduced into the body and their half-life from the body. Nowadays, chemical kinetics has become one of the effective "tools" for the study of catalytic reactions, including enzymatic ones, occurring in the human body. It is not for nothing that the expression appeared among scientists: all processes in chemistry and biochemistry are divided into catalytic and those where the fact of catalysis has not yet been discovered.

Goal: on the basis of the laws of thermodynamics, study the interconversion of various types of energy in chemical and physicochemical processes, apply the laws and principles of thermochemical calculations to form a holistic approach to the study of chemical and biological processes; get acquainted with the most important concepts and laws of chemical kinetics; analyze the influence of various factors (concentration, pressure, temperature) on the speed of a chemical reaction; to classify types of chemical processes by kinetic feature; interpret the influence of catalysts on the speed of chemical processes and explain the mechanism of their action; to know the features of enzymatic catalysis.

Basic concepts: thermodynamic system, thermodynamic process, phase, component, thermodynamic parameters, system state functions, heat, work, internal energy,

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enthalpy, the rate of chemical reaction, enzymatic catalysis, chemical equilibrium.

Plan and organizational structure of the lecture:

1. Basic concepts and definitions of chemical thermodynamics.
2. The first law of thermodynamics.
3. Fundamentals of thermochemistry. Hess's law. Thermochemical calculations
4. The important factors that affect the rate of reaction.
5. Enzymatic catalysis.
6. Acid-basic catalysis
7. Chemical equilibrium

Content of lecture material (lecture text)

Thermodynamics is a science that studies the general laws of transformation of different types of energy in a system. It describes changes and transformations without considering the structure of the bodies of the system.

Knowledge of energy changes is crucial for understanding the most important biological processes.

From the point of view of bioenergy, all living things are divided into autophores, which accumulate energy in organisms due to biochemical processes (for example, plants) and heterophores, which produce it as a result of oxidation of nutrients - fats and carbohydrates. Animal organisms are heterophores.

Basic concepts

A thermodynamic system is a body or a group of bodies that are in energy interaction and are mentally or physically separated from the surrounding bodies, which are called the external or surrounding environment.

System classification:

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1) if possible heat and mass transfer: isolated, closed, open. **An isolated system** does not exchange matter or energy with the environment. The concept of an isolated system is used in theoretical chemistry as a theoretical one. **A closed system** exchanges energy with the environment, but does not exchange matter. **An open system** exchanges with the environment and matter and energy. *Living organisms are open thermodynamic systems. An integral sign of a living organism is exchange with the environment: the ingestion of food products and oxygen with air and the release of metabolic products from it.*

2) by internal structure and properties: homogeneous and heterogeneous. **A homogeneous system** is called a system inside which there are no surfaces dividing the system into parts that are different in properties or chemical composition. Examples of homogeneous systems are aqueous solutions of acids, bases, salts; gas mixtures; individual pure substances. **Heterogeneous systems** contain natural surfaces within themselves. Examples of heterogeneous systems are systems consisting of substances of a different state of aggregation: metal and acid, gas and a solid substance, two liquids insoluble in each other.

A phase is a homogeneous part of a heterogeneous system, having the same composition, physical and chemical properties, separated from other parts of the system by a surface. The phases are solid, liquid and gaseous. A homogeneous system always consists of one phase, but a heterogeneous system consist several phases.

The properties of the system in physical chemistry can be described by setting the **system parameters**. The parameters most often are temperature (T), pressure (P), volume (V), amount of substance (ν) and others.

If the parameters of the system are constant, they say that the system is in a state of **equilibrium**.

The processes can be **isothermal** (occur at $T = \text{const}$), **isobaric** ($P = \text{const}$), **isochoric** ($V = \text{const}$), **adiabatic** (proceed without heat exchange with the environment). Of greatest importance in chemical thermodynamics are **isobaric-**

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isothermal ($P, T = \text{const}$) and **isochoric-isothermal** ($V, T = \text{const}$) processes. It is under such conditions that all chemical reactions occur.

The state of the system changes with at least one of its parameters.

For example, the Mendeleev-Clapeyron equation

$$P \cdot V = \frac{m}{M} RT$$

is the equation of state of an ideal gas.

For most systems, the thermodynamic description uses state functions that can be uniquely determined through the parameters (T, P, V).

A function of the state of a system is a function whose change depends only on the initial and final states of the system and does not depend on the path of the system from the initial to the final state.

State Functions:

- *E is the total energy of the system*
- *U - internal energy*
- *H - enthalpy*
- *S - entropy*
- *G - Gibbs free energy*
- *F - Helmholtz free energy.*

Internal energy (**U**) is the energy reserve of the system. It includes all types of energy associated with the structure of the system, and does not include the kinetic and potential energy of the system as a whole. Since there is no absolute knowledge of the structure of matter, the absolute value of internal energy cannot be found.

Enthalpy is the energy reserve of a system in the form of heat. Internal energy, enthalpy, heat, and work are measured in J / mol.

Entropy (**S**) is a thermodynamic function that quantifies the degree of disorder in a system. It is a function of the state of the system, measured in J/mol·K.

Helmholtz energy (**F**) is a function of the state of a system that characterizes the flow of chemical processes under isochoric-isothermal conditions.

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Gibbs energy (**G**) is a function of the state of a system that characterizes the occurrence of chemical processes under isobaric-isothermal conditions. Helmholtz and Gibbs energies are measured in kJ/mol.

The total energy (**E**) is a fundamental function of the state of the system:

$$\mathbf{E} = \mathbf{K} + \mathbf{P} + \mathbf{U}$$

where **K** is the kinetic energy of moving particles of the system;

P is potential energy of influence on the system of external force fields;

U is the internal energy of the system.

In thermodynamics, it is assumed that the system is in relative peace ($\mathbf{K} = 0$), and the influence of external power (gravitational, electromagnetic, and other forces) on the system can be neglected ($\mathbf{P} = 0$).

Under the given limiting conditions it will take the form:

$$\mathbf{E} = \mathbf{U}$$

The internal energy of the **U** system is the total energy reserve, which consists of the kinetic energy of the translational and rotational motion of molecules, the energy of attraction and repulsion of particles, the energy of electronic excitation, internuclear and intranuclear interaction, etc.

Accounting for all these components is impossible, but for thermodynamic analysis it is enough to know only the change in internal energy during the transition from one state to another.

The first law of thermodynamics is a special case of one of the most important laws of natural science - the law of conservation and transformation of energy. **The heat absorbed by the system is expended on the change in internal energy and the completion by the system of work:**

$$\Delta\mathbf{Q} = \Delta\mathbf{U} + \mathbf{A}$$

If the only type of work is the work of expansion forces, then

$$\Delta\mathbf{Q} = \Delta\mathbf{U} + \mathbf{P}\Delta\mathbf{V}$$

$\mathbf{A} = \mathbf{p}\cdot\Delta\mathbf{V}$ – mathematical expression of the I-th law of thermodynamics

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The body receives the energy necessary for the course of life processes with food in the form of the energy of the bonds of macromolecular compounds. In the body, these substances are oxidized to simpler ones. The released energy is converted into other types of energy, mainly into the heat necessary to maintain body temperature, as well as into work during various movements, including labor processes. At the same time, new complex ones are formed in the human body with partial absorption of the released energy, for example, in the muscles, which are the main source of heat production.

In the body there are fluctuations in the internal energy contained in its various parts. However, over a rather long period, for example, a day, all these fluctuations are mutually balanced, i.e. a constant state of the body is maintained. Therefore, when compiling, for example, the daily energy balance of an organism, we can assume that its internal energy remains on average unchanged.

As applied to a living organism, the law of conservation of energy (or the first law of thermodynamics) can be formulated as follows:

The amount of heat Q released in the body during the assimilation of food is spent on compensating for the loss of heat q in the environment and the body performing work A , i.e. $Q = q + A$.

This equation is the equation of the energy balance of the human body, on the basis of which the necessary energy value (calorie content) of the diet is determined. Food is also spent on the restoration and growth (at a young age) of body tissues, the formation of reserves (fat deposition), etc.

In general, it is believed that heat loss of the human body in a temperate climate averages 7,100 kJ per day. If we add to this $A = 2500 - 3340$ kJ, equivalent to the mechanical work performed by the body (for people who do not have physical activity), then we get the daily energy expenditure of the order of 9600 - 10400 kJ. When performing physical work, costs increase to 25,000 kJ per day. These energy costs should be replenished by food.

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Foods include mainly fats, proteins, carbohydrates, mineral salts, vitamins, water. The body receives energy mainly due to the first three groups of substances. From the point of view of energy, the most valuable are fats - 39 kJ / g, carbohydrates (18 kJ/g) and proteins (18 - 22 kJ/g) are less valuable.

The change in the internal energy of the system or enthalpy is usually attributed to the standard state of the starting materials and reaction products. The standard state of a substance at a given temperature is its state in the form of a pure substance at $p = 101,325 \text{ kPa}$ and $t = 25^{\circ}\text{C}$ (298 K).

Changes in the corresponding quantities referred to standard conditions are called standard and are denoted by ΔH^0 and ΔU^0 .

The standard heat of formation of a substance is the standard enthalpy of formation of 1 mole of a substance from simple substances (kJ / mol).

Enthalpy of formation of simple substances = 0.

If the element forms several simple substances, then the standard state is the state of the element in the form of the most stable under the given modification conditions and for it $\Delta H^0 = 0$.

The study of thermal changes in chemical reactions involved in thermochemistry.

Chemical equations that indicate the thermal effects of the reaction are called thermochemical.

There is a form for writing the equation:



$$\Delta H^0 = - 674 \text{ kcal}$$

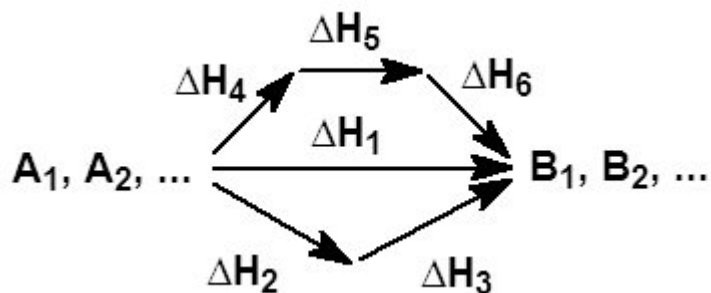
Exothermic reaction

Internal energy (U) and enthalpy (H) are functions of the state of the system; therefore, ΔU and ΔH depend only on which substances react under given conditions and which products are obtained, but do not depend on the path of the chemical process. This provision is known as the law of Hess (1810):

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The thermal effect of a chemical reaction that proceeds at constant pressure or at a constant volume does not depend on the number of intermediate stages, but is determined only by the initial and final state of the system.

Hess law has a graphical representation in the form of a diagram:

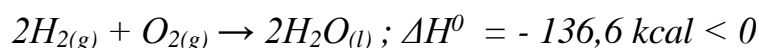


$$\Delta H_1 = \Delta H_2 + \Delta H_3 = \Delta H_4 + \Delta H_5 + \Delta H_6 \quad (11)$$

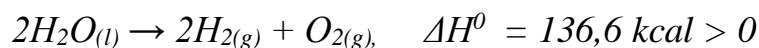
The practical value of the Hess law is that it allows you to calculate the thermal effects of chemical processes.

In thermochemical calculations, a number of consequences from the Hess law are usually used:

1. The thermal effect of the direct reaction is equal in magnitude and opposite in sign to the thermal effect of the reverse reaction.



Exothermic reaction



Endothermic reaction

2. The thermal effect of the chemical reaction is equal to the difference in the sums of the heats of formation of the reaction products and the process inputs, multiplied by stoichiometric coefficients.

$$\Delta H = \sum (v_i \Delta H_f)_{\text{products}} - \sum (v_i \Delta H_f)_{\text{process inputs}} \quad (12)$$

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3. The thermal effect of a chemical reaction is equal to the difference in the sums of the heats of combustion of the starting materials and reaction products, multiplied by stoichiometric coefficients.

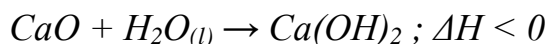
$$\Delta H = \sum (v_i \Delta H_c)_{\text{process inputs}} - \sum (v_i \Delta H_c)_{\text{products}} \quad (13)$$

Application - dietetics - calculation of calorie content of food products.

When studying all processes, they want to get an answer to 2 questions:

1. How complete is the process?
2. How quickly will equilibrium come?

In 1867, Bartlo formulated the principle according to which: all spontaneous processes are exothermic:



But it turned out that there are a large number of physical and chemical phenomena occurring spontaneously and with heat absorption.



Those ΔH does not play a role in determining the spontaneous course of the process.

In all cases considered, it is logical to talk about a change in entropy - S - the state function of the system.

S is a quantitative measure of system disorder [J / mol · K]

The second law of thermodynamics determines the conditions for the occurrence of spontaneous processes. Clausius postulate: **spontaneous transfer of heat from a less heated body to a hotter body is impossible.**

All spontaneous processes occur with an increase in entropy in the system.

If $\Delta S > 0$ – spontaneous process is thermodynamically possible;

If $\Delta S < 0$ – process is impossible;

If $\Delta S = 0$ – the process is reversible.

$$S_{cr} < S_l < S_g$$

An important conclusion follows from the second law of thermodynamics:

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The total change in entropy necessary for the formation of the human body and the maintenance of its life or the existence of any other living system is always positive.

The second law of thermodynamics allows us to determine the direction of chemical reactions and the conditions for establishing chemical equilibrium.

The stability of the system is determined by the ratio of enthalpy and entropy factors. The enthalpy factor characterizes the system's desire for ordering, because accompanied by a decrease in internal energy, and the second factor reflects a tendency to disorder, because this condition is most likely. It was advisable to introduce a state function that takes into account the combined influence of both factors.

In thermodynamics, there are two functions that reflect both the change in the internal energy (enthalpy) of a given process and its inherent probability (entropy).

This is the isochoric-isothermal potential F (Helmholtz free energy) and the isobaric-isothermal potential G (Gibbs free energy).

$$\Delta G^0 = \Delta H^0 - T\Delta S^0$$

ΔG^0 – Gibbs free energy – isobaric-isothermal potential ($P, T = \text{const}$).

$$\Delta F^0 = \Delta U^0 - T\Delta S^0$$

ΔF^0 – Helmholtz free energy – isochoric-isothermal potential ($V, T = \text{const}$).

The value of ΔG determines the possibility of a spontaneous process:

$\Delta G = 0$ – the process is equilibrium;

$\Delta G < 0$ – the process is spontaneous, the system spontaneously passes from one state to another;

$\Delta G > 0$ – the process cannot run spontaneously in the forward direction under standard conditions.

