MINISTRY OF HEALTH OF UKRAINE ODESA NATIONAL MEDICAL UNIVERSITY Department of Medical Biology and Chemistry

METHODOLOGICAL DEVELOPMENT FOR PRACTICAL CLASSES ON EDUCATIONAL DISCIPLINE APPLIED CHEMISTRY IN MEDICINE

Department, course Specialty

Discipline

International faculty, 1st course 222 «Medicine» Medical chemistry

The program was approved: at a meeting of **the Department of Medical biology and chemistry** Odesa National Medical University Minute N_{2} dated <u>26</u> august 2024 Head of Department __________ Hennadii STEPANOV

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Practical lesson No. 1

Topic: Toxicologically important substances: inorganic, organic and carcinogenic compounds, metals, teratogens and addictive substances.

Goal: get acquainted with the goals and tasks that modern toxicology solves, historical aspects of its formation as an educational discipline, describe the main concepts used in toxicology, reveal the pathogenesis of toxic action.

<u>**Basic concepts:**</u> toxicity, toxodose, poison, threshold dose, toxic concentration, carcinogenic substances, xenobiotics.

Equipment: Laboratory of the department

Plan:

1. General concepts of toxicology, history of development.

2. Inorganic substances - ozone, silicon oxide, hydrocyanic acid, carbon monoxide, nitrides, sulfides.

3. Metals - cadmium, barium, mercury, lead.

4. The selected organic compounds are benzene, toluene, polycyclic hydrocarbons, methanol, ethylene glycol.

5. Carcinogenic substances.

The student should know:

• basic characteristics of toxicity;

• relationships between exposure to chemicals and the development of various forms of toxic effects;

• factors affecting the toxicity of a substance: properties of toxicants, conditions of their interaction, state of the environment;

• mechanisms of penetration of toxicants into the body, patterns of their distribution, metabolism and excretion.

The student should be able to:

• regularities of the impact on the human body of various toxic compounds;

• predict the likely nature of the impact on the body of the environment of newly created chemical compounds;

• to ensure the preservation of life, health and working capacity of the population in

• conditions of everyday contact with chemicals and during emergency situations.

Content of the practical session

Toxicology, on the one hand, makes it possible to detect deception or crimes, and on the other hand, deters criminals people from crime, and in this case it is moral impact on social life and health preservation (A. Nelyubin)

1. General concepts of toxicology, history of development

Toxicological chemistry is a science related, on the one hand, to toxicology, and on the other hand, to chemistry. Toxicology is a medical science, its name comes from the Greek "toxikon" - poison, "logos" - teaching. Thus, toxicology is a science that studies the patterns of development and course of the pathological process of poisoning caused by the influence of poisonous substances on the human and animal body.

It has a centuries-old history. The age of toxicological chemistry equates to the age of medicine. One of the oldest literary sources of medicine, the Eber Papyrus (1500 BC), contains information about poisonous plants, many of which were later used as medicine or weapons.

However, the formation of toxicology as a science took place only at the beginning of the 19th century. Today, the founder of modern toxicology is considered to be Professor Matthew Joseph Bonaventure Orfilou (1787-1853). In 1814, he published his work "Treatise on Poisons", where he first defined toxicology as an independent science of the toxic properties of chemical substances. He also tried to determine the regularities between the physico-chemical properties and the biological action of poisons known at that time.

We should also mention our Kyiv school of toxicology, which was represented by the works of Oleksandr Ilyich Cherkes (1894-1974) on acute poisoning by compounds of heavy heavy metals. For clinical practice, the antidote unitiol was proposed, which in many respects is superior to foreign analogues. His followers at the Sanitary and Chemical Institute (now the Institute of Pharmacology and Toxicology of the National Academy of Sciences of Ukraine) were M.I. Luhansky, as well as P.V. Rodionov, V.E. Petrunkin, I.H. Mizyukova, Yu.S. Kagan, B.S. Braver-Chornobulska, G.A. White-legged A characteristic feature of Ukrainian toxicologists is the fact that the direction and content of their research activity is related to the work carried out by their colleagues in the field of preventive medicine, in particular occupational hygiene, food hygiene and environmental hygiene.

Toxicological chemistry is a pharmaceutical discipline, but in its development it occupies a border area between medical, biological and chemical disciplines.

It is related to pharmacology, which studies the effect of drugs on the human body. Analytical chemistry reactions and methods are widely used in the detection and quantification of poisons. Together with biological chemistry, the processes of metabolism of medicinal substances and poisons are studied.

Thus, medical disciplines, primarily toxicology, pose questions to toxicological chemistry, and chemical and pharmaceutical sciences (primarily analytical chemistry) provide methods for solving these questions.

Toxicity- the main concept of modern toxicology, it can be considered as the ability of chemical substances to act on biological systems in a non-mechanical way, causing their damage or, in relation to the human body, - impairment of working capacity, disease or death.

Toxic dose (D) is the amount of a substance that entered the body and caused a toxic effect. It is measured in units of toxicant mass per unit of body mass (mg/kg).

Toxic concentration (*C*) is the amount of a substance found in a unit of volume (mass) of any environmental object (water, air, soil), during contact with which a toxic effect develops, the units of measurement are mg/l or mg/kg.

To characterize the toxicity of substances that exist in the form of vapor, gas or aerosol, a value called toxodose (W) is often used. It takes into account not only the content of the toxicant in the air, but also the time of a person's stay in the contaminated atmosphere. You can calculate the amount of the toxodose using the formula:

$\mathbf{W} = \mathbf{c} \cdot \mathbf{t} \; ,$

where W is the toxodose, c is the concentration of the substance in the air, and t is the time of the substance's action.

Toxodose measurement units are mghv/l, mghv/m3.

Military toxicology also assesses the toxic effects that develop during the action of poisonous substances on the body, primarily:

- threshold dose (concentration)- the number of ORs that cause the initial manifestations of the action of the toxicant without loss of effectiveness in a certain percentage of people. Threshold concentrations denote Lim D100 (Lim C50). Numerical indices indicate the percentage affected;
- 2) lethal dose (concentration) LD(L from Latin lethalis deadly) is the amount of a poisonous substance that causes a fatal outcome with a certain probability. The concepts of absolutely lethal doses (concentrations) that cause the death of an organism with a probability of 100% (LD100) and the lethal result of the introduction of which occurs in 50% of those affected (LD50) are usually used.
- 3) *effective dose (concentration) ED* is a dose of a substance that causes any pathological effect on the human body.

A poisonous substance– a chemical agent intended for use during hostilities. *Toxin*is a highly toxic substance of bacterial, animal, or plant origin.

Xenobiotics- foreign compounds that enter the human body with food, air, through the skin, and also when taking medicines.

The consequence of the toxic effect of substances on biological systems is a toxic process.

Formation and development of reactions of the biosystem to the effect of a toxicant, leading to a violation of viability or death, is called a toxic process. The clinical picture of intoxication depends, first of all, on which organs and tissues are involved in the pathological process. Manifestations of the toxic process initiated by toxicants of various groups will be considered below.

Summing up

Questions for self-control

1. General concepts of toxicology: toxodose, poison, threshold dose, toxic concentration, xenobiotics;

2. Mechanisms of toxicityinorganic substances: ozone, silicon oxide, HCN, CO, etc.;

3. Ways of entry of metal poisons into the body, mechanisms of toxicity of the mentioned metals: Cd, Ba, Hg, Pb;

4. Toxicity mechanisms of aromatic hydrocarbons, mono- and diatomic alcohols;

5. Chemical carcinogens: types, ways of entering the body, metabolism and prevention.

Clinical tasks

Task 1

Patient S., 35 years old, who works at a city chemical plant, was brought to the hospital. He complains of weakness, dizziness, nausea, tinnitus, shortness of breath during physical exertion. Gradually the weakness increased, there was anxiety, a feeling of fear, pain in the heart area, frequent and deep breathing. There is a smell of bitter almonds from the clothes. During the examination, the skin and visible mucous membranes are bright pink. The pupils are dilated. Extrasystole. Blood pressure 140/90 mm Hg. Art.

Task:

1. Formulate and justify the diagnosis;

2. Determine the amount of first aid.

Task 2

Patient N., 36 years old, was found unconscious in a car with the engine running by colleagues. She was taken to the hospital: her condition is serious, she is unconscious. Does not respond to painful stimuli. The skin has a bluish tint, anisocoria,

the pupils are dilated to 5 mm, they react sluggishly to light. The pulse is 96 bpm, arrhythmic, filamentous, heart sounds are weakened. Blood pressure 100/50 mm Hg. Art. The breathing rate is 26 per minute. Dry rales are heard over the entire surface of the lungs. Body temperature is 38.2°C.

Task:

- 1. Formulate and justify the diagnosis;
- 2. Determine the amount of first aid.

Task 3

A man, P., 55 years old, drank about 600 ml of vodka to get drunk. Within 20-30 minutes, intoxication developed, weakness, drowsiness, nausea, vomiting appeared. Then there was the lossconsciousness His wife took him to the hospital 2 hours after the poisoning. During the examination: the condition is serious, there is no consciousness. The skin of the face is hyperemic, moist. The smell of alcohol is pronounced from the mouth. Pulse 116 bpm, rhythmic. I tone at the top is weakened. Blood pressure 110/50 mm Hg. The rate of breathing is 30 per minute, breathing is hard. The stomach is soft. The liver and spleen are not enlarged. Involuntary urination is noted.

Task:

- 1. Formulate and justify the diagnosis;
- 2. Determine the amount of first aid.

List of recommended literature

<u>Main:</u>

1. Medicinal chemistry: a textbook for universities / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others; under the editorship of Prof. V.O. Kalibabchuk - 4th ed. - K. VSV "Medicine", 2019 - 336p.