Let us analyze the ratio:

1. If $\Delta H < 0$ (exothermic process), and $\Delta S > 0$, then $\Delta G < 0$ at any temperature, i.e. the isobaric process in the case of an exothermic reaction proceeds spontaneously at any temperature.

2. If $\Delta H > 0$ (endothermic process), then $\Delta G < 0$ if $|\Delta H| < |T\Delta S|$ and $T\Delta S > 0$. This is done if the reaction proceeds at very high temperatures or in the gas phase, when

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the entropy increases significantly, i.e. in the case of an endothermic reaction, the process proceeds spontaneously only at very high temperatures.

3. If $\Delta H > 0$ and $|\Delta H| > |T\Delta S|$, then $\Delta G > 0$ and a spontaneous process is impossible, i.e. a process that is accompanied by a simultaneous increase in enthalpy and a decrease in entropy at a constant value of pressure and temperature is impossible.

As follows from relations (14) and (15), spontaneous flow of the process is possible both with increasing and decreasing entropy (under the conditions $P=\text{const}$ or $V=\text{const}$), which distinguishes the systems under consideration from the isolated ones in which the spontaneous process is always accompanied increase in entropy.

So, based on the second law of thermodynamics, we can conclude that in a system in which constant pressure and temperature are maintained, the processes proceed with a decrease in G . The change in entropy can be either positive or negative (there is no contradiction to the principle of increasing entropy, which follows from the second law of thermodynamics and refers to isolated systems). In accordance with this principle, if a process occurs in the system with a decrease in entropy, then in the environment, which can be considered together with the system as a united isolated system, a compensating increase should occur.

In addition, the negative sign ΔG only indicates the possibility of a spontaneous process under standard conditions. Whether this process will actually go on depends on specific conditions and other factors.

FREE ENERGY AND EQUILIBRIUM CONSTANT

The direction of a chemical reaction, like any other process, at a given pressure and temperature is determined by the change in the Gibbs energy of the system as a result of the reaction.

The minimum value of the Gibbs total energy indicates that chemical equilibrium has occurred in the system (the condition for the minimum of a function is that its derivative is equal to zero).

$$\Delta G = \Delta G^0 + RT \ln K \quad (16)$$

if $\Delta G=0$

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$$\Delta G^0 + RT \ln K = 0$$

$$\Delta G^0 = - RT \ln K$$

$$\Delta G^0 = -2,303 RT \lg K \quad (17)$$

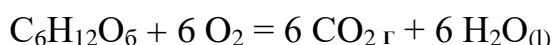
where K – equilibrium constant; ΔG^0 – Gibbs free energy.

From the relation follows:

1. The process is carried out as spontaneous in the forward direction, if $K > 1$, then $\lg K > 0$ and $\Delta G < 0$;
2. If $K < 1$, then $\lg K < 0$ and $\Delta G > 0$, that is, there will be a spontaneous process of converting products into starting materials;
3. If $K = 1$, $\Delta G = 0$ - the process is equilibrium.

ON THE APPLICABILITY OF THE THERMODYNAMICS OF EQUILIBRIUM PROCESSES TO BIOLOGICAL SYSTEMS

The considered laws of classical and chemical thermodynamics are the criteria for the possibility of a spontaneous process and the conditions for the implementation of the equilibrium process. Moreover, the universal criterion for any process is the change in Gibbs free energy. However, quite often, when $\Delta G > 0$ and a spontaneous flow of the process is impossible, this reaction is combined with another so that the total reaction turns out to be spontaneous. The combination of two or more reactions plays an important role in biochemical systems. For example, many reactions in the body are carried out only because they are combined with reactions that occur spontaneously with the release of energy. Thus, the release of energy from food during metabolism is the primary source of necessary free energy. For example, spontaneous oxidation of glucose in the body by the reaction:



is characterized by the release of a significant amount of energy: $\Delta H^0 = -2800$ kJ/mol, $G^0 = -2880$ kJ/mol.

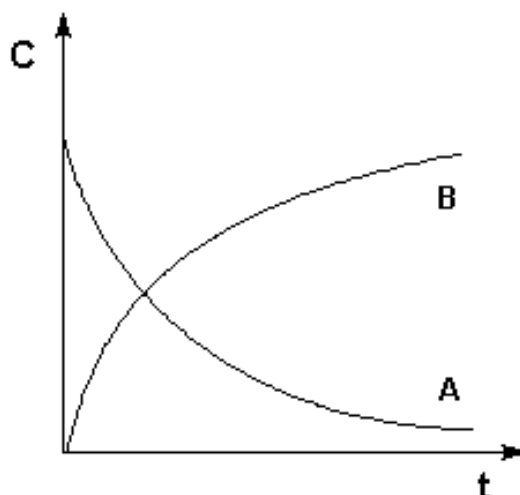
This energy is expended by the body to do useful work (converting ADP to ATP, maintaining a constant body temperature, etc.)

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The transformation of energy in living systems, its formation and deposition is the subject of bioenergy. As the molecular mechanism of many biological and biochemical processes is clarified, scientists are trying to apply thermodynamic concepts in studies of living systems. Living organisms are open systems, their state is defined as stationary, rather than equilibrium. Under stationary understand the equilibrium state with a constant concentration of particles, which is maintained by the influx and outflow of matter from the system. In fact, any cell in equilibrium is already a dead cell. The study of open systems requires methods of thermodynamics of irreversible processes. So far, such methods have not been developed. Therefore, at present, there are different opinions on the value of equilibrium thermodynamics for solving biological problems. Nevertheless, there are certain biochemical issues in which classical thermodynamics methods are very effective. For example, thermodynamic calculations are based on the assessment of the energy value of food products, which underlies dietetics, the assessment of the energy intensity of biochemical processes, the effectiveness of many macroergic drugs (ATP, cocarboxylase, vitamin B₁₂, etc.), the modeling of biological structures and processes.

Chemical thermodynamics gives information about the possibility of a reaction, but it is important to know the speed of a process. Chemical kinetics is the doctrine of the speed of chemical reactions, their mechanism and patterns of flow over time. To determine the speed of a chemical reaction, it is necessary to know not only the initial and final state of the system, but also the path along which the reaction proceeds; therefore, it is much more difficult to obtain kinetic laws than thermodynamic ones.

The rate of a chemical reaction shows the number of chemical interactions leading to the formation of reaction products per unit time in a unit volume (for a liquid medium) or on a unit surface, if the process involves a solid substance. The ratio of changes in the concentration of reacting substances to the final (measured) period of time is called the average speed: $V_{av} = \pm \Delta C / \Delta t$, mol/(L·s).



True rate is the ratio of changes in the concentration of reacting substances to an infinitely small period of time: $V_{\text{trr}} = \pm dC / dt$, mol/(L·s) – in SI system.

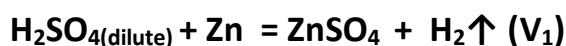
In medicine, other units of measurement of the reaction rate are also used, for example, ESR - the erythrocyte sedimentation rate. It is measured by the height of the column of red blood cells that have settled in the capillary per hour (normal ≈ 5 mm / hour). Pharmacokinetics is a special discipline which is based on the kinetic laws of the distribution of drugs in the body. It studies the distribution of drugs over time, the processes of absorption, the time of metabolism (withdrawal), the relationship between concentration and the magnitude of the therapeutic effect.

THE IMPORTANT FACTORS THAT AFFECT THE RATE OF REACTION

The factors are :

- 1) The nature of the reactants;
- 2) Concentration of reactants or pressure (for gases);
- 3) Temperature;
- 4) The presence of a catalyst in a system.

1. The nature of the reactants

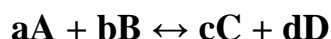


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$V_1 > V_2$ as H_2SO_4 is more strong electrolyte

2. *The effect of concentration on the rate of a chemical reaction.*

The effect of concentration on the rate of a chemical reaction is determined by the law of mass action - at a constant temperature, the speed of this reaction is directly proportional to the product of the concentrations of the reacting substances, taken in degrees equal to their stoichiometric coefficients.

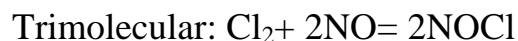
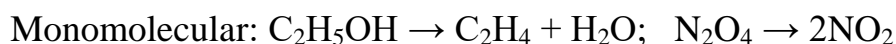


$$V_f = k_f \cdot [A]^a \cdot [B]^b$$

k - reaction rate constant shows the number of effective collisions (those that led to the reaction) per 1 mol of reacting substances. k depends on the temperature and nature of the substance, but does not depend on the concentration.

In the equation of the law of acting masses, the most difficult to determine the reaction rate constant. To determine it, you need to know the following concepts: reaction order and molecularity.

Molecularity is determined by the number of molecules whose simultaneous interaction at the time of the collision is a chemical transformation.



Most often, chemical processes consist of mono and bimolecular stages.

When conducting a chemical reaction, one of the most significant is the question of how quickly the studied transformation occurs. The answer to this question is given by the dependence of the concentration of the determined component on time, i.e. equation of the kinetic curve of the accumulation or expenditure of this component.

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The exponent is called the order for a given component or private *order*. The sum of the partial orders for all components is the general or formal order of the reaction.

For example, reaction $\text{N}_2 + \text{O}_2 = 2\text{NO}$

$$V = k C_{\text{N}_2} C_{\text{O}_2}$$

It is a second order reaction, but it is also a first order reaction with respect to the N_2 component, as well as the O_2 component.

The true order of the reaction can only be determined experimentally. It can be integer, zero or fractional.

The reaction order, which is established experimentally, makes it possible to establish its possible mechanism.

The effect of temperature on the rate of a chemical reaction.

This influence is determined by the Vant-Hoff rule: with an increase in temperature by 10°C , the rate of a homogeneous chemical reaction increases by 2–4 times.

$$V(t_2) = V(t_1) \cdot \gamma^{(\Delta t/10)}$$

$V(t_2)$ and $V(t_1)$ – reaction rates at temperature t_2 and t_1 .

γ – **temperature coefficient** = $2 \div 4$, shows how many times the reaction rate increased with increasing temperature by 10°C .

$$\Delta t = t_2 - t_1.$$

For biochemical reactions, the temperature coefficient with increasing temperature by 10°C cannot be received, but only at 5°C , and $\gamma = 1,1 \div 1,8$ times.

Vant Hoff rule works at temperatures from 0°C to 100°C .

For higher temperatures the Arrhenius rule is used. Arrhenius suggested that not every collision of molecules leads to chemical interaction. Only a small fraction of the total number of molecules that have the necessary or large energy reserve for the

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reaction to enter the reaction. **Activation energy** – E_a – is excess energy compared to the average value that a molecule must possess at the moment of collision in order to be capable of chemical interaction. The lower the activation energy leads to the higher the reaction rate.

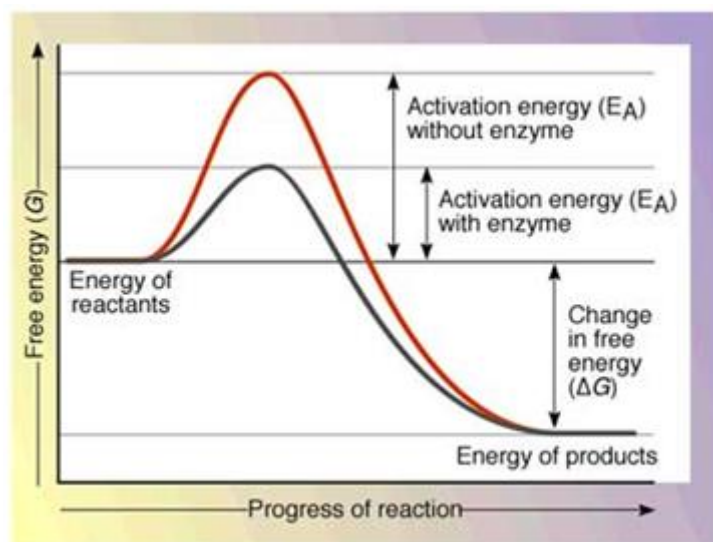


Fig.1. Activation Energy.

Activation energy is spent on weakening the bonds between atoms in the molecules of the reacting substances. In this case, the substances pass into an unstable intermediate state called the activated complex.

Arrhenius equation for calculating the activation energy:

$$k = Ae^{-\frac{E_a}{RT}} \quad \text{or} \quad \ln k = -\frac{E_a}{RT} + \ln A$$

Where:

- k = Chemical Reaction Rate
- A = Pre-exponential Factor
- E_a = Activation Energy
- R = Gas Constant
- T = Temperature in Kelvin

A high value of the activation energy of the reaction is undesirable, as this means that a high energy barrier stands in the way of its implementation. For most of the biochemical reactions, E_a is 2–3 times lower than for chemical ones, since they proceed

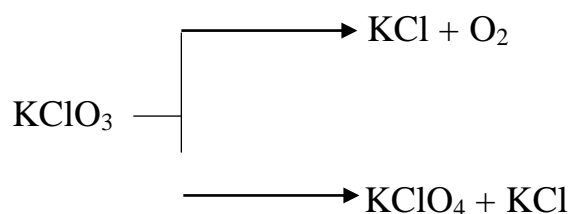
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in the presence of enzymes that lower E_a . However, the activation energy for the destruction of biological structures is very high, which helps protect cells from damage. The reaction rate can be increased by reducing the activation energy, which is carried out by introducing a catalyst into the reaction medium.

Complex reactions belong to three main types:

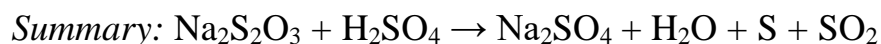
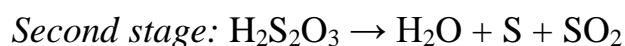
1. **Parallel reactions** - a related system of reactions in which different products can be obtained from the same starting materials.

For example,



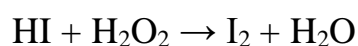
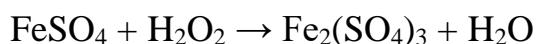
2. **Sequential reactions** - a connected system of reactions in which the products of the previous stages are the starting materials for the subsequent ones.

For example, the reaction of sulfuric acid and sodium thiosulfate is carried out sequentially:



3. **Conjugated reactions** are reactions of the type $A + B \rightarrow M$, $A + C \rightarrow D$, of which one, for example the second, proceeds only together with the first. In such reactions, substance B is an inducer of another reaction.

An example of such a reaction is the oxidation of ferrum (II) sulfate and iodohydrogen with hydrogen peroxide.



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Ferrum sulfate is oxidized by hydrogen peroxide, regardless of the presence of iodohydrogen, but iodohydrogen by hydrogen peroxide is not oxidized if there is no ferrum (II) sulfate. In this reaction, the inducer is ferrum (II) sulfate.