2. Toxicological chemistry: a textbook / I.V. Nizhenkovska, O.V. Velchynska, M.M. Coachman. — 3rd edition. - K. "Medicine",2020 – 372 p.

3. Mykhailovska T.M. Chemistry of toxic substances. Part 2 // Study guide - Chernivtsi: Ruta, 2007. - 84p.

4. Essentials of Medical Chemistry and Biochemistry /J. Dostal, H.Paulovand, E.Tandborskand – Brno, 2014- 211

5. Toxicological chemistry of food products and cosmetics: textbook / S.A. Voronov, Yu.B. Stetsyshyn, Yu.V. Panchenko, V.P. Vasiliev; under the editorship Prof. S.A. Voronov - Lviv: Publishing House of Lviv Polytechnic, 2010. - 316p.

6. Toxicological chemistry: educational method. manual for pharmacy students. part-time study program / comp. O. I. Panasenko [and others]. – Zaporizhzhia: ZDMU, 2015. – 235 p.

Additional:

Medical chemistry: textbook for students. higher education honey. closing
 / A.S. Moroz, D.D. Lutsevich, L.P. Yavorska – Ed. 4 – Vinnytsia: Nova Kniga, 2013.
 – 776 p.

2. Toxicological chemistry: an abbreviated summary of lectures for students majoring in "Chemistry" / Incl.: Yusina G.L. – Kramatorsk: DDMA, 2020. – 86 p.

3. Medicinal chemistry: a textbook / V. I. Homonai, S. S. Milovych. – Vinnytsia: Nova Kniga, 2016. – 672 p.

4. Medical chemistry: textbook / V.P. Muzychenko, D.D. Lutsevich, L.P. Yavorska; under the editorship B.S. Zimenkovsky. — 3rd ed., corr. — K.: VSV "Medicine", 2018. — 496 p.

Practical lesson No. 2

<u>Topic:</u> Water in living systems. The role and content of water in the human body. Determination of general, temporary and permanent hardness of water.

<u>Goal:</u> to acquaint students with the structure and biological properties of water, the content and functions of water in the human body; concepts of "free and bound water" in food products; determination of the total moisture content in food products, methods of determining and eliminating water hardness.

Basic concepts: hydrogen bond, dipole, total water, bound water, water activity, water hardness, temporary and permanent water hardness, ionites, deionized water.

Equipment: Laboratory of the department

Plan:

- 1. Structure of water. Biological value of water;
- 2. Structure of water. Biological value of water.
- 3. Water content in the human body. The role of water in the human body.
- 4. Free and bound water in food products.
- 5. Determination of total moisture content in food products.
- 6. Determination of water hardness.
- 7. Determination of temporary and permanent hardness of water.

The student should know:

- basic characteristics of the structure of the water molecule;
- determination of total and carbonate hardness of water;

- the principle of the trilonometric method of determining the total hardness of water;
- methods of removing water hardness.

The student should be able to:

- use acquired theoretical knowledge for practical purposes;
- determine the main indicators of the chemical composition of water and physical and chemical properties;
- to evaluate, on the basis of the obtained results, the quality of natural water; carry out measures to improve the biological properties of water.

Content of the practical session

Functions of water:

• is the structural basis of the optimal physiologically active cell volume;

• universal solvent. If this unique liquid is given enough time, it will dissolve any solid substance. No other substance in nature is capable of this;

• necessary for the course of chemical reactions. For example, thanks to it, carbohydrates, proteins, and lipids are digested in the human body, as a result of which the energy needed to sustain life is released;

• determines the spatial structure, and therefore the functions of biomolecules;

• ensures the specificity of enzyme action due to association with polar groups, especially in their active centers;

• forms a directed flow of substances inside the cell, between cells;

• the fluidity of cell membranes is based on the ability of phospholipids to automatically form a polar surface of the membrane and a hydrophobic internal phase;

• participates in thermoregulation. Thanks to it, heat is evenly distributed throughout the body, the temperature does not change depending on the environmental conditions;

• performs a transport function - as a result, every cell of the organism can receive nutrients. It is the main component of lymph and blood;

• maintenance of cell elasticity. Performing the function of the cellular skeleton, water supports the shape of organs. Binding of water to organic structures of the intercellular matrix - collagen, hyaluronic acid, chondroitin sulfates and other compounds ensures tissue turgor. This is clearly manifested in extreme dehydration of the body, when the eyeballs drop and the skin becomes inelastic.

1. <u>Water content in the human body</u>

Normally, the water content in an adult's body is 30-45 liters (45-65% of body weight), most of which is contained inside the cells. There are 10-15 liters of water outside the cells, and about 75% is in the intercellular space, another 25% is in the blood plasma. In the case of water exchange disorders, the pathological condition occurs precisely in the extracellular space.

In the process of vital activity, the body releases water through the lungs, skin and kidneys. Water exchange is extremely important for a person, because together with water, harmful substances or metabolic products are removed from the body. Retention of these substances or their untimely removal lead to severe forms of poisoning, and sometimes even to the death of the organism. Experiments have established that animals, when their entire skin was covered with varnish, died due to blockage of sweat glands, their bodies were oversaturated with toxic substances that should have been secreted by sweat glands.

Water exchange depends on the balance between the amount of fluid entering the body and the amount of its excretion. There is no single norm of water consumption for everyone. The body's fluid needs are influenced by various factors: individual characteristics, level of physical activity, ambient temperature, climatic conditions, etc. The main signal and controller of water consumption is the feeling of thirst.

According to the recommendations of the World Health Organization, the daily norms of water for adults and children are shown in Fig. 2

Approximate amount of fluid per day for an adultis 4% of the total body weight. That is, for a person weighing 70-75 kg, this indicator will be 2800-3000 ml/day. It is not only water, but also the liquid that we get with food. To maintain an optimal balance of water in the body, nutritionists recommend drinking 1-2 glasses of water on an empty stomach in the morning. The basic balance of intracellular and extracellular fluid is regulated by potassium and sodium ions. Potassium removes water, and sodium, on the contrary, promotes water retention. Normally, excess water is easily removed through the kidneys, lungs, and sweat glands. Fluid retention in the body occurs due to imbalance mainly due to salty foods. Note that the need for water increases by an average of 10% when the body temperature rises for every degree above 37 °C. Too much water is a big burden on the body. The recommended daily volume of water consumption reflects the amount that a person's kidneys and heart can withstand. In case of excessive fluidity of water, minerals and vitamins are removed from the body. In the case of limiting consumption, the concentration of urine increases, salt deposits may fall out in it, and excretion of metabolic products from the blood decreases. However, these provisions are correct, but not for all people to the same extent. Much depends on the individual characteristics of a particular person, his health and the nature of his diet.



Fig. 2. Daily water standards for adults and children

Children under six months cannot consume drinking water, the liquid must be compensated from breast milk or baby food. Boiled water for newborns is not only unnecessary, but also dangerous. Children from the beginning of complementary feeding until they reach the age of two should consume water at will, so it should be offered regularly. Starting from 2-4 years old, children should drink about 1 liter or 2-4 glasses/day. Adolescents 9-13 years old should consume 1.3-1.5 l/day. Children older than 14 years, like adults, should drink at least 1.5 - 1.7 l/day.

It is important to note that the amount of water per day for children also depends on the weight of the child, for example, overweight children need more water. Physical activity also plays a role. Also, the increased need for liquid is characteristic of hot periods of the year.

The intake of water into the body is determined by the feeling of thirst, which is formed by the nerve cells of the hypothalamus. They are located in front of the hunger centers and form the thirst center (Fig. 3). These are the paraventricular and supraoptic nuclei of the hypothalamus. When the concentration of sodium chloride begins to increase - 1%, 1.1% and so on, hyperosmia of the extracellular fluid occurs, which creates thirst. The thirst center of the hypothalamus begins to send signals through the amygdala to the frontal cortex of the large hemispheres. At the same time, vegetative and endocrine changes occur, which make it possible to save water until the next water intake.

Summing up

1. What is the role of water in human nutrition?

2. Basic properties of water.

3. What do you mean by "bound water"? What is its importance in food products?

4. How does the moisture content of food products affect their quality? How does the water content change with different methods of processing food raw materials?

5. How is the moisture content of food products determined?

6. What does the term "water hardness" mean? What types of water hardness are distinguished?

7. Specify the sources of ions that determine water hardness.

8. What is the impact of hard water on the human body and technological processes?

9. What is the general hardness of water? In what units is it defined?

10. What is temporary hardness? Specify the main methods of its elimination.

11. What does permanent (non-carbonate) hardness mean? How is it eliminated?

12. What methods of water softening are used?

13. What is the principle of the carbonate hardness determination method?

14. Specify the principle of the method of determining the total hardness of water.

List of recommended literature

<u>Main:</u>

1. Analytical chemistry and analysis of food products: textbook.Slobodniuk R. E., Goralchuk A. B..– K.: Condor Publishing House, 2021. – 336 p.

2. Gvozdyak P.I. Biochemistry of water. Biotechnology of water (automonography). Kyiv: Pub. House "Kyiv-Mohyla Academy", 2019. - 228 p.

3. Ensuring and chemical control of the quality of food products: training. manual / R.P. Vlodarchyk, I.M. Kobasa, M.M. Vorobets et al. – Chernivtsi: Chernivtsi national. University, 2015. – 336 p.

4. Never Yu.B. Food chemistry: reference outline for independent study of the discipline by students of the training direction 6.051701. "Food technologies and engineering" / Yu.B. Nikozyat, L.M. Kopantseva, Yu.I. Crazy – Poltava: PUET, 2015. – 37 p.

Practical lesson No. 3

<u>Topic:</u> Solutions. Preparation of solutions with a specified quantitative composition. Solutions for providing pre-medical care.