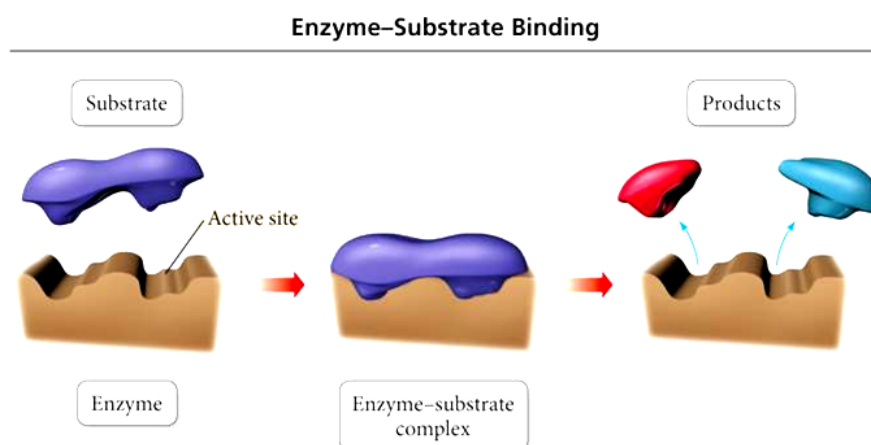
The kinetics of conjugated reactions is very complex.

ENZYMATIC CATALYSIS

The role of catalysts in the body is given to enzymes. Enzymatic catalysis has a number of features:

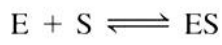
1. High catalytic activity. Enzymes are millions of times superior in their activity to chemical catalysts, so very few are needed for reactions.
2. High specificity. Each enzyme acts on a strictly defined reaction or group of reactions.
3. Enzymes are active at a strictly defined pH.
4. Enzymes are most active at a temperature of $37^{\circ}\text{C} \div 40^{\circ}\text{C}$, at a lower temperature, the enzymes become less active, and at a higher temperature, enzymes are denatured.

Enzymes: Biological Catalysts

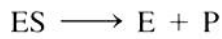


- Binding is H bonds or weak covalent bonds

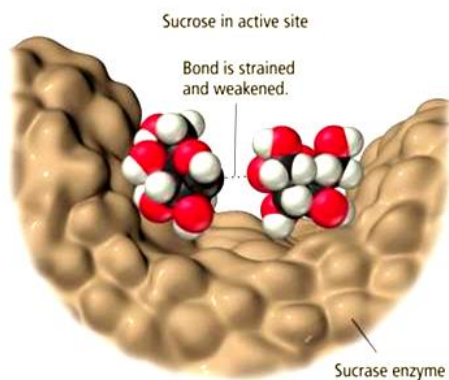
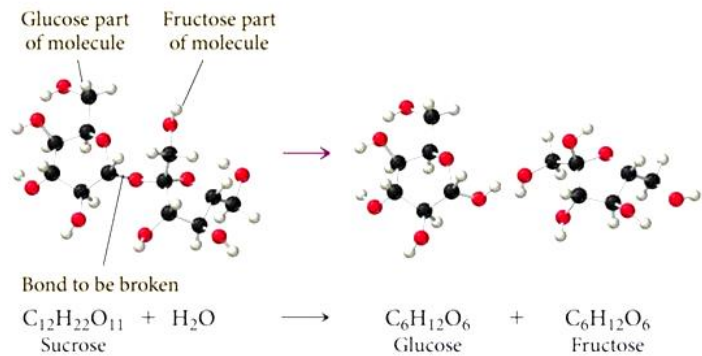
Enzymatic Hydrolysis of Sucrose



Fast



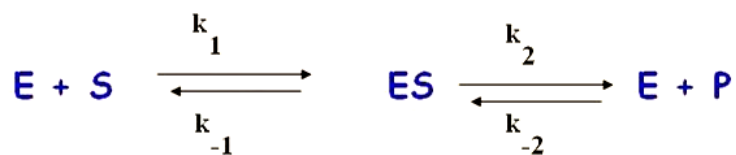
Slow, rate limiting



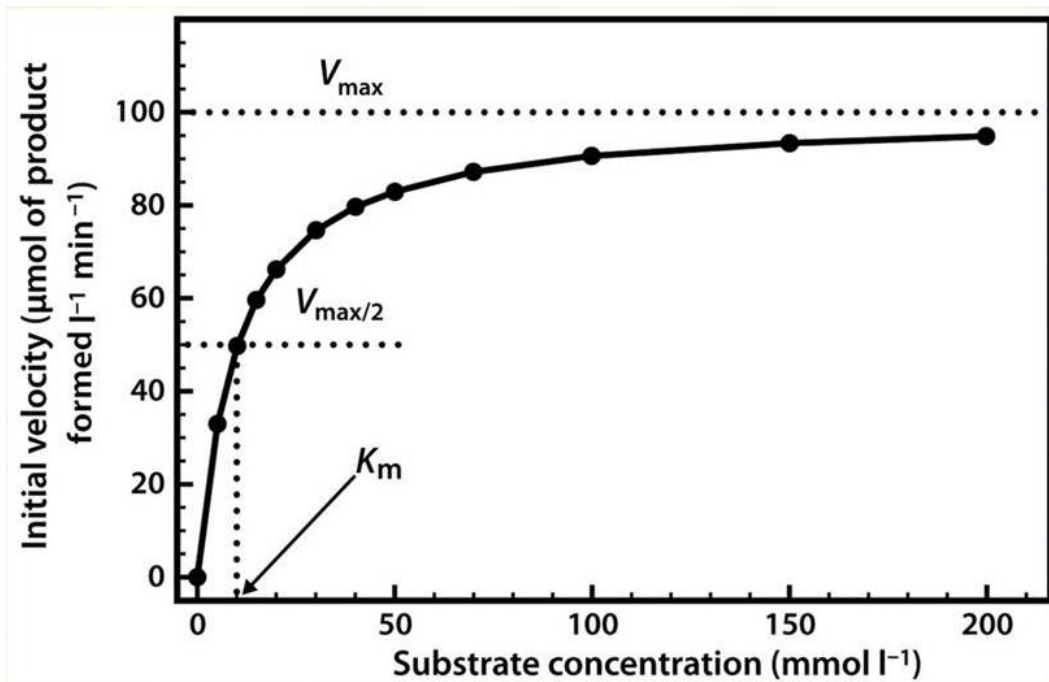
To lower the activation energy

Leonor Michaelis and Maud Menten - first researchers who explained the shape of the rate curve (1913)

During reaction enzyme molecules, E, and substrate molecules, S, combine in a reversible step to form an intermediate enzyme-substrate (ES) complex



k_1, k_{-1}, k_2, k_{-2} - rate constant - indicate the speed or efficiency of a reaction



The Michaelis-Menten Equation

The basic equation derived by Michaelis and Menten to explain enzyme-catalyzed reactions is

$$v_o = \frac{V_{\max} [S]}{K_m + [S]}$$

- K_m - Michaelis constant;
- V_o - initial velocity caused by substrate concentration, $[S]$;
- V_{\max} - maximum velocity

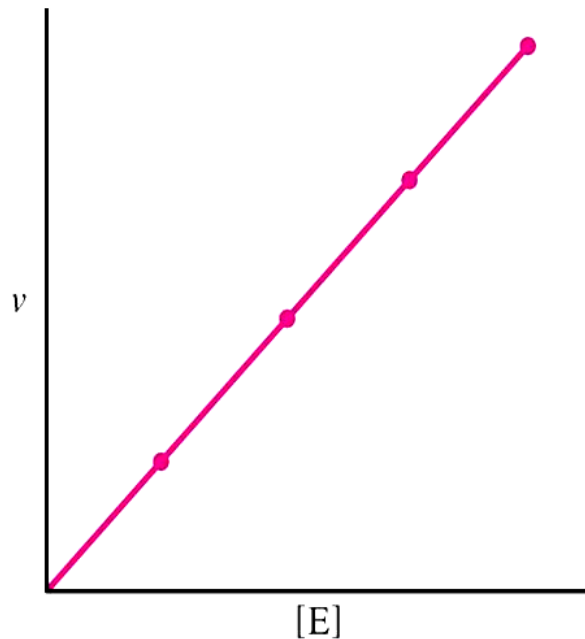
- At a fixed enzyme concentration $[E]$, the initial velocity V_o is almost linearly proportional to substrate concentration $[S]$ when $[S]$ is small but is nearly independent of $[S]$ when $[S]$ is large

- Rate rises linearly as $[S]$ increases and then levels off at high $[S]$ (saturated)

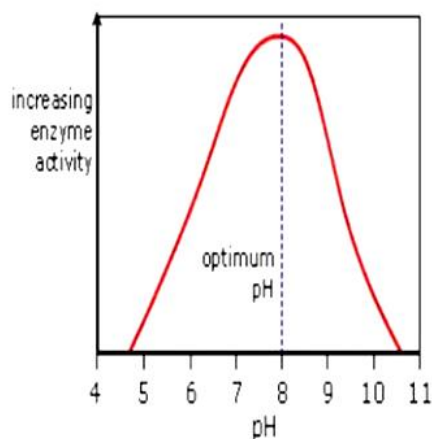
Effect of enzyme concentration [E] on velocity (v)

In fixed, saturating [S], the higher the concentration of enzyme, the greater the initial reaction rate

This relationship will hold as long as there is enough substrate present



Effect of pH on enzyme activity



- Hydrogen ion concentration also have an influence on enzyme activity.
- For most enzymes, the effective pH range is 4.0-9.0.
- Beyond these limits, denaturation of enzymes take place.
- Optimum pH for pepsin is 2.0 and for trypsin 8.0

ACID-BASIC CATALYSIS

Medical chemistry

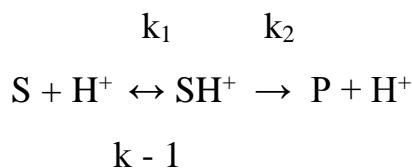
According to the proton theory of acids by Bronsted and Lowry, an acid is a substance that can give off a proton, and a base is a substance that can attach it. (Note that according to the aprotic theory of Lewis acids, an acid is an acceptor of a lone pair of electrons, and a base is a substance that is a donor of an electron pair in the formation of a compound with a donor-acceptor bond BF_3 (acid) + NH_3 (base) \rightleftharpoons $\text{F}_3\text{B}-\text{NH}_3$.)

Typical Lewis aprotic acids are (AlBr_3 , FeCl_3 , BF_3)

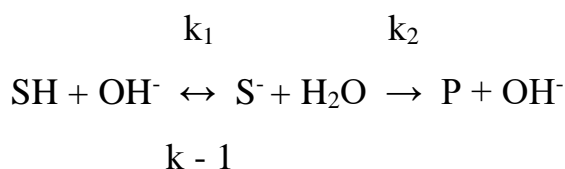
The following types of reactions are distinguished in acid-base catalysis.

1) Specific acidic and basic catalysis.

The former include reactions in which the activation of the substrate is carried out only by hydrogen ions, and to the second, only by hydroxyl ions. The simplest mechanisms of these reactions include the reversible interaction of the substrate (S) with the catalytic particle and the conversion of the resulting complex into a product:

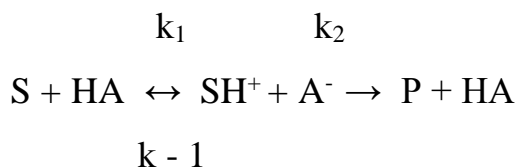


specific acidic catalysis



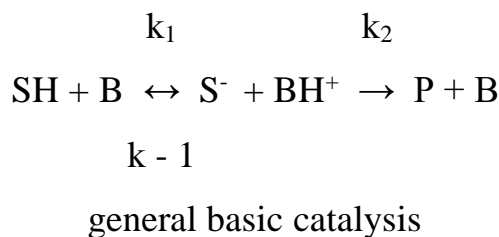
specific basic catalysis

2) General acid and basic catalysis - reactions with activation of the substrate by any proton donor, except for hydrogen ions, i.e. under the influence of generalized Bronsted acids; and reactions with activation by any proton acceptor other than OH^- , i.e. the generalized Bronsted base, respectively:



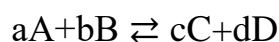
general acidic catalysis

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CHEMICAL EQUILIBRIUM

For a reversible reaction



we write the kinetic equations for the forward and reverse reactions:

$$V_{forw} = k_{forw} \cdot c(\text{A})^a \cdot c(\text{B})^b$$

$$V_{rev} = k_{rev} \cdot c(\text{C})^c \cdot c(\text{D})^d$$

For a given state of the system, $\Delta G = 0$. No visual changes are visible.

Since both direct and reverse reactions proceed in a state of chemical equilibrium, this equilibrium is called dynamic or mobile equilibrium, i.e. its establishment does not mean termination of the reaction. The concentrations of all participants in the reaction remain constant, are called equilibrium and are denoted by [A], [B], etc., the dimension of these quantities is mol / L.

Since at the moment of equilibrium the rates of direct and reverse reactions are equal, we can write:

$$V_{forw} = V_{rev}$$

$$k_{forw} \cdot [\text{A}]^a \cdot [\text{B}]^b = k_{rev} \cdot [\text{C}]^c \cdot [\text{D}]^d$$

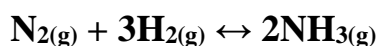
The ratio of the rate constants of direct and reverse reactions is called the equilibrium constant:

$$K_{eq} = \frac{k_{forw}}{k_{rev}} = \frac{[\text{C}]^c [\text{D}]^d}{[\text{A}]^a [\text{B}]^b}$$

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This expression is called the law of mass action for a system in a state of chemical equilibrium. The value of the equilibrium constant expressed in terms of the concentration of the participants in the reaction will be denoted by K_{eq} . K_{eq} is a thermodynamic quantity that does not depend on the path of the process. The value of the equilibrium constant indicates the direction of the process: if $K_{\text{eq}} \rightarrow \infty$, then the reaction products prevail in the reaction mixture, therefore, a direct reaction proceeds mainly (the equilibrium is shifted to the right).

For example,



$$K_{\text{eq}} = \frac{[\text{NH}_3]^2}{[\text{N}_2][\text{H}_2]^3}$$

The equilibrium constant depends on the temperature and nature of the reacting substances, but does not depend on the concentration of substances. The catalyst does not affect the value of the equilibrium constant, since it equally increases the rate of both direct and reverse reactions.

The expression for the equilibrium constant of a heterogeneous reaction includes only the concentrations of substances in solution or in the gas phase, since the concentrations of solid and liquid substances agreed to be considered constant (equal to 1).