- **Topicality:** Liquid pharmaceutical forms (LPF) of pharmacies make up more than 60% of the total number of all medicinal products prepared in pharmacies.
- <u>Goal:</u> To form a general idea of what solutions are, what components they are made of and how they are classified, to ensure an understanding of the meaning of solutions in medical practice, to develop the ability to calculate the amount of a substance for preparing solutions of different concentrations.

Basic concepts: liquid dosage form, solvent, purified water, solutions, concentration.

Lesson plan and organizational structure:

- 1. Characteristics of liquid dosage forms, their classification.
- 2. Solvents and their classification.
- 3. Purified water and its quality control.
- 4. Solutions. Manufacturing methods.
- 5. Expression of concentrations of solutions.
- 6. Preparation of solutions for first aid.

Content of the practical session

<u>The wide use of RLF is due to a number of advantages over other medicinal</u> <u>forms:</u>

- due to the application of certain technological methods (dissolution, peptization, suspension or emulsification), the medicinal substance, which is in any aggregate state, can be brought to the optimal degree of particle dispersion, dissolved or evenly distributed in the solvent, which is of great importance for providing a therapeutic effect medicinal substance on the body and confirmed by biopharmaceutical research;

- liquid dosage forms, characterized by a wide variety of composition and methods of application;

- as part of RLF, it is possible to reduce the irritating effect of some medicinal substances (bromides, iodides, etc.);

these dosage forms are simple and convenient to use;

- in RLF, it is possible to mask the unpleasant taste and smell of medicinal substances, which is especially important in children's practice;

- when taken orally, they are absorbed and act faster than solid dosage forms (powders, tablets, etc.), the effect of which is manifested after their dissolution in the body;

- the softening and enveloping effect of a number of medicinal substances is most fully manifested in the form of liquid medicines.

At the same time, liquid medicines have a number of disadvantages:

- they are less stable during storage, since substances are more reactive in dissolved form;
- solutions are more susceptible to microbiological deterioration, accordingly, they have a limited shelf life a little more than 10 days;
- RLF require quite a lot of time and special dishes for preparation, are inconvenient during transportation;
- liquid medicines are inferior to other medicinal forms in terms of dosing accuracy, as they are dosed with spoons and drops.

Thus, RLF is a widely used medicinal form today. Due to their advantages, liquid medicines have great prospects in the future for the creation of new medicines.

In addition, such a drawback of RLF, as instability during storage, does not allow to reduce the amount of extemporaneous medicines and increase the amount of readymade liquid medicines.

1. CHARACTERISTICS OF LIQUID MEDICINAL FORMS, THEIR CLASSIFICATION

Liquid dosage forms (LPF) are drugs that are obtained by mixing or dissolving active substances in a solvent, as well as by extracting active substances from plant material.

According to the physical and chemical nature of RLF, they are free, comprehensively dispersed systems in which the medicinal substance (dispersed phase - solid, liquid or gaseous - solventum) is evenly distributed in a liquid dispersion medium (solvent - solvents).

Concentration of the solution

One of the most important characteristics of a solution is its concentration. The concentration of a solution is its composition, that is, the relative content of each of the components present in the solution (the content of a dissolved substance in a certain mass or in a certain volume of a solution or solvent).

Quantitatively, the concentration of a solution is expressed in many ways. Six ways of expressing the concentration of solutions are most often used: mass fraction (ω , %), molar concentration (CM, M), molar concentration of equivalent or normal (CH, H), molal concentration (Cm), titer (T), mole fraction (N). In

practice, we often have to deal with solutions that have a clearly defined content of dissolved substances in them.

4. Expression of concentration of solutions

Mass fraction() ω component of the solution is defined as the ratio of the mass of this component m(X) contained in this mass of the solution to the mass of the entire solution mp-pa. Mass fraction is a dimensionless quantity and is expressed in fractions of a unit:

$$\omega = \frac{m(X)}{m_{p-Hy}} (0 < 0 < 1)$$

Mass percentage is the mass fraction multiplied by 100:

$$\omega(X) = \frac{m(X)}{m_{p-Hy}} \cdot 100(0\% < 0 < 100\%),$$

or $\omega(X) = \frac{m(X)}{V_{p-Hy} \cdot \rho} \cdot 100$

where ρ – solution density, g/cm3 (g/ml), – solution volume. $V_{\rho-Hy}$

The mass fraction of the dissolved substance is also called the percentage concentration of the solution.

Molar concentration or molarity(cm) is defined as the ratio of the amount of dissolved substance X to the volume of the solution V:

$$C_{M} = \frac{n(X)}{V_{p-Hy}}, \text{mol/l}$$

An example of writing molar concentration: Cm(H2SO4) = 0.8 mol/l or 0.8M.

Normal concentration or normality(CH) is defined as the ratio of the number of equivalents of dissolved substance X) to the volume of the solution. The unit of normality is mol-eq/l. An example of writing a normal concentration: Sn (H2SO4) = 0.8 mol-eq/l or $0.8n.n_{_{\rm 2KB}}$ (

$$C_{H} = \frac{n_{eKB}(X)}{V_{p-Hy}}$$
$$n_{eKB} = \frac{m}{M_{E}} \text{ or } C_{H} = \frac{m}{M_{E} \cdot V}$$
$$M_{E} = M/Z$$

*Acids*have in their composition active hydrogen, capable of being substituted in neutralization reactions.

Equivalent number *Z* for an acid is equal to the number of hydrogen cations in its composition or its basicity:

z acids = n(H+) = basicity

Foundations contain the hydroxo group OH-.

Therefore, the equivalent number z for a base is equal to the number of hydroxo groups in its composition: zbase = n(OH-) = acidity.

The normal concentration is calculated according to the law of equivalents.

If two dissolved substances react, then nE(1) = nE(2), and

Sn(1) V1 = Sn(2) V2 Sn(1) V1 = m / ME(2) V2nE(1) nE(2) nE(1) nE(2)

where *CH*(*1*) and CH(2) – normal concentrations of reactant solutions, ; V1 and V2 – volumes of reactant solutions; nE(1) and nE(2) are the number of mole equivalents of reactants. $\frac{MORb - eKB}{R}$

To change from molar to normal concentration and vice versa, use the rule: the normal concentration is as many times (x) greater than the molar concentration, how many times the molar mass of the substance (M) is greater than its molar mass of equivalents (ME).

$$CH = CM \cdot 1/z$$

Caption(T) shows how many grams of solute X is contained in 1 ml or 1 cm3 of solution:

$$T = \frac{m(X)}{V}$$
, or $T = \frac{m_B}{V}T = \frac{C_{\rm H} \cdot M_{\rm E}}{1000}$

where m(X) is the mass of dissolved substance X, g; Vr-nu – volume of the solution, ml.

Molal concentration or molality solution m shows the amount of dissolved substance X in 1 kg of solvent:

$$m=\frac{n(X)}{m_0},$$

where n(X) is the number of moles of dissolved substance X, mol; mo is the mass of the solvent, kg.

List of recommended literature

Main:

1. Medicinal chemistry: a textbook for universities / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others; under the editorship of Prof. V.O. Kalibabchuk - 4th ed. - K. VSV "Medicine", 2019 - 336p.

2. Applied chemistry: teaching. manual / I.V. Kosogina, I.M. Astrelin - K.:

NTUU "KPI", 2015. - 282 p.

Practical lesson No. 4

<u>Topic:</u> Solubility of drugs. Relationship between pharmacological activity and ionization of molecules. Infusion solutions.

- **Topicality:** Consolidate theoretical knowledge and learn to organize aseptic preparation conditions, observe safety rules, prepare solutions for injections with different physical and chemical properties,
- **Goal:** Infusion solutions are the most complex group of drugs for parenteral use. These include the so-called physiological solutions, which by their composition are capable of maintaining the viability of cells and organs, are administered in large quantities and do not cause any violations of the physiological balance in the body.

Basic concepts: solubility, pharmacopoeia, infusion solutions.

Lesson plan and organizational structure:

- 1. History of medicines.
- 2. Ways of creating new medicines.
- 3. Solubility of substances.
- 4. State Pharmacopoeia of Ukraine.
- 5. Infusion solutions.

Content of the practical session Ways of creating new medicines

Pharmacopoeias of different countries count, according to various data, from 2 to 15 thousand medicinal products. Every year, 50-70 new, truly original medicines are registered in the world, and the work on creating new ones does not stop.

What is the reason for the need to create more and more new drugs? First of all, the appearance of new diseases. According to the WHO, from 1975 to 1996, more than three dozen new diseases were registered. Diseases of greatest concern include HIV-AIDS, Ebola, SARS, and prion infections such as spongiform encephalopathy. Recently, humanity has been carefully watching whether a mutation of the dangerous H5N1 bird flu virus will occur, which could lead to a pandemic.

No less dangerous is the emergence of new strains of microorganisms resistant to drugs widely used in medical practice. In 1963, for the first time, cases of inflammation of the lungs that were not amenable to treatment with tetracycline antibiotics were described. Later, the causative agents of this disease acquired resistance to erythromycin and lincomycin, and now multiresistant strains have spread widely in Europe and the USA. The recent spread of tuberculosis caused by strains resistant to the most common anti-tuberculosis drugs, which has become an epidemic, is particularly dangerous.

Another factor that encourages the creation of new drugs is the development of medical science. The emergence of new medical technologies requires appropriate pharmacological support. Thus, the development of transplantology necessitated the search for new, highly effective immunosuppressants that would prevent rejection of the transplanted organ. Implantation of artificial heart valves requires pharmacological regulation of blood clotting.

The general increase in the standard of living makes the question of increasing not only the duration, but also the quality of life even more urgent, which, in turn, requires the creation of new, more effective, more convenient, less toxic drugs.