CHEMICAL EQUILIBRIUM SHIFT

The state of chemical equilibrium is maintained as long as the thermodynamic parameters at which it is established remain unchanged. When conditions (*temperature, pressure, concentrations of substances involved in the reaction*) change, the rates of the forward and reverse reactions change, as a rule, differently and the equilibrium is disturbed. As a result, after a while the state of a new chemical equilibrium is established in the system, which is characterized by new equilibrium concentrations of all substances

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The process of transition from one equilibrium state to another is called a shift in chemical equilibrium. The direction of this displacement obeys the principle of **Le Chatelier** (1884):

If a system in a state of chemical equilibrium is exposed to external influences, then the equilibrium is shifted in such a way that this effect decreases.

Factors Affecting Chemical Equilibrium

Change of conditions		Equilibrium offset direction
Temperature	increases	Towards the endothermic reaction
	decreases	Towards exothermic reaction
Pressure	Increases	Towards reducing the volume of gaseous substances
	decreases	Towards increasing the volume of gaseous substances
The reactants concentration	increases	Towards direct reaction
	decreases	Towards the reverse reaction
The products concentration	increases	Towards the reverse reaction
	decreases	Towards direct reaction
Catalysts		Balance does not shift

General material and educational and methodological support of the lecture:

- Working program of the discipline
- Silabus
- Methodical recommendations for independent work of higher education applicants
- Multimedia presentations
- Situational tasks

Medical chemistry

Recommended literature

Basic literature:

1. Medical Chemistry: textbook / V.Y. Tsuber, A.A. Kotvytska, K.V. Tykhonovych et al. - - Kyiv, AUS Medicine Publishing, 2022. – 392 p.
2. Medical chemistry: a textbook for universities / V. O. Kalibabchuk, I. S. Chekman, V. I. Galynska and others; for ed. Prof. V. O. Kalibabchuk – 4th ed. – K. VSV "Medicine", 2019 – 336 p.
3. Medical chemistry / V.O. Kalibabchuk, V.I. Halynska, L.I. Hryshchenko et al. – Kyiv, AUS Medicine Publishing, 2020. – 224 p.
4. General and Inorganic Chemistry: textbook / V.O. Kalibabchuk, V.V. Ohurtsov, V.I. Halynska et al. – Kyiv, AUS Medicine Publishing, 2019. – 456 p.

Additional literature:

1. Medical chemistry: a textbook / V. P. Muzychenko, D. D. Lutsevich, L. P. Yavorska; for order. B. S. Zimenkovsky. – 3rd ed., Ed. – K.: BCB «Medicine», 2018. – 496 p.
2. Mironovich L. M. Medical Chemistry: A Textbook. – Kyiv: Karavella, 2008. – 159 p.
3. Moroz A. S. Medical chemistry: a textbook / D. D. Lutsevich, L. P. Yavorska. – Vinnytsia: New book, 2006. – 776 p.
4. Gotsulyak L. O., Mardashko O. O., Yerigova S. G., Kuzmenko G. I., Kuzmina A. V., Zhilinskaya K. I. Bioinorganic, physicoloid and bioorganic chemistry. Teaching. manual. Odessa. Odessa State Medical University 1999. – 248 p.
5. Textbook of Medicinal Chemistry / V. Alagarsamy // CBS Publishers & Distributors Pvt Ltd, India; 3rd edition, 2018 – 584 p.
6. Richard Post. Chemistry: Concepts and Problems / Richard Post, Chad Snyder, Clifford C. Houk // A Self-Teaching Guide, Jossey-Bass, 2020. – 432 p.

Medical chemistry

Lecture № 3

Topic: «Solutions. Acid-base equilibria in biosystems.»

Actuality of theme: Solutions are one of the most important states of matter, which is of great importance in human life and practical activities. The processes of assimilation of food by humans and animals are related to the transfer of nutrients into a solution. The solution is all the most important biological fluids (blood, lymph, etc.). The composition of the solution can be expressed in different ways, both with the help of dimensionless units and with the help of dimensional units - concentration. Knowledge of how to express the concentration of solutions and the ability to prepare solutions of a certain concentration are necessary for students to study biochemistry, hygiene, pharmacology, and doctors for the correct interpretation of laboratory analysis data, calculation of drug dosages.

Goal: To form systematic knowledge about the concepts: solutions, solubility, properties of solutions. Know different ways of expressing the concentration of solutions and the relationship between them. Familiarize yourself with the methods of determining pH; learn how to calculate the degree and constant of dissociation; pH of the solution. Explain the mechanism of action of buffer systems and their role in maintaining acid-base balance in biosystems.

Basic concepts: electrolyte solution, strong electrolytes, weak electrolytes, Ionic product of water, dissociation constant, pH, buffer systems.

Plan and organizational structure of the lecture:

1. Arrhenius Theory of Electrolytic Dissociation
2. Factors affecting the degree of dissociation
3. Weak electrolytes. Dissociation constant.
4. Ionic product of water. pH
5. Biological role of pH.
6. Buffer systems.
7. Blood buffer systems

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Content of lecture material (lecture text)

Arrhenius Theory of Electrolytic Dissociation

Most natural chemical systems and biological objects are **electrolyte solutions**.

Electrolytes	Substances that in solutions or melts decay into ions, and therefore conduct an electric current. Almost all acids, bases, salts belong to electrolytes.
Non-electrolytes	Substances that in solutions or melts do not decay into ions and do not conduct electric current. These include most organic compounds (sugar, benzene), oxides, simple substances.

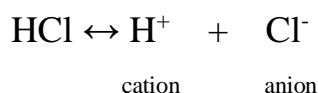
The ability of electrolyte solutions to conduct electric current was explained by the theory of electrolytic dissociation, proposed by the Swedish chemist Svante Arrhenius (1883 - 1887), which is based on the postulates:

- *Electrolytes, when dissolved in water or melted, decompose into positive and negative ions.*

Electrolytic dissociation is the decomposition of electrolyte molecules into ions by the action of polar solvent molecules (water).

Under the influence of an electric current, the ions acquire directional motion: positively charged move to the cathode and are called cations, and negatively charged to the anode and are called anions.

For example,



- *The dissociation of molecules into ions is incomplete and is characterized by the degree of dissociation α .*

The degree of dissociation is the ratio of the number of molecules disintegrated into ions (n) to the total number of molecules (N)

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$$\alpha = \frac{n}{N} \cdot 100\%$$

Factors affecting the degree of dissociation:

- the nature of the electrolyte;
- the nature of the solvent;
- degree of dilution.

Depending on the degree of dissociation, Arrhenius divided all electrolytes into 3 groups - strong, weak and medium strength:

1. **Strong electrolytes** - when dissolved in water, they dissociate almost completely. The degree of dissociation is greater than 30% ($\alpha > 30\%$). These include almost all soluble salts, strong acids, alkalis:

HCl, HNO₃, H₂SO₄, HMnO₄ – acids;

NaOH, KOH, LiOH, Ba(OH)₂ – base (alkali);

NaCl, K₂SO₄, KNO₃, KMnO₄ – salts.

2. **Weak electrolytes** - when dissolved in water, they partially dissociate. The degree of dissociation is less than 3% ($\alpha < 3\%$). These include covalent compounds that undergo partial dissociation in water. These are weak acids (H₂S, H₂CO₃, HCN) and weak bases (NH₄OH), sparingly soluble salts, H₂O; almost all organic acids (CH₃COOH), phenols, amines.

3. **Electrolytes of medium strength** - degree of dissociation $3\% < \alpha < 30\%$. These include H₂CrO₄, H₂SO₃, H₃PO₄, HI.

- *The forces of interaction between ions are absent and electrolyte solutions behave like ideal gas systems. This position was not expressed directly, but it underlies all the quantitative relations obtained by the authors of the theory of electrolytic dissociation.*

The theory of electrolytic dissociation made it possible to explain many features of the chemical properties of electrolytes, however, the Arrhenius theory had a number

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of drawbacks, in particular, it did not take into account the interaction between ions in solution caused by their electric charges.

Weak electrolytes. Dissociation constant

Strong electrolytes exist in solutions only in the form of ions, and in solutions of weak electrolytes there are ions and molecules between which dynamic equilibrium is established at a given temperature:



Because weak electrolytes obey the law of acting masses; this equilibrium can be quantitatively characterized by an equilibrium constant, which in this case is called the dissociation constant.

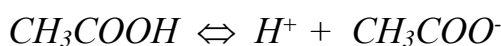
Dissociation constant is the ratio of the product of the concentration of electrolyte ions to the concentration of undissociated molecules:

$$K_{diss} = \frac{[Ct^+][An^-]}{[CtAn]}$$

where: $[Ct^+]$ - the concentration of cations;

$[An^-]$ - the concentration of anions.

For example, for acetic acid:



$$K_{diss} = \frac{[H^+][CH_3COO^-]}{[CH_3COOH]}$$

If the degree of dissociation is known, the dissociation constant (K_d) is calculated from the Ostwald dilution law:

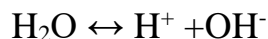
$$K_d = \frac{\alpha^2 c}{1 - \alpha},$$

where c is the electrolyte concentration, mol/L.

4. Ionic product of water. pH

Water, being a very weak electrolyte, dissociates into ions to a very small extent:

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We apply the law of the acting masses to this reversible process.

$$K = \frac{[\text{H}^+] \cdot [\text{OH}^-]}{[\text{H}_2\text{O}]},$$

where K is the dissociation constant of water, which can be calculated, for example, using the values of electrical conductivity.

At 22°C $K = 1,8 \cdot 10^{-16}$.

Since water dissociates extremely little, in the equation the concentration of water $[\text{H}_2\text{O}]$ can be considered as a constant value. Numerically $[\text{H}_2\text{O}] = \frac{1000}{18} = 55,56$ mol/L. The equation can be rewritten as following:

$$K \cdot [\text{H}_2\text{O}] = [\text{H}^+][\text{OH}^-] = K_w.$$

K_w – a constant value - is called the ionic product of water. Substituting the values of K and $[\text{H}_2\text{O}]$ in the equation, we obtain the numerical value of the ionic product of water at 22 °C:

$$K_w = [\text{H}^+][\text{OH}^-] = 1,8 \cdot 10^{-16} \cdot 55,56 = 10^{-14}.$$

$$\text{Then, } K_w = [\text{H}^+][\text{OH}^-] = 10^{-14},$$

Where K_w is constant value at constant temperature.

The medium of aqueous solutions is determined by the ratio of the concentrations of two ions H^+ and OH^- , which are always present in water and in an aqueous solution of any substance.

1) *neutral medium*

For pure water, the concentration of hydrogen ions is equal to the concentration of hydroxide ions, since one mole of H^+ ions and one mole of OH^- ions are formed from one mole of water. Consequently, the concentration of these ions at 22°C $[\text{H}^+] = [\text{OH}^-] = 10^{-7}$ mol/L.

2) *acidic medium*

if acid is added to pure water, then $[\text{H}^+] > [\text{OH}^-]$ and $[\text{H}^+] > 10^{-7}$ mol/L.

3) *alkaline medium*

if alkali is added to pure water, then $[\text{H}^+] < [\text{OH}^-]$ and $[\text{H}^+] < 10^{-7}$ mol/L.

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To avoid the inconvenience associated with the use of numbers with negative exponents, the concentration of hydrogen ions is usually expressed in terms of the hydrogen index and denoted by the pH symbol.

pH is the decimal logarithm of the concentration of hydrogen ions, taken with the opposite sign:

$$\text{pH} = -\lg[\text{H}^+] \text{ или } [\text{H}^+] = 10^{-\text{pH}},$$

where $[\text{H}^+]$ – hydrogen ion concentration, mol/L.

The concept of "hydrogen indicator" was introduced by the Danish chemist Zørensen in 1920: the letter "p" is the initial letter of the Danish word *potenz* is a mathematical degree, the letter H is the symbol of hydrogen.

Using pH, the reaction of solutions is characterized as follows:

neutral $\text{pH} = 7$,

acidic $\text{pH} < 7$,

alkaline $\text{pH} > 7$.

Qualitatively, the nature of the medium is determined using indicators - weak organic acids and bases, which change their color depending on the medium of the solution, i.e. pH of the solution. For example, colour of litmus in an acidic medium - red, in an alkaline - blue, it is not used to determine neutral; phenolphthalein: in an acidic medium is colorless, in an alkaline - raspberry.

In addition, the hydrogen indicator can be simply and conveniently determined using indicator paper - strips of special paper containing a number of indicator paints. If you wet a strip of such paper with the test solution, then it acquires a characteristic color, which is compared with pH color standards (scale).

The true pH value is determined using pH meter instruments using by the potentiometric method.

BIOLOGICAL ROLE OF pH

The pH value is of great importance in chemical and biological processes, because depending on the nature of the medium, these processes can proceed at

Medical chemistry

different speeds and in different directions.

Therefore, the determination of the pH of solutions is very important in medicine, science, technology, agriculture.

All body fluids in a living organism have constant pH values. Changing the pH of blood or gastric juice is a diagnostic test in medicine. Deviation of pH from normal values even by 0.01 units indicates pathological processes in the body.

For example, some pH values:

Gastric juice	1,0 — 2,0
Coca-Cola	2,1 — 2,4
Lemon juice	2,5±0,5
Vinegar	2,9
Apple juice	3,5±1,0
Coffee	5,0
Shampoo	5,5
Tea	5,5
Healthy skin	~ 6,5
Saliva	6,35 — 6,85
Milk	6,6 — 6,9
Blood	7,36 — 7,44
Sea water	8,0
Baking soda solution	8,5
Hand soap	9,0 — 10,0
Ammonia	11,5

BRØNSTED-LOWRY ACID BASE THEORY

Arrhenius theory is valid only for aqueous solutions.

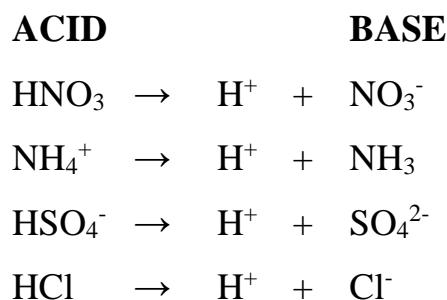
Bronsted and Lowry in 1923 proposed the proton theory of acids and bases.

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According to this theory, acids are substances that can be proton donors, and bases are substances that can attach protons (proton acceptors):



Here are a few examples showing the Bronsted-Lowry definition:



The same compound may exhibit acid or base properties, under conditions are changed. For example,

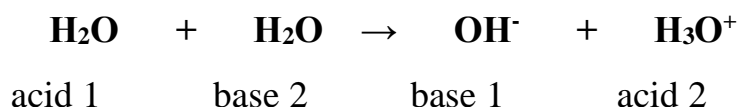


acid

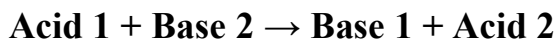


base

In the total equation:



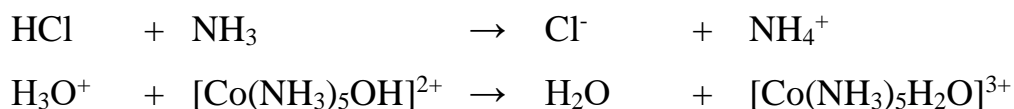
Because there are no free protons in solutions, then the interaction of acids with bases can be represented by the general scheme:



Such pairs of acids and bases are called conjugated. So, in the equations below, pairs acid 1 and base 1, acid 2 and base 2 are conjugated.



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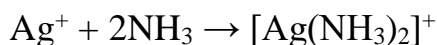


Therefore, the acid and base can be any molecules or ions capable of cleaving or attaching a proton, and reactions of this type are called protolytic.

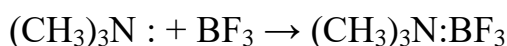
LEWIS ELECTRONIC THEORY

However, there are substances that have strongly pronounced acidic and basic properties, but they cannot be attributed to Bronsted acids and bases due to the absence of a proton. A more general idea of acids and bases was given by D. Lewis (1923).

An acid is a particle capable of attaching an electron pair (electron acceptor); A base is a particle capable of donating an electron pair (electron donor). According to Lewis, the acid and base interact with each other with the formation of a donor-acceptor bond.



The reaction between neutral molecules:



The neutralization reaction in the Lewis theory is considered as the addition of an electron pair of a hydroxide ion to a hydrogen ion, which provides a free orbital for placing this pair:



Lewis bases include halide ions, ammonia, amines, oxygen-containing organic compounds. Lewis acids include halides of boron, aluminum, silicon, and tin.

BUFFER SYSTEMS

Buffer systems are a combination of several substances in a solution, giving it buffering properties, i.e. ability to withstand changes in the active reaction of the

Medical chemistry

medium (pH) upon dilution, concentration of the solution or when small amounts of strong acid or alkali are added to it.

Buffer systems are widespread in nature: they are found in the waters of the oceans, soil waters, and especially in living organisms, where they act as regulators that support the active reaction of the environment under certain conditions necessary for the normal course of life processes. Buffer systems provide the state of acid-base equilibrium corresponding to the norm - protolytic homeostasis. The shift of protolytic equilibrium to the acidic region causes acidosis, to alkaline - alkalosis. The constancy of the pH of biological fluids, tissues and organs is due to the presence of several buffer systems that make up these bioobjects. Buffer systems exhibit their buffer properties in a certain range of pH values (≈ 2 units) - called the buffer action zone.

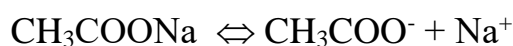
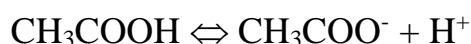
Buffer solutions are solutions that maintain a constant pH when diluted with water or when acids and alkalis are added to them.

Typically, buffer solutions are solutions containing:

- 1) a weak acid and its salt formed by a strong base;
- 2) a weak base and its salt formed by a strong acid.

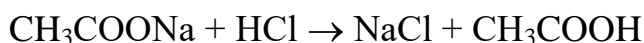
We consider the mechanism of the buffer action using the acetate buffer solution $\text{CH}_3\text{COOH} + \text{CH}_3\text{COONa}$ as an example.

The following processes take place in this solution and equilibrium is established:



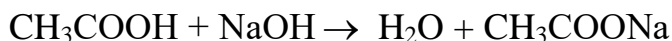
a) When a strong acid (for example, HCl) is added, the CH_3COONa salt will counteract the change in acidity.

An exchange reaction occurs, as a result, strong acid (HCl) is replaced by weak acid (CH_3COOH) and the pH remains almost unchanged:



b) When a small amount of alkali (NaOH) is added, the pH also does not change significantly, because alkali reacts with acetic acid (neutralization reaction), as a result of which OH^- - ions combine with H^+ ions to form an H_2O molecule:

Medical chemistry



These processes lead to a shift in the dissociation equilibrium towards the formation of new ions and thereby restore the pH value.

Each of the buffer mixtures is characterized by a certain concentration of hydrogen ions, which the buffer system seeks to preserve when acid or alkali is added to it.

Let us consider how the pH of buffer systems is determined by the example of acetate buffer. It consists of acetic acid (weak electrolyte) and its salt - sodium acetate (strong electrolyte). The acid dissociates partially, and the salt completely.



In such a system, the pH is determined by acid dissociation. We apply the law of acting masses to equation (1) and write the expression for the dissociation constant:

$$K_d = [\text{CH}_3\text{COO}^-][\text{H}^+] / [\text{CH}_3\text{COOH}] \quad (3)$$

Where

$$[\text{H}^+] = K_d \cdot [\text{CH}_3\text{COOH}] / [\text{CH}_3\text{COO}^-] \quad (4)$$

That is, the concentration of H^+ ions depends on the dissociation constant of a weak acid and the ratio of the concentrations of acid molecules and its anions.

However, in the buffer solution, the concentration of anions is determined mainly by the concentration of the salt, which completely dissociates. In this case, a salt with the ion of the same name completely suppresses acid dissociation. Therefore, we can assume that the concentration of anions is equal to the concentration of salt, and the concentration of acetic acid molecules is equal to the initial acid concentration.

$$[\text{CH}_3\text{COO}^-] = [\text{Na}^+] = [\text{salt}] \quad (5)$$

$$[\text{CH}_3\text{COOH}] = [\text{acid}] \quad (6)$$

Substituting (5) and (6) into (4), we can write

$$[\text{H}^+] = K_d \frac{[\text{acid}]}{[\text{salt}]}$$

Or in logarithmic form

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$$-\lg[\text{H}^+] = -\lg K_d - \lg \frac{[\text{acid}]}{[\text{salt}]}$$

By using the notation, we obtain

$$\text{pH} = \text{pK}_A - \lg \frac{[\text{acid}]}{[\text{salt}]} \quad (7)$$

or
$$\text{pH} = \text{pK}_A + \lg \frac{[\text{salt}]}{[\text{acid}]} \quad (8)$$

Equations (7) and (8) are called **the Henderson-Hasselbach equations**.

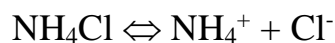
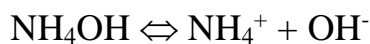
According to the Bronsted theory, the anion of an acid is its conjugate base, therefore, in general terms, the Henderson-Hasselbach equation takes the form:

$$\text{pH} = \text{pK}_A + \lg \frac{[\text{conjugated base}]}{[\text{acid}]} \quad (9)$$

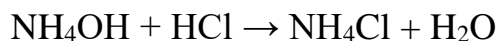
It follows from (7) and (8) that the pH of the buffer solution is determined by the ratio of the concentrations of the components and the dissociation constant of the weak acid that is part of this buffer.

Consider the mechanism of action of the main buffer on the example of ammonia buffer solution.

The following processes take place in this solution and equilibrium is established:

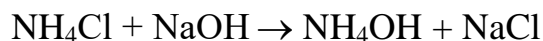


a) When a strong acid is added (e.g. HCl):



The neutralization reaction takes place and the pH practically does not change.

b) When a small amount of alkali (NaOH) is added, the pH also does not change significantly:



Buffer capacity (B) is the amount of equivalent substance (N) of a strong acid or strong base that needs to be added to 1 liter of buffer solution so that its pH changes by one:

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$$B = \frac{N}{pH_2 - pH_1},$$

where N is the amount of an equivalent substance of a strong acid (or strong base);

pH₁ is pH before adding a strong acid or base;

pH₂ is pH after adding strong acid or alkali.

The buffer capacity is determined by two factors:

1. The concentration of the acid-base pair - the higher the concentration of the acid-base pair, the higher the buffer capacity.

2. The ratio of the concentrations of the components.

The buffer capacity is higher, the higher the concentration of the components (acid and its salt or alkali and its salt). The solution with the same concentration of components has the highest buffer capacity.

BLOOD BUFFER SYSTEMS

BLOOD PLASMA

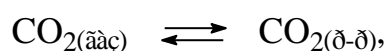
The normal blood pH is 7.40 ± 0.05 , i.e. $[H^+] \approx 3.7 \cdot 10^{-8} - 4 \cdot 10^{-8}$ mol/L. The constancy of these values is ensured by the simultaneous action of hydrocarbonate ($H_2CO_3/NaHCO_3$), phosphate (NaH_2PO_4/Na_2HPO_4), protein ($PrCOOH/PrCOONa$) and amino acid buffer systems.

1. Hydrocarbonate.

The peculiarity of this system is that one of the components of the system – H_2CO_3 is formed during the interaction of CO_2 with H_2O .



In turn, the concentration of CO_2 is determined by the equilibrium



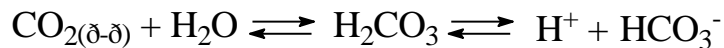
which is described by Henry's law

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$$C_{\text{CO}_2(\text{d-d})} = s \cdot P(\text{CO}_2)$$

$$s = \frac{C_{\text{CO}_2(\text{d-d})}}{P(\text{CO}_2)}$$

equilibrium is established in the blood:

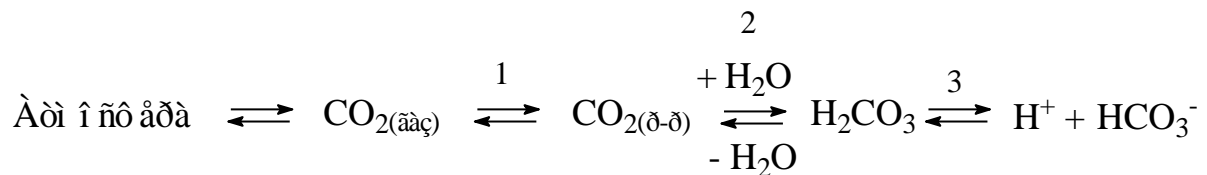


In accordance with equation 1, the pH of the hydrocarbonate buffer is ultimately determined by the concentration of HCO_3^- and the partial pressure of CO_2 :

$$\text{pH} = \text{pK}_{\text{a1}} + \lg \frac{C(\text{HCO}_3^-)}{s \cdot P(\text{CO}_2)}$$

$$\text{pK}_{\text{a1}} = 6.1 \implies \frac{C(\text{HCO}_3^-)}{C(\text{H}_2\text{CO}_3)} = 10^{1.3} = 20$$

Between CO_2 in the alveoli and bicarbonate buffer in blood plasma, equilibrium is established:



When proton donors enter the bloodstream, equilibrium 3 shifts toward H_2CO_3 . At the same time, the concentration of H_2CO_3 increases, and the concentration of HCO_3^- decreases. This leads to a shift of equilibrium 2 to the left, as a result of which equilibrium 1 shifts towards the formation of gaseous CO_2 , which leads to an increase in CO_2 pressure in the lungs and its removal due to increased pulmonary ventilation.

Upon receipt of proton acceptors, the equilibrium shifts in the opposite direction, which leads to the dissolution in the blood plasma of an additional amount of CO_2 contained in the lungs.

As a result of the described processes, the hydrocarbonate buffer system effectively ensures a constant pH of blood plasma. This system is also found in red blood cells and kidney tissue.

2. Phosphate buffer system

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$$\text{pH} = \text{pK}_a(\text{H}_2\text{PO}_4^-) + \lg \frac{\text{C}(\text{HPO}_4^{2-})}{\text{C}(\text{H}_2\text{PO}_4^-)}$$

$$\frac{\text{C}(\text{HPO}_4^{2-})}{\text{C}(\text{H}_2\text{PO}_4^-)} \approx 4 : 1$$

The phosphate buffer system is less powerful than bicarbonate, due to the low content of phosphates in the blood plasma.

The phosphate system is also found in tissues, kidneys, and red blood cells.

3. Protein buffer system.

It is a combination of albumin and globulin.

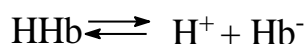
4. Aminoacid buffer systems.

Almost all amino acids have pH values significantly different from 7.4 and their power is small.

Thus, the power of the blood plasma buffer systems decreases in the series $\text{H}_2\text{CO}_3/\text{HCO}_3^- > \text{proteins} > \text{H}_2\text{PO}_4^-/\text{HPO}_4^{2-} > \text{aminoacids}$.

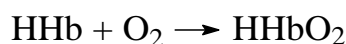
RED BLOOD CELLS

Normal erythrocyte pH is 7.25 ± 0.05 . There are hydrocarbonate and phosphate buffer systems. Their power is small compared with the power in blood plasma. The hemoglobin - oxyhemoglobin system plays an important role, which accounts for about 80% of the whole buffer capacity of whole blood. Hemoglobin is a weak acid ($\text{pK}_a = 8.2$), dissociates according to the scheme:



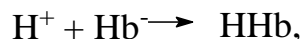
The undissociated part is bigger, i.e. $\frac{\text{C}(\text{Hb}^-)}{\text{C}(\text{HHb})} \approx \frac{1}{9}$.

In the lungs HHb reacts with O_2 ,



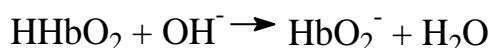
Medical chemistry

forming oxyhemoglobin, which is carried by the blood to the capillary vessels, from where O_2 enters the tissue. $HHbO_2$ is a weak acid $-pK_a (HHbO_2) = 6.95$. Therefore, under the action of proton donors, they will be neutralized first of all by the Hb^- anion

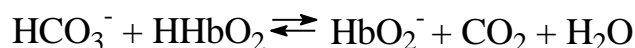


because has a greater affinity to H^+ .

But under the action of bases - proton acceptors - oxyhemoglobin will primarily react:



The $HHbO_2 / HbO_2^-$ system also protonates the HCO_3^- ions, followed by the release of CO_2 through the lungs:



It should also be noted the participation of phosphoric acid esters in maintaining a constant pH. Phospholipids are weak acids. pK_a dissociations of polar phosphate groups are in the range of 6.8–7.2. Therefore, at a physiological value of $pH = 7.25$, the phospholipids of the erythrocyte membranes are in both ionized and non-ionized forms. The ratio of ionized to non-ionized forms is approximately 3:1.

Conclusion - the erythrocyte membrane itself has a buffering effect, maintaining a constant pH of the internal environment of red blood cells.

Summary - the combined effect of several buffer systems provides acid-base homeostasis in the body.