One of the factors that prompts the search for new drugs is socio-economic. It is known that Ukraine belongs to the countries with a low average standard of living of the population. Patients in Ukraine cannot afford to buy highly effective, but expensive drugs manufactured by leading Western companies, so the search for new, effective, safe, but inexpensive drugs remains relevant.

The original medicines first patented by the developer and released to the market in the USA, and after them throughout the world, are called "brands" (from First Brand - the first factory brand). The term of patent protection in the USA is 17 years, in European countries - 20. At this time, other companies can produce this medicine only after acquiring a license. After the expiration of the patent, any pharmaceutical company can produce the same medicine according to its technology and under its trade name. Such medicines are called "generics". The vast majority of drugs currently released on the market by Ukrainian pharmaceutical companies are generics. In the USA, the strict requirements of the standards of domestic legislation force the company producing generics to achieve a minimum of 92-98% efficiency in relation to the brand, after which the abbreviation NBE (National Brand Equivalent) is added to the name of the drug, which means equivalence to the brand. Medicinal products that have become widely distributed can, at the request of the manufacturing company, receive from the WHO an international non-proprietary name (INN - International Nonproprietary Names), which is recommended to be indicated in the labeling of the medicinal product and in informational materials along with the brand name. This makes it easier to understand the variety of names.

Among the advantages of generic drugs is the fact that during their use (about 20 years), the peculiarities of their pharmacological action, all the pros and cons become known. Another way to create new drugs is related to this - the new use of already known medicinal substances. In the process of using the anthelmintic drug Levamisole (Dekaris), it was established that it can act as an immunomodulator - to

strengthen a weak reaction of cellular immunity, weaken a strong one and not affect the normal one. Midantan, originally proposed as an antiviral, is now used to treat parkinsonism. The most successful in this regard is sildenafil citrate, which was originally used as a cardiovascular drug, and is now known worldwide as "Viagra".

One of the traditional, but still not exhausted, sources for the search for new medicinal substances is plant raw materials. Research of still unstudied medicinal plants used in folk medicine, research of species close to those already used in medical practice, in-depth study of insufficiently researched types of plant raw materials allows to identify and divide into individual components the amount of biologically active substances with a valuable pharmacological effect. In some cases, when the structure of the isolated substances is simple enough, in the future, they proceed to their synthesis, which in many cases is economically more expedient. Yes, they are already synthesizing some alkaloids, vitamins, antibiotics, components of essential oils.

A very promising source of biologically active substances promises to be the just-started study of hydrobionts - organisms that live in the water element (algae, corals, molluscs, fish, etc.). Their research has already produced the first promising results: for example, a new antibiotic squalamine was isolated from the tissues of some species of sharks, and substances with high antitumor activity were isolated from certain species of Australian corals.

One of the ways to create new medicinal substances is to modify the structure of natural biologically active substances. Such works began a long time ago and went in parallel with the selection, establishment of the structure and introduction into medical practice of medicinal substances of natural origin. Thus, bromination of the well-known analeptic drug camphor, by analogy with inorganic bromides, produced the sedative drug bromocamphor. Ethylation of morphine hydrochloride made it possible to obtain ethylmorphine hydrochloride - an antitussive and ophthalmic agent. Modification of the structure of atropine - esterification of tropine alcohol with other acids - led to the appearance of such drugs as homatropine, tropacin, tropafen. Diprophylline, xanthine nicotinate, and pentoxifylline were obtained by alkylation of purine alkaloids theophylline and theobromine. The well-known angioprotector troxevasin was synthesized by introducing hydroxyethyl groups into the bioflavonoid rutin. Particularly large-scale works on the modification of natural structures are carried out in two groups of medicinal substances - hormones and antibiotics.

Immediately after the discovery of the first steroid hormones, it became clear that their content in animal raw materials is very low, and the extraction has significant difficulties, so now they are obtained synthetically. Natural compounds that already have a steroid cycle are used as raw materials - cholesterol, alkaloid solasodine or saponin diosgen. In the process of medical use of glucocorticosteroids as antiinflammatory, anti-allergic, desensitizing agents, it became clear that their influence

on carbohydrate and fat metabolism causes harmful side effects. Modification of the structure of corticosteroids made it possible to obtain compounds whose activity is tens and hundreds of times higher than that of cortisone with almost no effect on carbohydrate metabolism; they include, in particular, fluorinated derivatives. At the same time, modification of the structure made it possible to obtain anabolics that do not have an androgenic effect, as well as significantly more active progestogens and estrogens, which are used in birth control pills.

Widespread use of antibiotics quickly led to the emergence of strains of microorganisms resistant to their effects. This, in turn, prompted scientists to modify the structure of natural antibiotics in search of more stable substances with a broad spectrum of action, active against resistant forms. Among P-lactam antibiotics, natural compounds are almost no longer used, they have been replaced by drugs of the third and fourth generations.

A method of finding new drugs that is very close to the modification of natural compounds is the creation of synthetic agents that are structurally similar to natural compounds. In particular, an analogue of the natural alkaloid papaverine, which has an antispasmodic effect, is synthetic drotaverine hydrochloride (HO-ShPA). An analog of adrenaline unstable to oxidation is synthetic mesaton and a number of β -adrenostimulators (izadrine, orciprenaline, salbutamol, etc.). Isolation of the pharmacophore in the structure of cocaine made it possible to create a number of local anesthetics - anesthesin, novocaine, dicaine, etc.

The most common is the empirical search for new drugs, which is carried out by trial and error ("scientific tic" method). Based on certain empirically established regularities and ideas about the influence of certain functional groups on biological activity, a certain large number of new compounds are synthesized, which are subjected to screening (sieving), that is, they are checked for biological activity by several (preferably as many) tests in order to identify the most active . For the first time, screening in the creation of medicinal products was used by P. Ehrlich at the beginning of the 20th century, when he was engaged in the search for antisyphilitic agents in a number of organic compounds of arsenic. As is known, compound 606 was introduced into medical practice under the name "salvarsan". Currently, statistics show that only approximately one out of 50-70 thousand synthesized compounds, subject to spending 300-500 million dollars, has a chance to become a brand.

In the modern world, the so-called total, current or continuous screening (High Throughput Screening) has been developed, which consists in mass testing of the biological activity of all chemical compounds synthesized for any purpose (for example, as a pesticide or plastic stabilizer). In many pharmaceutical centers, the substance is tested for 30-70 or more types of specific biological activity. In these tests, inactive, weakly active, toxic, too expensive or time-consuming compounds are

rejected. When a therapeutic effect is detected, a lead compound is selected, which is subjected to in-depth study. In parallel, related compounds (analogues) are synthesized to identify the most active and safe substance in this series.

State Pharmacopoeia of Ukraine

In each state, all products produced by the pharmaceutical industry must meet certain quality standards. The main document regulating the quality standards of medicinal products is the State Pharmacopoeia (national).

In addition to national pharmacopoeias, there are regional pharmacopoeias that contribute to the unification of the nomenclature and quality requirements of medicinal products produced in different countries of the region.

For example, the European Community has a pharmacopoeial commission that prepared and published the first volume of the EU Pharmacopoeia in 1969, and the second in 1971.

The European Pharmacopoeia has a legislative character for the countries of the European Community, but does not replace national pharmacopoeias.

The idea of creating the International Pharmacopoeia was caused by the need to unify the nomenclature and requirements for the quality of medicinal products in all countries of the world. Unlike national pharmacopoeias, the requirements of the International Pharmacopoeia are not legislative, but rather advisory in nature.

The State Pharmacopoeia of Ukraine is a legal act that contains general requirements for medicinal products, pharmacopoeial articles (monographs), as well as methods of quality control of medicinal products.

The main goal of modern pharmacological, including pharmacokinetic, research is to find new drugs for pharmacotherapy that are more active but less toxic than existing ones. Until now, in such studies, searches were conducted empirically. After determining the pharmacological activity of compounds of a certain chemical structure, a number of numerous derivatives are synthesized and their activity is investigated. In this way, many highly active drugs were discovered. However, a clear correspondence between the structure of molecules, their pharmacological action and pharmacokinetic parameters has not been established. However, it cannot be confidently stated that it was possible to synthesize the most optimal compound in terms of pharmacokinetics (even in one chemical group). To solve this problem, it is necessary to more accurately determine the electronic structure of compounds that are different in structure but have the same pharmacokinetic parameters. On the basis of such calculations, it is possible to determine the correlation between various indicators characteristic of the electronic structure and pharmacokinetics. It is likely that molecules that contain different atoms have common parameters of the electronic structure (for example, charges on atoms, energies of frontier orbitals, polarizability) and, as a result, have the same pharmacokinetics.

The question of the correlation between pharmacological activity and molecular or electronic structure is quite complex. In order for a medicinal substance (PR) to exert its effect, in almost every case such a chemical compound must penetrate the cell membrane at an appropriate speed and enter those parts of the cell in which the therapeutic effect is manifested. It is also necessary to investigate whether the molecule has the appropriate diffusion properties, which, in turn, depend on the electronic and spatial structure. An important requirement for drugs is the complete absence of side effects. This means that the future LR should specifically bind only to certain parts of the cell. The absence of significant side effects, including toxicity, probably depends on the spatial and electronic structure of the molecule. Thus, the main pharmacological, including pharmacokinetic, problems can in principle be solved by quantum chemical calculations of the electronic structure, if the spatial structure of this molecule is known. Progress in the development of quantum chemistry, quantum physics, quantum mechanics, molecular biology, and computer technologies became the basis for the research of a new science - quantum pharmacology. The term "quantum pharmacology" appeared in the scientific literature in 1977. The English chemist WG Richards, who headed the chemistry department at the University of Oxford, defined quantum pharmacology as a science in which knowledge of the electronic structure of drugs is used for de novo drug design, the study of the connection between the structure and biological activity of substances, as well as the establishment of pharmacophores and the explanation of the mechanism of action of LR. Based on the analysis of data from modern literature and own research, the following definition of quantum pharmacology can be given: "a science that applies the principles of theoretical chemistry and quantum mechanics and computer modeling methods to study the molecular structure of drugs, the mechanisms of their interaction with receptors and other biomolecules of the body with the aim of establishment of the primary pharmacological reaction of medicines". Since quantum pharmacology was created and developed in order to increase the efficiency and speed of development of new drugs with predicted properties, the methodological approaches of this science were widely used for the study of pharmacokinetic processes.

List of recommended literature

Main:

1. Medicinal chemistry: a textbook for universities / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others; under the editorship of Prof. V.O. Kalibabchuk - 4th ed. - K. VSV "Medicine", 2019 - 336p.

2. Applied chemistry: teaching. manual / I.V. Kosogina, I.M. Astrelin - K.:

NTUU "KPI", 2015. - 282 p.

Practical lesson No. 5

- <u>Topic:</u> Medical solutions: antiseptics, disinfectant liquids. Water purification and sterilization of medical products and instruments in the field.
- **Topicality:** Carrying out disinfection and sterilization measures as one of the means of non-specific prevention of the development of infectious diseases is a necessary condition for ensuring the sanitary and epidemiological well-being of the population. Disinfection and sterilization are necessary conditions for protecting patients from the entry of pathogenic microorganisms into the body through surgical instruments, the hands of medical personnel, and contaminated surfaces.

Goal: Formulate the definition of the concept of "sterilization", master the theoretical knowledge and practical skills of sterilization of water and medical instruments.

Basic concepts: disinfection, sterilization, field conditions.

Lesson plan and organizational structure:

- 1. Disinfection. Levels of disinfection.
- 2. Characteristics of medical disinfectants.
- 3. ATwater purification in derived conditions.
- 4. Sterilization.
- 5. Prevention of surgical infection.

Content of the practical session

Medicine is a branch of science and practical activity, the main goal of which is to preserve and strengthen human health, as well as diagnosis and treatment of diseases. All medical institutions must comply with established sanitary and epidemiological requirements for the organization of premises and equipment. In order for patients to be treated in conditions that do not pose an additional threat to their condition, it is necessary to pay special attention to disinfection and sterilization.

Disinfection is a set of measures aimed at processing premises, surfaces, instruments and other objects of the external environment, with the aim of cleaning them from various pathogenic microorganisms.

Special attention is paid to disinfection in healthcare facilities. It is medical workers who are most exposed to the risk of infection with various viral infections, due to the fact that their work is associated, in particular, with constant contact with human biological materials (blood, damaged tissues, etc.). All premises in medical organizations are subject to mandatory sanitation. Failure to properly disinfect or sterilize rooms, surfaces, and reusable medical equipment can lead to contamination of medical personnel and patients, as well as rapid development of nosocomial infections.

Disinfection levels: high, medium, low

There are three levels of disinfection suitable for different types of medical instruments:

High - the level of disinfection at which all vegetative forms of bacteria (including tuberculosis mycobacteria), viruses (including resistant hydrophilic viruses), fungi and most spores are destroyed. This disinfection method is suitable for decontamination of "semi-critical" medical items.

Medium - the level of disinfection at which all vegetative forms of bacteria (including tuberculosis mycobacteria), most viruses and fungi are destroyed, but spores are not destroyed. Medium-level disinfection is suitable for decontamination of all "non-critical" items, as well as some "semi-critical" items.

Low - the level of disinfection at which most vegetative forms of bacteria (except mycobacteria and spore forms), some fungi, and lipophilic viruses (hepatitis B, C, Hantavirus and HIV) are destroyed. Suitable exclusively for disinfection of "non-critical" medical items.

How to choose the right disinfectant? What properties of the tool to pay attention to?

Today, there is a large selection of disinfectants of different chemical compositions and fields of application. The characteristics on the basis of which a disinfectant is selected include, first of all, the spectrum of antimicrobial activity. An effective disinfectant should provide a bactericidal, virucidal (including against hepatitis A, B, C and human immunodeficiency viruses) and fungicidal action, and, if necessary, a tuberculocidal action. In order to choose the optimal agent that not only protects against pathogens of infectious diseases, but also does not harm human health, objects of processing and the environment, it is necessary to understand the key characteristics of an effective disinfectant.

Key characteristics of an effective disinfectant:

- a wide range of antimicrobial action (bactericidal, including tuberculocidal, virulicidal, fungicidal and sporicidal action);
- effectiveness with minimal exposure (minimum disinfection time);
- safety for the user and the environment, as well as environmental friendliness of the product (absence of volatile components, persistent unpleasant irritating smell, minimal toxicity (4th class of danger));
- a combination of disinfecting, washing and deodorizing action;
- compatibility with the materials of the processed products (absence of corrosive and other harmful effects);

- convenience of preparing working solutions (convenience of dosage, quick and complete solubility in water);
- manufacturability and ease of use, no need for users to use expensive personal protective equipment;
- stability of the agent and its working solutions during storage, lack of need for periodic control of the content of the active substance.

Aldehydes

Modern aldehyde-containing disinfectants are based on glutaric or succinic aldehyde, formaldehyde, glyoxal, orthophthalic aldehyde. Additional components are most often quaternary ammonium compounds, surface-active substances (surfactants) and other activating impurities.

Properties of aldehydes:

- dissolve well in water
- destroy bacteria, in particular the causative agent of tuberculosis, viruses, fungi, spores
- do not contain oxidants (have a milder effect on construction materials)

Modern aldehyde-containing disinfectants usually contain detergents. Most of these disinfectants are universal, as they can be used for <u>disinfection</u> medical devices, surfaces, etc. Individual means of this group are used to sterilize medical instruments.

This group of disinfectants is also distinguished by the duration of storage of the activity of working solutions (up to 14 days) and the possibility of repeated use.

Aldehydes are used during general, ongoing cleaning in surgical, procedure rooms, etc.

Peroxides, peroxy compounds, oxygen-containing and other oxidants

The disinfectants of this group are based on active oxygen. Modern oxygencontaining disinfectants have high bactericidal, tuberculocidal, virulicidal and sporicidal activity. It is believed that their use does not cause the formation of resistant strains of microorganisms. In addition, these drugs are environmentally safe, because they break down into oxygen, carbon dioxide and water.

Such means are usually used for disinfection of rubber, plastic, glass medical products, as well as surfaces, linen, dishes, patient care items, for chemical sterilization of medical products.

Disadvantages of oxygen-containing disinfectants:

- relatively low stability, which limits the shelf life of drugs
- aggressiveness towards corrosion-resistant materials
- high irritant effect of concentrated solutions on the mucous membranes of the respiratory organs, which requires the use of protective equipment

Alcoholic drugs

The active substance of these disinfectants are mono- and polyhydric alcohols. For <u>disinfection</u> mostly ethyl and isopropyl alcohols are used, but the latter is inactive against non-lipid viruses. Alcohols belong to the 3-4 class of danger and have a relatively quick effect. They are active against tuberculosis bacteria, viruses (in particular, hepatitis B and HIV), fungi.

70% solutions are the most active against microbes. It is impractical to use alcohols of a higher concentration, as they quickly fold the protein and do not penetrate into the microbial cell.

The advantage of alcohols is that microorganisms cannot form stable forms during long-term use of drugs of this group. Alcohols are the main active ingredient in antiseptics, that is, preparations for skin treatment, which are part of some complex disinfectants.

Boiling water

One of the simplest and most reliable methods is the thermal method of water purification, which consists in boiling it. The boiling time depends on the degree of contamination of the water source. In particular, if it is collected from a clean stream, it should be boiled for about 15 minutes, if it is from a polluted reservoir, then at least 30 minutes.

Various branches of trees and grass are added to the water during boiling to enhance the disinfecting effect. Example:

- ▶ young branches of coniferous plants: spruce, juniper, pine, cedar (150-250 grams per bucket; boiling time 30-35 minutes);
- ► willow, oak, beech bark (150-250 grams per bucket, boiling time 40 minutes);
- ► stone moss (lichen), as well as forest or walnut shells (50-75 grams per bucket);
- ► field violet or perekotipole grass (300 grams per bucket);
- Calendula grass (150-250 grams per bucket; boil for about 30 minutes);
- ▶you can also use leaves of chamomile, raspberry, St. John's wort, celandine and other antiseptic medicinal plants;
- Is such mushrooms as rain mushrooms and porcini mushrooms also have bactericidal properties, so they can be used instead of herbs;
- ► if you did not find these plants or mushrooms, you can use them to clean the sand. First, collect the top layer of sand and filter water through it. Then boil the water with another portion of sand (so that it occupies 1/10 of the bucket) for half an hour, constantly shaking the sand from the bottom.
- ▶ in case of an unpleasant smell of water, add charcoal from the fire during boiling.

After you have boiled the water for enough time, leave it to settle for another 30 minutes. Then carefully drain the sediment from the water and in no case drink it. If it is not possible to make a fire to boil water, you can use other methods. **Salt**

The easiest way to disinfect water is to use salt. It is thrown into water at the rate of one tablespoon per liter and a half of water and left to infuse for up to 30 minutes. During this time, some types of microbes will partially die and heavy metal salts will settle. However, it is often impossible to drink such water, as it has excessive salinity and also has a low bactericidal effect.

Activated carbon

Activated carbon perfectly copes with the unpleasant smell of water, impurities and harmful substances that may be present in it. For disinfection by this method, you need to put 5 tablets wrapped in a flap of fabric in a liter of water. The water will be clean and drinkable after 8 hours.

Silicon/ Jerusalem artichoke

One of the powerful activators of water is the natural mineral silicon. It has excellent bactericidal properties, and water with silicon additives improves metabolism and at the same time is stored well and for a long time.