General material and educational and methodological support of the lecture:

- Working program of the discipline
- Silabus
- Methodical recommendations for independent work of higher education applicants
- Multimedia presentations
- Situational tasks

Medical chemistry

Recommended literature

Basic literature:

2. Medical Chemistry: textbook / V.Y. Tsuber, A.A. Kotvytska, K.V. Tykhonovych et al. - – Kyiv, AUS Medicine Publishing, 2022. – 392 p.
2. Medical chemistry: a textbook for universities / V. O. Kalibabchuk, I. S. Chekman, V. I. Galynska and others; for ed. Prof. V. O. Kalibabchuk – 4th ed. – K. VSV "Medicine", 2019 – 336 p.
3. Medical chemistry / V.O. Kalibabchuk, V.I. Halynska, L.I. Hryshchenko et al. – Kyiv, AUS Medicine Publishing, 2020. – 224 p.
4. General and Inorganic Chemistry: textbook / V.O. Kalibabchuk, V.V. Ohurtsov, V.I. Halynska et al. – Kyiv, AUS Medicine Publishing, 2019. – 456 p.

Additional literature:

7. Medical chemistry: a textbook / V. P. Muzychenko, D. D. Lutsevich, L. P. Yavorska; for order. B. S. Zimenkovsky. – 3rd ed., Ed. – K.: BCB «Medicine», 2018. – 496 p.
8. Mironovich L. M. Medical Chemistry: A Textbook. – Kyiv: Karavella, 2008. – 159 p.
9. Moroz A. S. Medical chemistry: a textbook / D. D. Lutsevich, L. P. Yavorska. – Vinnytsia: New book, 2006. – 776 p.
10. Gotsulyak L. O., Mardashko O. O., Yerigova S. G., Kuzmenko G. I., Kuzmina A. V., Zhilinskaya K. I. Bioinorganic, physicoloid and bioorganic chemistry. Teaching. manual. Odessa. Odessa State Medical University 1999. – 248 p.
11. Textbook of Medicinal Chemistry / V. Alagarsamy // CBS Publishers & Distributors Pvt Ltd, India; 3rd edition, 2018 – 584 p.
12. Richard Post. Chemistry: Concepts and Problems / Richard Post, Chad Snyder, Clifford C. Houk // A Self-Teaching Guide, Jossey-Bass, 2020. – 432 p.

Topic: Physicochemistry of surface phenomena. Fundamentals of adsorption therapy. Chromatography.

Relevance of the topic: Surface phenomena are processes that occur at the interface of two phases and depend on the characteristics and structure of their surface.

Biological objects are heterogeneous systems consisting of several phases and separated from each other by interfaces. Any living organism contains a huge number of heterogeneous systems, and the most important biochemical processes take place at the interfaces. All surface phenomena are characterized by low activation energy. That is why biochemical reactions occur at the distribution surface at a high rate compared to the ambient temperature. Interactions of enzymes with substrates, antibodies with antigens, polarization and depolarization of biological membranes - all these phenomena can be explained by sorption processes.

Objective: To form a systematic knowledge of sorption processes. To find examples of practical application of sorption processes in professional activities and in life. To evaluate the surface properties of substances based on the structure of their molecules, to be able to explain the behavior of biologically active substances in terms of surface activity, to interpret the use of adsorbents for analytical and medical purposes.

Key concepts: sorption, adsorption, sorbents, adsorption theories, surfactants, Duclot-Traube rule, chromatography.

Plan and organizational structure of the lecture:

1. Surface phenomena. Surface energy.
2. Surface tension of liquids. Surface activity.
3. Adsorption at the P-G and P-P interface.

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4. SURFACTANTS. Orientation of surfactant molecules in the surface layer.
5. Langmuir adsorption isotherm equation. "Langmuir's palisade". Structure of biological membranes. Polymolecular adsorption.
6. Adsorption at the T-P, T-G interface, its mechanism and patterns. Freundlich's equation.
7. Adsorption therapy.

Content of lecture material (lecture text)

Surface effects include those effects and behavior of substances that are observed on the interface. The cause of surface phenomena is the special state of molecules in the layers of liquids and solids directly adjacent to the interface. These layers sharply differ in many physicochemical characteristics (specific energy, density, viscosity, etc.) from the properties of phases in the depth of the volume. The differences are associated with a certain orientation of the molecules in the surface layers and their different energy state in comparison with the molecules in the bulk.

The importance of surface phenomena for medicine is determined by the fact that most dosage forms are dispersed systems with a large specific surface: powders, ointments, suspensions, emulsions, etc.

Sorption processes are those that occur on PRF in heterogeneous systems.

The absorption of substances by solids or liquids is called sorption.

There are such sorption processes:

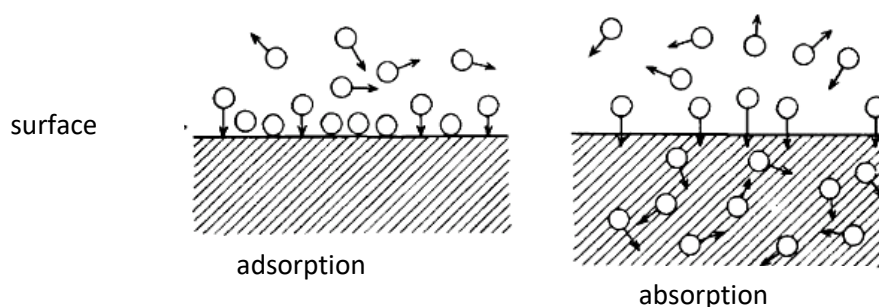
- absorption;
- adsorption;
- capillary condensation.

Absorption is the absorption of gas by the entire volume of a solid or liquid. During absorption, the distribution of gas molecules in the solid or liquid phase occurs

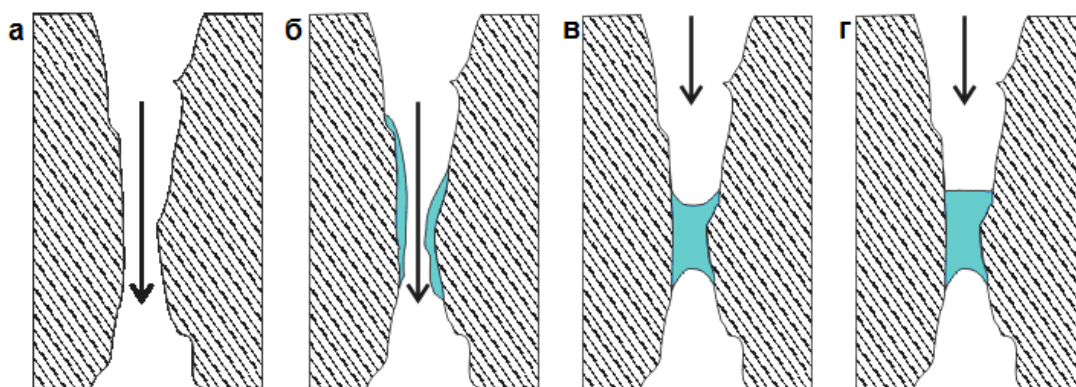
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mainly as a result of diffusion. For example, the absorption of hydrogen by palladium, carbon dioxide and ammonia by water.

Adsorption – spontaneous concentration of a substance on a solid or liquid PRF. The liquid or solid phase, which serves as an absorber, is called an adsorbent. An adsorbed substance (gas, liquid, dissolved substance) is called an adsorbent, and an already adsorbed substance is called an adsorbate.



Capillary condensation is the condensation of gaseous substances in the pores of solids (for example, in the pores of silica gel, alumina gel) under the action of sorption forces. The cause of capillary condensation is a reduced vapor pressure above the liquid located in the pores of solids.



Depending on the type of interaction between the adsorbent and the adsorbate, physical and chemical adsorption are distinguished.

SORPTION

Physical adsorption -Molecules retain their individuality;	Chemical adsorption(chemisorption) -Molecules lose their identity;
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Medical chemistry

-reversible; -decreases with temperature; -quantity of heat 8 – 25 kJ/mole	-nonreversible; -increases with temperature; -quantity of heat more than 80 kJ/mole
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Adsorption forces

Physical (orientational, induction) PHYSICAL ADSORPTION 1) reversible; 2) non-specific; 3) low heat of adsorption.	Chemical (ionic, covalent, coordination) CHEMOSORPTION 1) nonreversible; 2) specific; 3) heat of adsorption are comparable in magnitude with the heats of chemical reaction.
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Physical or van der Waals adsorption is the result of cohesive and adhesive forces. During physical adsorption, there is no chemical interaction between the adsorbent and the adsorbate; therefore, the adsorbate molecules do not lose their individuality. The equilibrium during physical adsorption is established quickly, and it is always reversible:

Adsorption ↔ desorption.

With increasing temperature, physical adsorption always decreases.

Chemical adsorption or chemisorption is due to the action of valence (chemical) forces, and is always accompanied by the formation of surface chemical compounds, but without the formation of a new bulk phase. Chemisorption in some cases proceeds rather slowly; it is usually irreversible. With increasing temperature, chemisorption tends to increase.

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The adsorption value is measured by the number of moles of adsorbate, which per unit surface or per unit mass of adsorbent. The units of adsorption are mol/m² or mol/g.

THEORY OF MONOMOLECULAR ADSORPTION OF LANGMUIR

The first theoretical equation for the adsorption isotherm was obtained by the American scientist Langmuir in 1915.

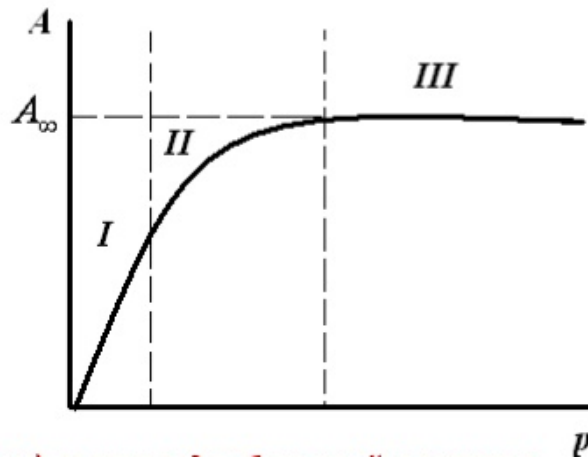
The main points of the theory are as follows:

1. Adsorption is localized and is caused by forces close in nature to chemical forces. These forces act at short distances.
2. Adsorption occurs on the active centers of a solid surface, where there are particles with uncompensated intermolecular forces. Active centers are located mainly on convex surface areas: protrusions, ribs, corners.
3. Only a monomolecular adsorbate layer can form on the surface of the adsorbent.
4. The adsorption process is in dynamic equilibrium with the desorption process.
5. The forces of interaction between the adsorbed molecules are neglected.

Langmuir isotherm equation

Based on the foregoing, Langmuir derived the equation of the adsorption isotherm for the gas – solid interface

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I – at a low pressures ($p \rightarrow 0$, $K_{eq} \ll 1$) the adsorption increases linearly with increasing concentration.

$$A = A_{\infty} * K_{eq} - \text{Henry`s equation}$$

II – at a middle pressures:

$$A = A_{\infty} \frac{kP}{1+kP}$$

III – at high pressures ($K_{eq} \gg 1$) the entire surface is occupied by adsorbate molecules:

$$A = A_{\infty}$$

The Langmuir adsorption isotherm equation can also be used to describe adsorption for the solution – solid interface:

Langmuir's isotherm of adsorption

$$G = G_{\infty} \frac{KC}{1 + KC}$$

At low concentrations $C \ll K$

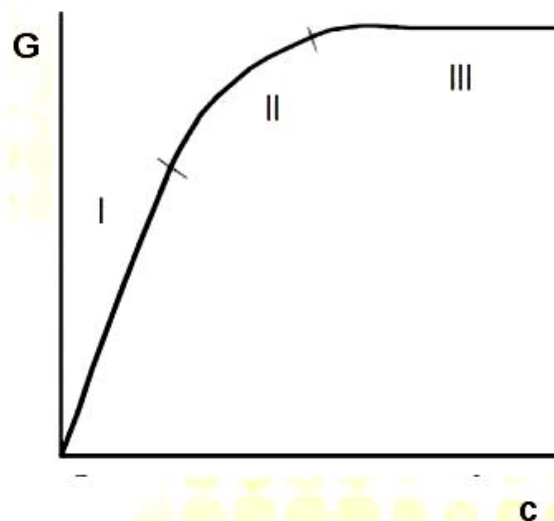
$$G = G_{\infty} \frac{K}{C}$$

At average concentrations $C = K$

$$G = 1/2 G_{\infty}$$

At high concentrations

$$G = G_{\infty}$$



INNOVATION

$$A = A_{\infty} \frac{kC}{1+kC}$$

Where C is the equilibrium concentration of the adsorbent.

FREINDLICH ISOTHERM ADSORPTION EQUATION

This empirical equation is used more often than other isotherms, because was derived based on experimental data.

$$A = \Gamma = \frac{x}{m} = k \cdot p^{1/n}$$

Where x is the amount of adsorbed substance;

m is the mass of the adsorbent;

p is the equilibrium gas pressure in the system;

k and 1/n are constants.

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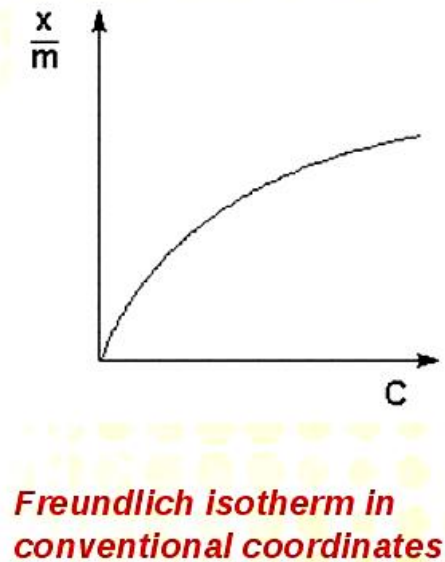
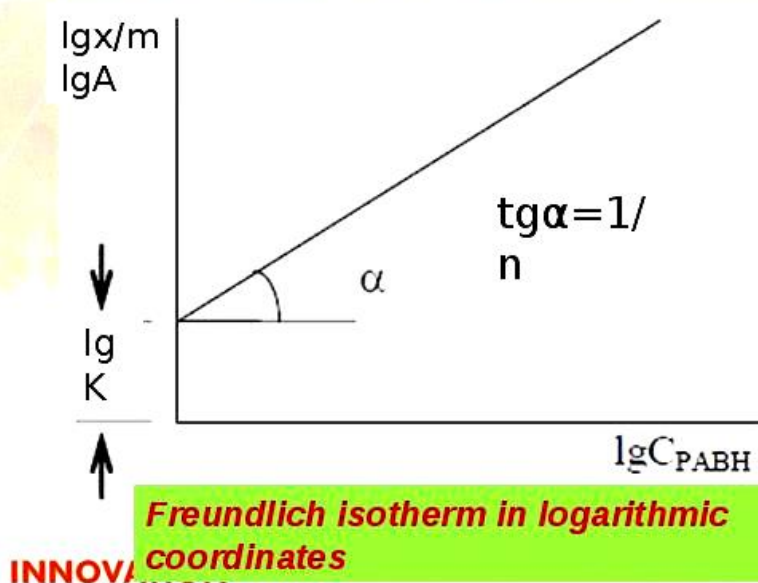
For adsorption from a solution on a solid adsorbent, the Freundlich equation has the form:

$$A = \Gamma = \frac{x}{m} = k \cdot c^{1/n}$$

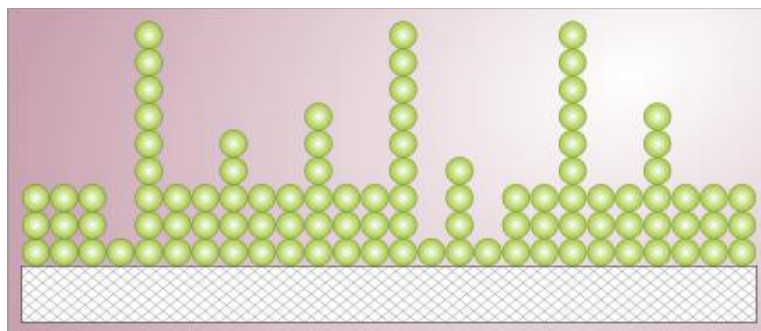
Where c is the equilibrium concentration of the solution.