To prepare silicon liquid, you need to wash it, and then drop 1-3 g of the mineral into a container with raw or boiled water (1 l). Cover the vessel with clean gauze and leave to infuse for 24 hours in a place protected from the sun. After a day, you can drink water with the addition of silicon, as well as wash wounds and gargle.

By the way, Jerusalem artichoke can be used instead of this mineral, as it has a high silicon content.

Manganese

According to experts, the most effective way to disinfect water in small quantities (for individual consumption) is to use potassium permanganate (permanganate) or iodine.

However, when using potassium permanganate, the main thing is to be careful in the proportions, because an excess of the dose can cause partial or complete death of the intestinal microflora. So, to clean 1 liter of water, you need 1-2 grams of a solution of potassium permanganate or 1-2 crystals of this liquid (the volume should be no more than a match head). The solution should be pale pink in color.

Iodine

Along with potassium permanganate, iodine in the form of an alcohol tincture or iodine tablets designed specifically for individual disinfection of water is also suitable for water purification. To treat water in this way, you need to add 3-4 drops of 5%

alcohol iodine tincture or 2 iodine tablets to 1 liter of water. After that, mix thoroughly and leave to infuse for about one hour.

You can drink such water, but cook food only after 40-60 minutes of boiling. Since iodized water has a characteristic smell and only during the boiling process, twothirds of the iodine evaporates.

Special tablets to purify water

Tablets are also used to kill microbes in field water. In particular, Hydroperit or Furacilin. A bucket of water can be disinfected with four to five hydroperite tablets. Then the vessel is covered with a lid, allowed to stand for 20-30 minutes, and then heated to boiling.

With the help of 10-12 furacilin tablets, you can also clean a bucket of water. At the same time, the water should be heated to 40-50 degrees, as the tablets dissolve quickly when heated. Then the container with water is left on low heat for another 20-30 minutes, and then the solution is precipitated with any natural alum at the rate of five to six grams per bucket of water. A special preparation for chemical sterilization of any water - pantocid - is also produced. Only 1 tablet is needed to disinfect a flask of water (0.5-0.75 l).

Silver

One of the good disinfectants is silver, as it disinfects water well. If it is cloudy, with the content of earth, sand, etc., then you need to first filter the liquid through a cloth, and then put a silver object on the bottom of the dish.

However, do not forget that silver also has a high degree of danger to human health. It, like other heavy metals, has the ability to accumulate in the body and cause argyrosis (silver poisoning). In addition, the bactericidal effect of silver requires considerable concentrations, and in acceptable amounts it can only stop the growth of bacteria without killing them. Therefore, the use of silver is possible only for the purpose of preserving already clean water for long-term storage.

Wine

Another interesting method of water purification is wine purification. If you have a hand, then you can dilute the water with red dry or fortified wine in the proportion of a liter of wine per bucket of water.

!!!After any method of disinfection, the water should be allowed to stand for at least 15-30 minutes.

Take something from our list with you when you go on vacation outside the city. It will help you avoid health problems and survive in an extreme situation.

STERILIZATION

Sterilization is the process of destroying biological agents (all types of microorganisms and their spores) on medical products. Sterilization is carried out for the purpose of:

1) prevention of introduction of microorganisms into the human body during medical interventions;

2) exclusion of microbial contamination of medicinal and diagnostic materials, nutrient media and cell cultures used in microbiological and immunological studies.

Sterilization of medical devices includes three stages:

1st - disinfection;

2nd - pre-sterilization cleaning;

3rd - sterilization.

Disinfection

All products are subject to disinfection after their use in patients. Disinfection of products is carried out with the aim of destroying pathogenic and opportunistic microorganisms, including the causative agents of viral hepatitis and HIV infection, mycobacterium tuberculosis and fungi, including fungi of the genus Candida. After disinfection, the product is washed with water, dried and used as intended or subjected to pre-sterilization cleaning and sterilization.

Pre-sterilization cleaning of products

Pre-sterilization cleaning of medical products is carried out in order to remove protein, fat and mechanical impurities, as well as drug residues.

Control materials for the final stage of the lesson. Questions to check the final level of knowledge:

- 1. What is disinfection?
- 2. Name the levels of disinfection.
- 3. Characteristics of medical disinfectants.
- 4. How to purify water in derivative conditions.
- 5. Sterilization and its types.
- 6. Prevention of surgical infection.

List of recommended literature

Main:

1. Medicinal chemistry: a textbook for universities / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others; under the editorship of Prof. V.O. Kalibabchuk -

4th ed. - K. VSV "Medicine", 2019 - 336p.

2. Applied chemistry: teaching. manual / I.V. Kosogina, I.M. Astrelin - K.: NTUU "KPI", 2015. - 282 p.

Practical lesson No. 6

<u>Topic:</u> Medical gases: production, application and safety. Dosage of gas mixtures for inhalation anesthesia. Solubility of gases.

Actuality of theme

Knowledge of the characteristics of the solubility of gases (oxygen, carbon dioxide, nitrogen) is important for future doctors' understanding of how certain physiological processes occur in living organisms in normal and pathological conditions. Therefore, from the first year we begin to understand these issues using interdisciplinary integration.

Air is extremely important, because, first of all, it supplies the necessary oxygen for the life of all living things on the planet, ensures vital processes. It has an important hygienic value, and is one of the most important factors of climate formation. Under the influence of air, geological processes occur on the Earth's surface. Self-cleansing processes from harmful chemicals, gases and steam, suspended solids, pathogenic microorganisms take place in it. A person can live without food for 40 days, without water - for 5 days, and without air - for 2-3 minutes. When we come into the world, the first thing we do is breathe. When we die, we stop breathing. That is, our life is completely dependent on air, even if we cannot see and feel it.

Oxygen-respiratory and anesthesia equipment is widely used in cases of emergency aid in case of oxygen deficiency, for pain relief in case of injuries and surgical interventions.

During the last decade, effective methods of treatment of therapeutic patients using inhalation of inert gases have been developed. The use of xenon, krypton and helium makes it possible to achieve a positive effect in the treatment of therapeutic patients without the use of powerful sedative and muscle relaxant drugs, to shorten the treatment period of inpatients with inflammatory diseases of the respiratory organs.

- **Goal:** familiarize yourself with the properties of gases and their laws; to study the purpose and use of medical gases (medical oxygen, nitrous oxide); to understand how the solubility of gases affects the human condition; to know the peculiarities of the use of inert gases in medicine.
- **Basic concepts:** gases, solubility of gases, laws of Henry-Dalton and Sechenov, caisson disease, medical oxygen, oxygen therapy, noble gases.

Equipment: Laboratory of the department

Lesson plan and organizational structure:

- 1. Properties of gases, gas laws.
- 2. Solubility of gases in liquids and its dependence on various factors.
- 3. Henry-Dalton law.
- 4. The influence of electrolytes on the solubility of gases (Sechenov's law). Solubility of gases in blood. Bends.
- 5. Air, its composition.
- 6. Analysis of the composition of exhaled air for diagnostic purposes.
- 7. Medical oxygen: production, operation, safety rules.
- 8. Oxygen therapy. Mountain air, hypoxytherapy. Singlet oxygen therapy, ozone therapy.
- 9. Noble gases in medicine.
- 10. Gas mixtures for anesthesia.
- 11. Xenon, production of medical xenon.
- 12. Radonotherapy.

The student should be able to and know:

a) electronic structure of H, O, N and elements of group VIII;

b) the concept of gaseous substances;

c) chemical properties of oxygen and ozone;

d) chemical properties of inert gases;

e) concepts of "volatile substances", "ideal gas", "solubility".

f) the principle of operation of the hemoglobin-oxyhemoglobin buffer system

Lesson content

Solubility of gases in liquids

Solubility of gases in liquids and its dependence on various factors.

Solubility refers to the ability of a substance to dissolve in a solvent. Quantitative solubility (ks) is defined as the mass of a substance contained in 100 g of solvent at a given temperature.

Substances based on solubility in water are classified into:

- well soluble (ks> 1) - nitrates, sugar, alcohol;

- sparingly soluble (ks = 0.1 - 1) - gypsum, benzene, nitrogen;

- insoluble (ks< 0.1) - most carbonates, phosphates, glass.

Factors influencing the solubility of gases in liquids

1. *The nature of gas*, the nature of the solvent (N2 and HH3 have different solubility).

Non-polar gases are difficult to dissolve in a polar solvent, particularly in water, and dissolve better in non-polar organic solvents.

2.*Pressure*. (Henry-Dalton law).

According to Henry's law, the solubility of a gas in a liquid is directly proportional to its pressure above the liquid:

m=kp

where m is the mass of the dissolved gas, p is the gas pressure above the liquid, k is the proportionality factor that depends on the nature of the gas.

<u>**Dalton's first law**</u>: the total pressure of a mixture of gases that do not interact with each other is equal to the sum of the partial pressures of all its components rzag=p1+p2+...ri

<u>The second law</u>Dalton: the solubility of each of the components of a gas mixture in a given liquid at a constant temperature is directly proportional to its partial pressure above the liquid and does not depend on the total pressure of the mixture and the content of other components.

mi = k and pi

where mi is the mass of each dissolved component of the gas mixture, pi is the partial pressure of each component of the gas mixture.

3.*Temperature*(Clausius-Clapeyron law)

It is described by the Clausius-Clapeyron equation: the solubility of gases at constant pressure decreases with increasing temperature:

$\ln N1/N2 = -\Delta H/R \cdot (1/T2 - 1/T1),$

where N are mole fractions of gas at T1 and T2, Δ H is the heat of dissolution of 1 mole of gas.

It has been proven that the solubility of gases decreases with increasing temperature.

4. Availabilityelectrolytein solution (Sechenov's law)

<u>Sechenov's law</u>: the solubility of gases in electrolyte solutions is lower than in a pure solvent.

This dependence is expressed mathematically by the equation:

$S = S_0 e^{-kc}$

where S is the solubility of gas in an electrolyte solution with a concentration of C (mol/dm3), S0 is the solubility of gas in water, k is a constant that depends on the temperature and the nature of the components of the solution, and e is the base of natural logarithms.

With an increase in the amount of oxygen in the blood, the return of carbon dioxide by the blood is facilitated, and, conversely, with an increase in the pressure of carbon dioxide, the solubility of oxygen in the blood increases. The formed bubbles clog capillary blood vessels (gas embolism), disrupt blood supply to organs, which can cause serious functional disorders. This phenomenon is also taken into account during intravenous administration of drugs, preventing air from entering the vein.

Solubility of gases in blood. Caisson and mountain sickness

Blood is an aqueous dispersed system with inorganic and organic substances, therefore the solubility of oxygen, CO2 and nitrogen in it is much lower than in water. Thus, 23.7 cm3 of oxygen dissolves in 1 dm3 of water, and 23.0 cm3 in blood plasma at a temperature of 37 oC. It is interesting that with an increase in the amount of oxygen in the blood, it gives off CO2 much more easily, and with an increase in the pressure of carbon dioxide in the blood, the solubility of oxygen increases.

For normal physiology, it is important to understand that the solubility of various gases (oxygen, nitrogen, carbon dioxide) in water is important. Gas exchange, which occurs mainly in the lungs, is based on the difference in the partial pressures of oxygen

and carbon dioxide. It is necessary to understand that when a person falls into special conditions (change in atmospheric pressure), changes in the solubility of gases in the blood are observed. So, when a person climbs high in the mountains, at a certain height, mountain sickness can occur due to reduced pressure. Oxygen starvation (decrease in blood oxygen concentration) is observed, pulmonary ventilation increases, blood alkalinity increases, therefore alkalosis develops (shift of blood pH in the alkaline direction). In order to prevent this phenomenon, climbers use citric acid the day before.

An interesting example is caisson disease. Divers descend to depth - the concentration of gases in their blood changes significantly due to the increase in pressure. To prevent the development of caisson disease, the diver must slowly rise from the depth, so that there is no sharp decrease in pressure and, as a result, a rapid release of gases dissolved in the blood in the form of bubbles. It should be remembered that these bubbles can close capillaries, which contributes to gas embolism of blood vessels, as a result of which the blood supply of organs is disturbed - this is the cause of important violations of the normal functioning of organs and systems.

Analysis of the air exhaled by a person as a useful source for diagnosing these diseases

Today, more than 800 gases are known, which are products of physiological and biochemical processes in the body. Their concentration reveals the level of homeostasis, as well as the presence of various pathological diseases. Analysis of the air exhaled by a person is used to detect these diseases, predict the body's reaction to a specific type of treatment, and monitor the effectiveness of medical therapy. Such an analysis is safe for personnel, is relatively cheap and takes little time.

With the help of a special device - a halimeter - the intensity of the unpleasant smell or how successfully the treatment is progressing is assessed. The breath test is the main method for determining the presence of Helicobacter pylori bacteria in the human body. At the same time, the composition of the air exhaled by a person is analyzed. To conduct the test, a plastic tube is used, into which the patient breathes for several minutes, and then a carbide solution is injected. Comparing the air that was before contact with urea and after, appropriate conclusions are drawn. This analysis is completely safe and is carried out during the initial diagnosis and quality control of anti-helicobacter therapy.

For the diagnosis of intestinal cancer using a chromato-mass spectrometer, it is possible to use the analysis of the air exhaled by a person. Air analysis is also used to diagnose malabsorption.

Features of medical oxygen in treatment

Medical oxygen is a transparent, odorless natural gas. Under conditions of normal atmospheric pressure, at a general temperature of -183° Celsius, the substance becomes liquid, and at -219° - solid. How does technical oxygen differ from medical oxygen used for medical therapy?

Medical oxygen is a ready-made concentrated substance, free from foreign impurities. It is delivered to specialized medical clinics in the form of balloons. The cylinder with medical oxygen is subjected to strict tests and checks for the presence of other gaseous impurities in them, as well as the containers themselves for storing the substance are checked directly. For this reason, the cost of medical oxygen is an order of magnitude higher than technical oxygen.

It is used for inhalation in conditions accompanied by oxygen deficiency: diseases of the respiratory tract (pneumonia, bronchial asthma), cardiovascular system, surgical operations, poisoning with carbon monoxide, hydrocyanic acid, chlorine, phosgene, etc.

Medical gaseous oxygen is produced in accordance with the requirements of regulatory documentation (GOST 5583-78). For medical purposes, it is obtained from atmospheric air by the method of low-temperature rectification. Medical oxygen is delivered to the pharmacy chain in blue steel cylinders, on which the inscription "Oxygen" is written in black paint, which indicates that this gas is intended for medical purposes. Packaging: 2 1, 3 1, 4 1, 5 1, 6 1, 7 1, 8 1, 9 1, 10 1, 12 1, 40 1 in cylinders

INERT GASES IN MEDICINE

Action on the human body.

It would be natural to believe that noble gases should not affect living organisms, because they are chemically inert. However, this is not entirely true. In a mixture with oxygen, inhalation of higher inert gases leads a person to a state similar to alcohol intoxication. This narcotic effect of inert gases is due to their dissolution in nervous tissues. And the higher the atomic weight of an inert gas, the higher its solubility, and the greater the narcotic effect it is capable of providing.

Field of application of inert gases.

Helium- a source of low temperatures. Helium is the most common element in space after hydrogen, its presence in the atmosphere of the Sun, stars, and meteorites has been proven by spectral analysis.

Since 1930, inert helium gas has been used in medicine as part of respiratory gas mixtures with oxygen. To date, more than 500 scientific works and the results of international studies have been published on the use of helium-oxygen mixtures in pulmonology, diving and sports medicine, as well as during the correction of emergency conditions. Due to its low density, the oxygen-helium mixture affects the

ventilatory function of the lungs, contributing to the regression of obstructive disorders. Helium inhalation optimizes the activity of the respiratory center, improves oxygen diffusion through the alveolar-capillary membrane, reduces breathing resistance and relaxes smooth muscles. Helium reduces the viscosity of sputum and the load on the respiratory muscles. This method of treatment makes it possible to effectively fight respiratory failure and help patients with chronic obstructive pulmonary disease, bronchial asthma, pneumonia, acute and chronic congestive heart failure.

It is also important to note the use of an oxygen-helium mixture as a kind of "transport" (carrier gas) for the delivery of an inhaled drug into the respiratory tract. Helium is well tolerated, does not cause side effects and makes it possible to significantly improve the condition of patients.

Argonwidely used in production.

Argon is the most common noble gas on Earth.

Arc electric welding in argon is very convenient, because thin-walled products and metals that were previously considered difficult to weld can be welded in an argon jet. By blowing argon through the liquid steel, gas inclusions are removed from it. This improves the properties of the metal. Argon (mixed with hydrogen) blown along the column of the arc protects the edges of the cut and the tungsten electrode from the formation of oxide, nitride and other films. At the same time, it compresses and concentrates the arc on a small surface, due to which the temperature in the cutting zone reaches 4000-6000° C. And when welding in an argon jet, there is no need for fluxes and electrode coatings, and therefore, for cleaning the seam from slag and flux residues.

Xenon

Xenon is actively used in medicine - for a long time it was used as the most effective and safest anesthesia during operations. Since 2010, after long studies, permission was obtained for the use of xenon-oxygen mixture inhalations (xenonotherapy) in therapeutic practice. This method of treatment is used to relieve stress, anxiety and depressive disorders, to relieve pain syndrome of various genesis, rehabilitation after heart attacks, strokes and difficult surgical interventions.

Medical xenon is used in almost all branches of modern medicine:

- It is actively used in pediatric anesthesiology as an effective and safe anesthetic.

- In cardiology for the treatment of heart rhythm disorders and ischemic heart disease.

- In therapy - for the treatment of bronchial asthma, irritable bowel syndrome, gastric ulcer, as well as various autoimmune diseases accompanied by pain syndrome.

- Dermatologists and cosmetologists use xenon inhalation to treat neurodermatitis, female alopecia, and acne.

- For neurologists, xenonotherapy is an effective method of combating panic attacks, neurotic disorders, as well as treating sciatica and headaches.

- The use of medical xenon helps during rehabilitation after a stroke, as well as in the complex treatment of tremors and impaired muscle tone due to Parkinson's disease.

- In psychiatry, xenonotherapy is used to combat depression, stop the withdrawal syndrome in case of drug or alcohol addiction.

- Xenon was also used in sports medicine to restore physical strength after exhausting training; however, since 2014, inhalation of xenon has been recognized as doping, and it is not allowed to be used by athletes; which also indicates its effectiveness.

- Active use of xenon was also found in dentistry. Indications for the use of this gas in dental practice are quite broad - it is stress relief before a dental appointment, relief of spasm of masticatory muscles, and for the prevention of pain syndrome, and in the treatment of bruxism. Xenonotherapy is especially effective for dentophobia - panic fear of dental treatment. Until recently, the only way to treat dentophobia was general anesthesia, but its use has a number of disadvantages: it cannot be used often and for a long time. Against the background of xenon inhalation, patients easily and comfortably tolerate not only therapeutic ones.

- Medical xenon has analgesic (analgesic), antidepressant, anxiolytic (antianxiety) and myorelaxant (one that relaxes muscle tone) effects. The action of xenon is carried out by temporarily blocking NMDA-glutamate receptors, which are involved in the process of pain syndrome transmission. By affecting the reticular formation, xenon activates the antinociceptive (antipain) system, which inhibits the activity of the neurons of the posterior horns of the spinal cord and thereby produces an analgesic effect. The anti-anxiety and anti-depressant effect of xenon is due to the effect on inhibitory mediators and a decrease in the level of hormones of body systems that implement stress.