Determination of the constants in the Freundlich equation

■ $\lg A = \lg k + 1/n \lg c$



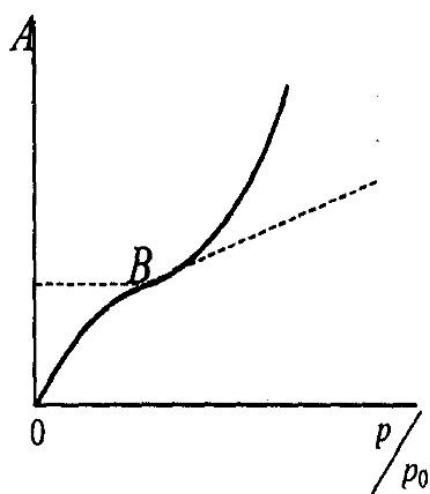
BET POLYMOLECULAR ADSORPTION THEORY



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In most cases, the monomolecular adsorption layer does not compensate for the completely excess surface energy and therefore there remains the possibility of the influence of surface forces on the second, third and subsequent adsorption layers. This possibility is realized when gases and vapors are adsorbed at temperatures below the critical temperature, i.e., polymolecular layers of matter are formed on the surface of the adsorbent, which can be represented as forced condensation of vapor under the influence of surface forces. As a result, if in the region of the formation of the monomolecular layer the adsorption substantially slows down its growth with increasing vapor pressure, then in the region of pressures close to the saturated vapor pressure, it begins to increase sharply.

Theory of polymolecular adsorption BET (Brunauer, Emmett, Teller)

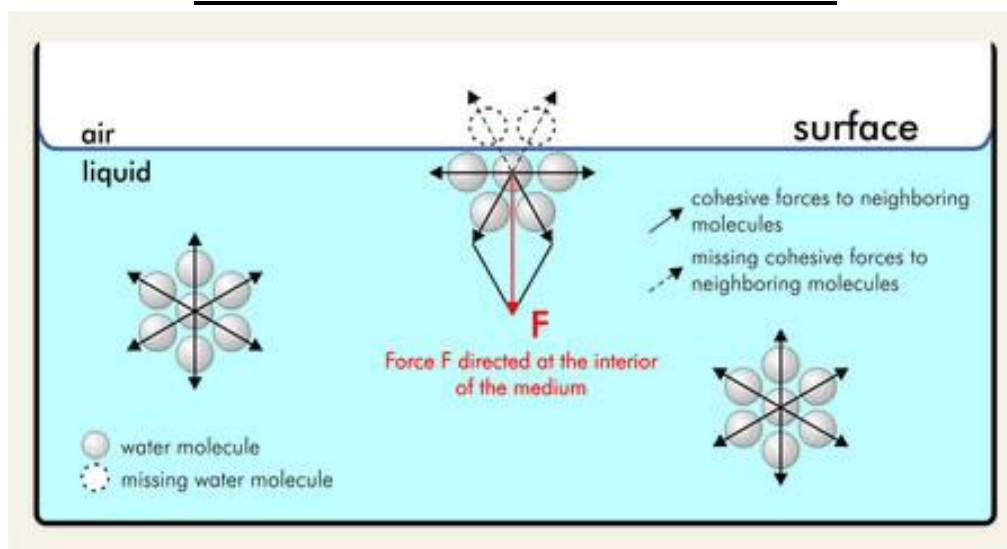


Many experimental evidence suggests that, after the monomolecular layer formation (point B) Adsorption continues to rise, due to the excess surface activity.

S-shaped polymolecular adsorption isotherm

This isotherm is described by the theory of BET polymolecular adsorption, named after the initial letters of the names of its authors (Brunauer, Emmett, Teller).

SURFACE TENSION OF SOLUTIONS



The properties of molecules in the surface layer and in the volume of the system differ significantly from each other. The molecules inside the liquid experience the same effect from all sides, as a result of the attractive forces are compensated and their resultant is zero. Looking at the surface between the liquid and the air, it can be seen that the liquid molecules in the surface layer experience unequal attraction from the liquid and from the gaseous phases.

Since the density of the gas is less than the density of the liquid, the resultant of all attractive forces will be directed inside the liquid perpendicular to its surface. Thus, surface liquid molecules are always under the action of a force tending to draw them in, i.e. the surface of the liquid always tends to contract. This explains the spherical shape of the drop (the ball has a minimal surface).

Every surface is characterized by a supply of energy called surface energy. It depends on the surface tension σ and the surface area A .

Surface tension is surface energy referred to a unit of surface: $\sigma = F/A$

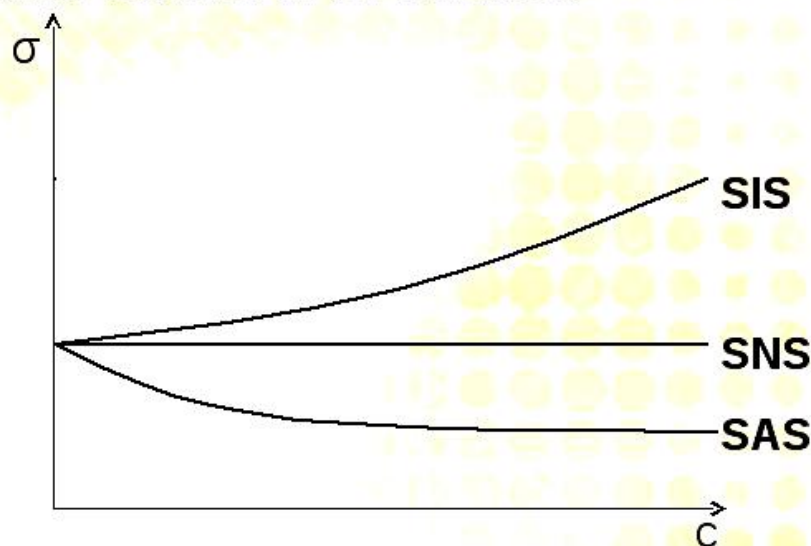
It is measured in N/m^2 .

Adsorption of the solute at the gas-gas interface is associated with a change in the free surface or surface tension.

The dependence of surface tension on the concentration of the solute can be represented by the following curves:

The isotherm of surface tension

The dependence of σ on the concentration of the dissolved substance at a constant temperature is called **isotherm of surface tension**.



INNOVATION

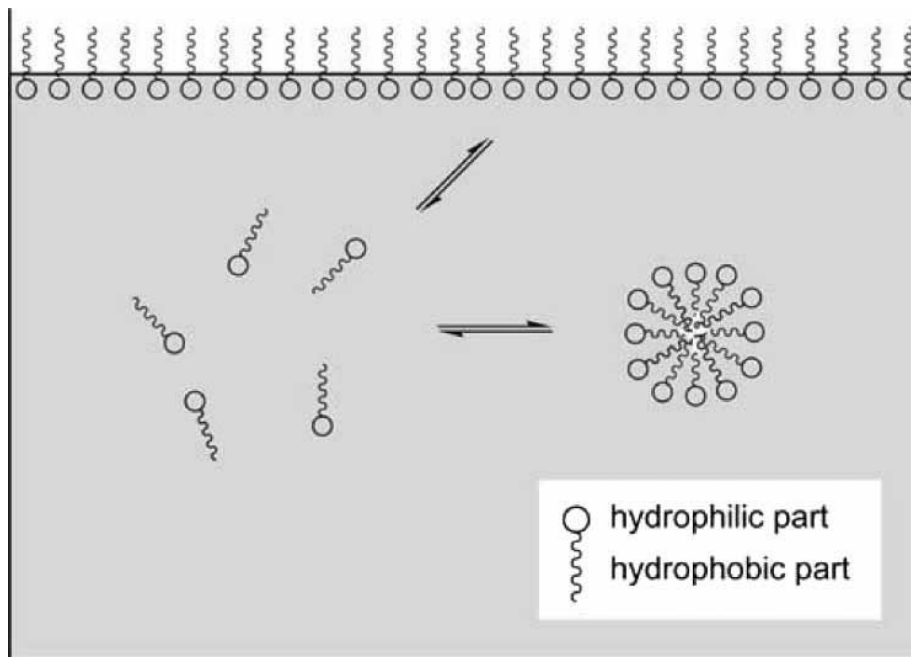
SAS are substances that lower the surface tension of a solvent when dissolved. If the force field of the molecules of the dissolved substance is weaker than the force field of the solvent, then the surface tension of the solution (σ) is less than the surface tension of the solvent. For example, soaps, alkyl sulfates, alkyl benzene sulfonates.

SIS - substances that increase the surface tension of a solvent upon dissolution. If the force field of the molecules of the dissolved substance is stronger than the force field of the solvent molecules. For example, inorganic acids, salts, bases.

SNS - substances that do not change the surface tension of the solvent upon dissolution. For example, glucose, sucrose, etc.

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A characteristic feature of the structure of surfactant molecules is their diphilic structure, which manifests itself in the presence of hydrophilic and hydrophobic parts of the molecule, i.e. polar group and non-polar hydrocarbon radical.



The polar groups include $-\text{OH}$, $-\text{COOH}$, $-\text{NH}_2$. A hydrocarbon radical is a non-polar tail.

The diphilic nature of the surfactant nature promotes their spontaneous concentration at the phase boundary, where each part of the molecule can interact with the phase to which it has the highest affinity.

Surfactants are classified according to various criteria. So, in terms of their ability to dissolve in water, surfactants are water-soluble and fat-soluble.

The ability of water-soluble surfactants to dissociate into ions distinguishes ionic (non-dissociating to ions) and non-ionic (non-dissociating to ions) surfactants.

Ionogenic can be:

1) Anionic (surface-active ions are negatively charged). For example, soaps are alkaline salts of fatty acids of the RCOOME type, alkyl sulphates are alkaline salts of sulfoesters of higher alcohols of the ROSO_3Me type;

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2) Cationic (surfactant ions are positively charged), for example, salts of amines of the type $[\text{RNH}_3]^+ \text{Cl}^-$, quaternary ammonium bases of the type $[\text{R}(\text{CH}_3)_3\text{N}]^+ \text{Cl}^-$;

3) Ampholytic (depending on the pH of the medium can be either anionic or cationic surfactants). For example, amino acids containing acidic (carboxylic) and basic (amine) groups.

GIBBS ADSORPTION ISOTHERM EQUATION

When dissolved in water, surfactants accumulate in the surface layer, and TIDs are concentrated in the volume of the solution. In 1878 American scientist Gibbs proposed an equation linking the adsorption value with the solution concentration and surface tension at the interface between the liquid and gas phases.

Gibbs Equation

$$G = -\frac{a}{RT} \cdot \frac{d\sigma}{da}$$

G - the amount of adsorbed substance [mole/m^2]
a - equilibrium activity of the substances in solution [mole/l]
R - universal gas constant = $8,31 \cdot \text{J}/\text{mole} \cdot \text{K}$

$\frac{d\sigma}{da}$ - surface activity of the dissolved substance.

$$G = -\frac{c}{RT} \cdot \frac{\Delta\sigma}{\Delta c}$$

G - the amount of adsorbed substance [mole/m^2]
c - the concentration of the substance in solution [mole/l]
R - universal gas constant = $8,31 \cdot \text{J}/\text{mole} \cdot \text{K}$

$$G = -\frac{p}{RT} \cdot \frac{d\sigma}{dp}$$

G - the amount adsorbed substance [mole/m^2]
p - the equilibrium gas pressure, Pa
R - universal gas constant = $8,31 \cdot \text{J}/\text{mole} \cdot \text{K}$

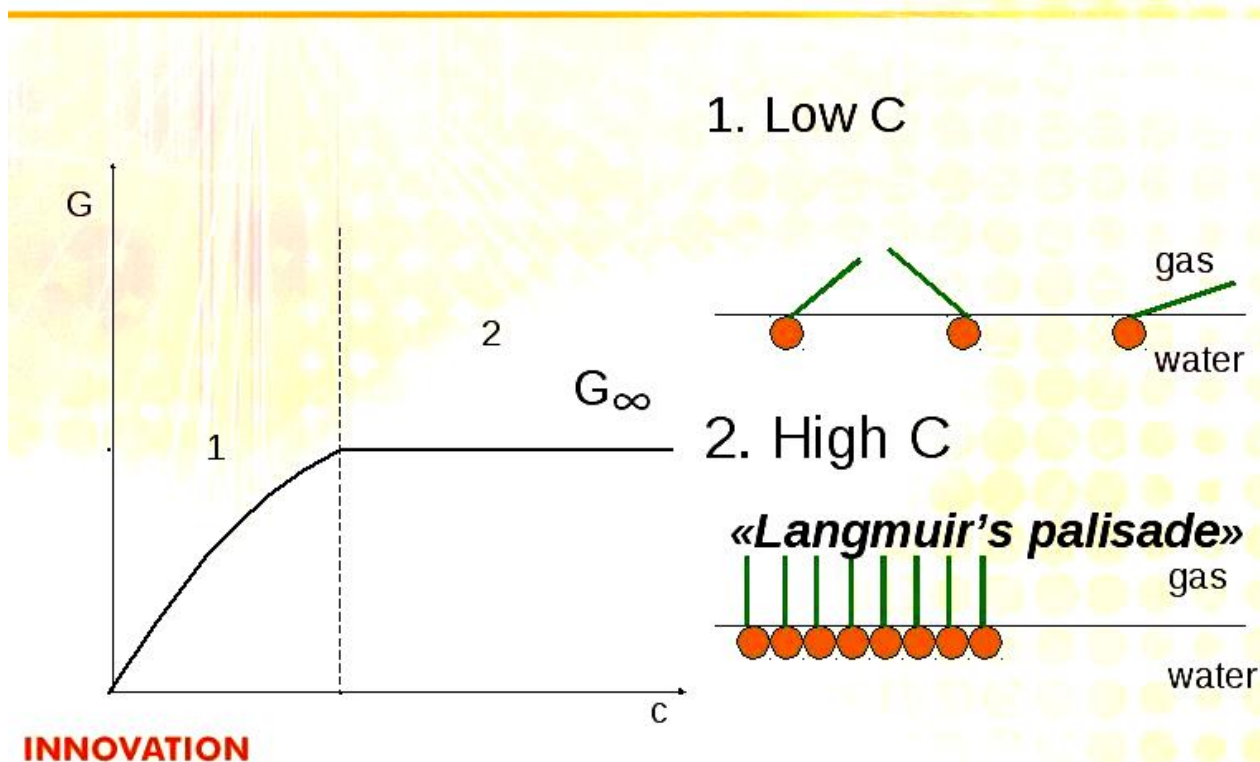
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$$\Gamma = -\frac{c}{RT} \cdot \frac{d\sigma}{dc}$$

Where C is the concentration of the solution; σ is the surface tension of the solution, R is the universal gas constant; T is the temperature.

The equation is called the adsorption isotherm.

Gibbs' isotherm of adsorption



DUKLOS-TRAUBE RULE

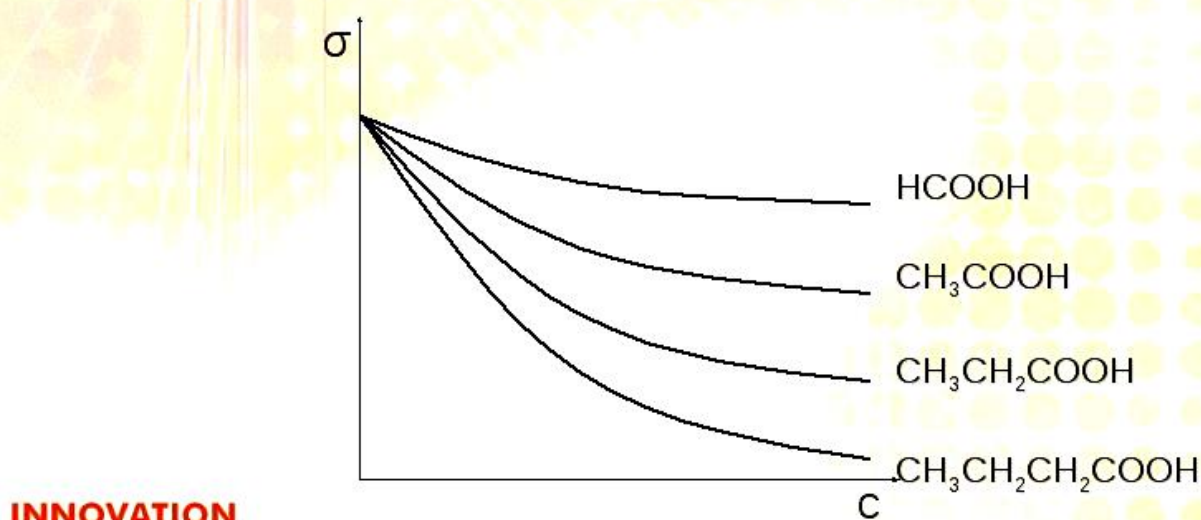
It was experimentally established that the surface activity ($\frac{d\sigma}{dc}$) of water-soluble surfactants, as a rule, increases with decreasing polarity of the substance. For molecules with a large number of polar groups, surface activity is low.

Based on a large amount of experimental material, Duclos and Traube formulated the rule:

The surface activity in the series of homologs increases by 3–3.5 times with chain elongation by one CH_2 - group (only at 200°C).

Traube-Duclos rule:

When extending the chain-CH₂ - in homological series of surface activity increases in 3-3,5 times, respectively, increases the ability to adsorption.



ADSORPTION OF STRONG ELECTROLYTES

As a result of the fact that strong electrolytes in solution are completely dissociated into charged particles, when considering the adsorption of electrolytes, it is necessary to take into account both specific adsorption and electrostatic forces.

ADSORPTION OF ELECTROLYTES

Adsorption from aqueous solution of electrolytes occurs so that mainly ions of the same type are adsorbed on a solid adsorbent. Predominant adsorption from a solution of either an anion or a cation is determined by the nature of the adsorbent and ions. The mechanism of adsorption of ions from electrolyte solution can be different: distinguish between exchange and selective adsorption of ions.

Medical chemistry



Ions, as a rule, are adsorbed on polar adsorbents. The adsorption of ions is characterized by high selectivity and is exchange in nature.

The selectivity, or specificity, of ion adsorption consists, first of all, in the accumulation on a solid adsorbent of predominantly either cations or anions.

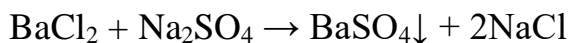
Selective Adsorption Factors:

- 1) The nature of the adsorbent (sign of its charge);*
- 2) The nature of adsorbed ions (their charge, radius, degree of hydration).*

Since electrostatic forces play a leading role in ion adsorption processes, predominantly cations are adsorbed on negatively charged adsorbents, and anions on positively charged ones.

The rule of selective adsorption by Peskov-Fajans-Paneth

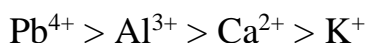
On a solid crystalline surface, ions are predominantly adsorbed, which are either part of the crystal lattice or isomorphic to it.



On the BaSO_4 precipitate, Ba^{2+} and SO_4^{2-} ions will be adsorbed, but not Na^+ or Cl^- ions.

The adsorption of ions depends on many factors:

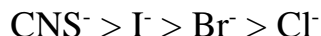
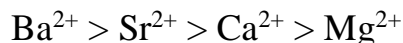
- 1) The larger the charge of an ion, the greater its adsorption capacity



- 2) For ions having the same charge, the adsorption capacity depends on their radius and degree of hydration. The larger the radius and the lower the degree of

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hydration, the better they are adsorbed on a solid surface. The hydration shell interferes with adsorption forces.



Such series are called lyotropic or Hofmeister series.

BASES OF ADSORPTION THERAPY

The development of civilization, primarily the growth of industrial production, the chemicalization of agriculture and everyday life, the intensive use of fossil fuels, has led to the appearance in the environment of many toxic substances for human health. Tens of thousands of foreign compounds fall into the internal environment of the human body. That is why in recent decades a new direction has appeared in medicine, which is developing intensively - efferent medicine (from Latin. Efference - to derive). Unlike traditional methods of treatment based on the introduction of drugs into the body, efferent medicine allows you to remove harmful and toxic substances from it - to protect the internal environment of the body with sorbents. It should be noted that the methods of efferent medicine dates the ability to cleanse the body not only of toxic substances that enter from the external environment, i.e. toxins of exogenous origin, but also from toxins of endogenous origin (toxic substances that form and accumulate in the body, for example, during burns, radiation sickness, kidney and liver failure, etc.)

Hemosorption is a direct blood purification method in which blood is released from toxins by passing it through an adsorbent column connected to a blood circulation system.

Hemosorption is an effective treatment for seriously ill patients with endogenous and exogenous intoxications of various origins. Currently, it is successfully used in the treatment of patients with exogenous poisoning, liver and kidney failure, autoimmune

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and allergic diseases, surgical patients with severe endotoxemia, patients with toxic forms of schizophrenia. According to clinicians, the use of hemosorption is most appropriate in the first stages of poisoning, when the maximum amount of poison circulates in the blood.

Plasma sorption is an effective method of detoxification of the body, the essence of which is the passage of plasma, previously separated from the formed elements of the blood, through a column with a sorbent, after which the purified plasma combines with the formed elements and returns to the vascular bed.

Plasma sorption is used in the treatment of patients with severe forms of poisoning with organophosphorus insecticides, barbiturates, antidepressants, chlorinated hydrocarbons, etc.

Lymphosorption is a type of sorption detoxification of the body, which consists in passing lymph removed from the body through the thoracic lymphatic flow on the neck, through a column with sorbent and then introducing lymph free of toxic substances into the vascular system of the patient.

Lymphosorption is the most effective way to detoxify the body when toxic substances of exogenous origin, such as pale toadstool alkaloids, carbon tetrachloride, etc. enter it. The advantages of the method include its relative non-injuries (absence of damage to blood cells, disturbances in the blood coagulation process, changes in the cardiovascular system). However, the widespread use of lymphosorption is limited by the insufficient rate of formation and outflow of lymph.

Liquorosorption is a type of detoxification of the body in which cerebrospinal fluid is passed through a layer of sorption material, and then returned to the cerebrospinal canal.

Application sorption is one of the types of sorption detoxification, which helps to heal infected wounds and burns, restore the integrity of the skin, as well as the mucous membranes by sorption absorption of toxins from the wound or burn zone.

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The use of application therapy contributes to the intensification of tissue regeneration processes, since with the help of applications, the wound is more quickly released from protein decomposition products. At the same time, the general intoxication of the body decreases.

The essence of application therapy consists in applying a gauze napkin with granular sorbent or dressings made of carbon fiber material to a wound or burn area. After application, the material is easily regenerated and therefore can be used repeatedly.

Enterosorption is a type of sorption detoxification of the body, in which the sorbent enters the oral cavity, after which, passing at different speeds through the digestive system, it adsorbs toxic substances and metabolic products.

The method is based on the idea that a decrease in the amount of toxic substances in one of the parts of the body (in this case, in the stomach and intestines) causes a decrease in their concentration throughout the body. Due to the absorption of toxins by sorbents in the intestine, their content in the blood decreases, the load on organs such as the liver, kidneys, etc. decreases.

Chromatography is a physicochemical method for analyzing and separating mixtures of substances based on their different distribution between two phases, one of which is stationary (solid or liquid), and the other mobile (gas or liquid), which is filtered through the stationary.

From the history of chromatography

Birthday of chromatography – 21.03.1903

The report of M.S. Tsvet "A new category of adsorption phenomena and their application to biochemical analysis"

His method of M.S. Tsvet called - "chromatography" (written by color)



Mikhail Semenovich Tsvet
(1872—1919)

Richard Kuhn (Institute of Basic Medicine , Heidelberg) (1938, Nobel Prize in Chemistry for the suggested color adsorption chromatography carotenoids and vitamins)

Alfred Vintershtayn (1915, Nobel Prize in Chemistry for his research of chlorophyll)

Archer Martin Porter , Richard Laurence Millington Singe (1938, first countercurrent extractor using water and chloroform to separate oligopeptides ; 1940. Using liquid-liquid chromatography for separation of amino acids ; November 19 , 1941. The article " A new form of use of the two liquid phases for chromatography " in «Biochemical journal»;1952 . Nobel Prize for the discovery of partition chromatography

Archer Porter Martin , Anthony James Trafford (50s first gas chromatograph)

Izmailov, Schreiber (1938g. first work on thin-layer chromatography)

Stahl (1956 Using thin-layer chromatography as an analytical method)

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The discovery of chromatography is a merit of the Russian botanist M.S. Tsvet (1903), which passed an alcoholic extract of chlorophyll through a column filled with calcium carbonate, received eight colored bands on an adsorbent, each of which corresponded to a particular pigment. Taking into account the color of the zones, M.S. Tsvet called the resulting picture of the distribution of pigments a chromatogram (from Greek chromos - color). Therefore, the method he founded was called chromatography. It should be noted that the author of the method also provided for the fundamental possibility of separating mixtures and colorless components.

Thanks to technological progress, chromatography has become a unique method of analysis (analytical chromatography) and separation (preparative chromatography) of mixtures of any substances and - most importantly - substances that are very similar in structure and properties.

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General material and educational and methodological support of the lecture:

- Working program of the discipline
- Silabus
- Methodical recommendations for independent work of higher education applicants
- Multimedia presentations
- Situational tasks

Questions for self-control:

1. Adsorbents and absorbents.
2. Theories of adsorption.
3. PAH, PIR, PNR.
4. Ionic adsorption. Panetta-Fayans rule.
5. Adsorption therapy.

Recommended literature

Basic literature:

1. Medical Chemistry: textbook / V.Y. Tsuber, A.A. Kotvytska, K.V. Tykhonovych et al. – Kyiv, AUS Medicine Publishing, 2022. – 392 p.
2. Medical chemistry: a textbook for universities / V. O. Kalibabchuk, I. S. Chekman, V. I. Galynska and others; for ed. Prof. V. O. Kalibabchuk – 4th ed. – K. VSV "Medicine", 2019 – 336 p.
3. Medical chemistry / V.O. Kalibabchuk, V.I. Halynska, L.I. Hryshchenko et al. – Kyiv, AUS Medicine Publishing, 2020. – 224 p.
4. General and Inorganic Chemistry: textbook / V.O. Kalibabchuk, V.V. Ohurtsov, V.I. Halynska et al. – Kyiv, AUS Medicine Publishing, 2019. – 456 p.

Additional literature:

1. Medical chemistry: a textbook / V. P. Muzychenko, D. D. Lutsevich, L. P. Yavorska; for order. B. S. Zimenkovsky. – 3rd ed., Ed. – K.: BCB «Medicine», 2018. – 496 p.

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2. Mironovich L. M. Medical Chemistry: A Textbook. – Kyiv: Karavella, 2008. – 159 p.
3. Moroz A. S. Medical chemistry: a textbook / D. D. Lutsevich, L. P. Yavorska. – Vinnytsia: New book, 2006. – 776 p.
4. Gotsulyak L. O., Mardashko O. O., Yerigova S. G., Kuzmenko G. I., Kuzmina A. V., Zhilinskaya K. I. Bioinorganic, physicoloid and bioorganic chemistry. Teaching. manual. Odessa. Odessa State Medical University 1999. – 248 p.
5. Textbook of Medicinal Chemistry / [V. Alagarsamy](#) // CBS Publishers & Distributors Pvt Ltd, India; 3rd edition, 2018 – 584 p.
6. Richard Post. Chemistry: Concepts and Problems / Richard Post, Chad Snyder, Clifford C. Houk // A Self-Teaching Guide, Jossey-Bass, 2020. – 432 p.