Control materials for the final stage of the lesson. Questions to check the final level of knowledge:

- 1. Solubility of gases in liquids and its dependence on various factors.
- 2. Henry-Dalton law.
- 3. Sechenov's law
- 4. Solubility of gases in blood. Bends.
- 5. Air, its composition.
- 6. Analysis of the composition of exhaled air for diagnostic purposes.
- 7. Medical oxygen
- 8. Oxygen therapy.
- 9. Singlet oxygen therapy, ozone therapy.

10. Noble gases in medicine.

- 11. Xenon, production of medical xenon.
- 12. Radonotherapy.

Literature:

Main:

1.Medicinal chemistry: a textbook (University I-III years) / V.P. Muzychenko, D.D. Lutsevich, L.P. Yavorska; under the editorship B.S. Zimenkovsky. — 3rd ed., edition, 2018 – 496 p. (p. 23-31).

2.Poretsky A.V., Bannikova-Bezrodna O.V., Filippova L.V. Medicinal chemistry: Textbook. — K.: VSV "Medytsina", 2012. — 384 p.

1. General anesthesia. Inhalation and non-inhalation anesthesia. Indications and contraindications. Complications and their prevention: method. order to practice occupations and independence. works of students of the 3rd year of II and IV med. facts from the discipline "General surgery" / edited by V. O. Syplivy, G. D. Petrenko, V. V. Dotsenko and others. – Kharkiv: KhNMU, 2020. – 24 p

2. Ozone therapy in veterinary practice:educational and practical manual / M.G. Ilnitskyi, R.V. Podborska – Bila Tserkva, 2018. – 50 p.

3. Chepkiy L.P., Novytska-Usenko L.V., Tkachenko R.O. Anesthesiology and intensive care. - K., "Health".-2003. - 399 p

Practical lesson 7

<u>Topic</u>: Surface-active substances and their importance in human life. Chemistry of surfactants and detergents (synthetic detergents, shampoos, gels, bath foams).

- **Goal:** providing students with an idea of the main properties of solutions of colloidal surface-active substances (surfactants) surfactants and detergents in aqueous solutions, processes of micelle formation and their driving forces, solubilization, the mechanism of surface tension reduction and washing action. Familiarization with the most important fields of use of surfactants in medicine and pharmacy, in particular for the modification of surface (interfacial) layers. The goal is also to get acquainted with certain types of complex surfactants, primarily polymers and phospholipids, as well as the processes of micelle formation in organic, in particular, nonpolar solvents, where inverse micelles and microemulsions are created.
- **Basic concepts:** micellar surfactants, surfactants, detergents, foaming, phase inversion. **Equipment:** Laboratory of the department

Plan:

<u>1. Organizational measures(greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).</u>

2. Control of the reference level of knowledge:

- Rules for performing laboratory work.
- Methods of experimental data processing.
- Surface tension, surface energy.
- Surface activity. Duclos-Traube rule.
- Lyophilic and lyophobic dispersion systems.
- 3. <u>Requirements for students' theoretical readiness to perform practical classes:</u>

PLAN:

- 1. Colloidal surfactants.
- 2. Classification of colloidal surfactants.
- 3. Causes of micelle formation.
- 4. Critical concentration of micelle formation.
- 5. The structure of South African micelles.
- 6. Solubilization.
- 7. Use of colloidal surfactants
- 8. Twines, surfactants, enzymes, detergents.

Colloidal surfactants

Classifying dispersed systems, we divided them into two groups - lyophilic and lyophobic (reversible and irreversible). Typical representatives of lyophilic dispersion systems are solutions of colloidal surfactants.

Colloidal surfactants 56 are called surfactants capable of forming micellar systems. The properties of surfactants are determined by the diphilicity of their molecules. Special characteristics are observed in long-chain surfactants with the number of carbon atoms nC - 10 - 20, which are characterized by an optimal balance of hydrophilicity and hydrophobicity.

At low concentrations, they form true solutions, with an increase in concentration, the process of association of molecules occurs and micellar systems are formed.

Micellar surfactant solution is a thermodynamically stable, balanced and reversible system. Surfactant micelles, unlike micelles of lyophobic sols, are thermodynamically stable and do not change until the equilibrium in the system is shifted under the influence of external factors.

Classification of colloidal surfactants

According to their ability to dissociate, surfactants are divided into ionic (anionic, cationic, amphoteric) and nonionic.

In anionic surfactants surface-active ions are negatively charged. These include alkaline salts of fatty acids (soap) - RCOOMe, alkyl sulfates-sulfoethers of higher alcohols and their salts of the R-O-SO3-Me type; alkyl and arylsulfonates R-O-SO3-Me - alkali salts of high molecular weight sulfonic acids, where R denotes a hydrocarbon radical of the typeCnH2n+1with the number of carbon atomsC10–C20, and Me - Na+ ions, K+, NH4+.

Cationic surfactants- these are salts of amines, quaternary ammonium bases, alkylpyridine compounds [RN+H3]Cl [R(CH3)3N+]Cl; [RN+-C6H5]Cl-.

Surface-active ions of such substances are positively charged.

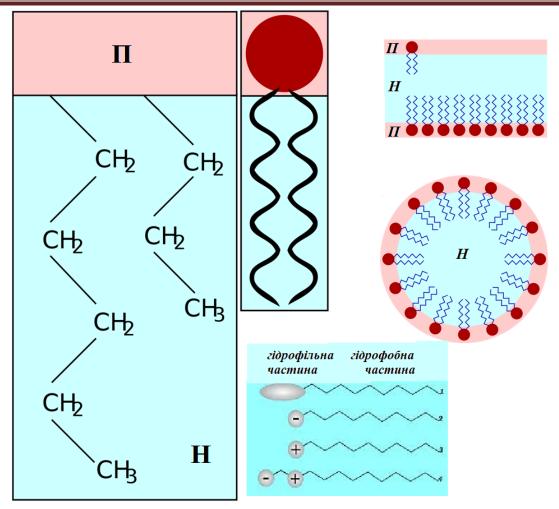
Amphoteric surfactants- these are alkylamino acids RN2COOH, sulfobetaines, etc. Depending on the pH, they show anionic or cationic properties.

Nonionic surfactants do not dissociate into ions. They are obtained by the interaction of ethylene oxide with alcohols, phenols, fatty acids and other compounds with polar groups. The general formula of nonionic surfactants is R(OCH2CH2)mOH. Hydrophilicity is determined by the length of the oxyethylene chain.

An important characteristic of a colloidal surfactant solution is the ratio of hydrophilic and hydrophobic properties, which is determined by the number of HLB. Depending on the number of HLB, colloidal surfactants are used as hydrophobic emulsifiers (3 - 6), wetting agents (7 - 9), detergents (13 - 15), hydrophilic emulsifiers (8 - 18).

Causes of micelle formation

The thermodynamic driving force of micelle formation in aqueous solutions of colloidal surfactants is hydrophobic interactions: the hydrocarbon part of the diphilic molecule is pushed out of the aqueous medium to avoid contact of the chain with water. As a result, micelles are formed, the inner part of which consists of liquid hydrocarbon (connected, densely packed hydrocarbon chains), and the outer part, facing water, consists of polar groups.



List of recommended literature:

<u>Main:</u>

1. Medical chemistry: a textbook / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others. ; under the editorship V.O. Kalibabchuk. - K.: VSV "Medicine", 2019. - 336 p.

2. Medical chemistry: textbook / V.P. Muzychenko, D.D. Lutsevich, L.P. Yavorska ; under the editorship B.S. Zimenkovsky. – 3rd ed., corr. - K.: VSV "Medicine", 2018. - 496 p.

3. V. I. Homonai Medical chemistry: a textbook / V. I. Homonai, S. S. Milovych – Vinnytsia: Nova kniga, 2016. – 672 p.

Practical lesson No. 8

<u>Topic:</u> High molecular compounds. Properties and features of biopolymer solutions. The use of solutions of the polymers in medical practice.

Actuality of theme

Without such high-molecular compounds as proteins, polysaccharides and nucleic acids, it is impossible to imagine the functioning of a living being. Biopolymers in the body perform the following most important functions: they catalyze biochemical processes, store and transmit genetic information, perform protective, support and structural functions, participate in blood clotting, are reserve nutrients, maintain the oncotic pressure of blood plasma.

When blood pH changes, proteins change their charge, and their structure and functions are disturbed. During starvation, protein does not come with food, with liver diseases, the formation of protein is disturbed, with kidney diseases, protein is lost in the urine. In these cases, the protein content in the blood and the oncotic pressure of the blood plasma decrease, therefore, water from the bloodstream enters the surrounding tissues - edema is formed. Artificial and synthetic polymers are used in medicine and pharmacy. They are used to make tooth and gum prostheses, tissue substitutes, blood plasma, blood vessels, and bones. They are also used in the "artificial kidney" device, etc. Polymers are used for the production of modern dosage forms, prolonging the action of drugs in the body.

- **Goal**: to study the general characteristics of the HMC, to get an idea of the structure of the HMC, to study the biological role and application of the most important solutions of the HMC, to interpret the physicochemical properties of proteins that are structural components of all body tissues, to form students' systematic knowledge about the physicochemical properties of HMC solutions, application in medicine, draw conclusions about the charge of dissolved biopolymers based on their isoelectric point.
- **Basic concepts:** HMC, biopolymers, solubility of polymers, viscosity, optical properties of HMC, molecular kinetic properties, isoelectric point, structure of biopolymers.

Equipment: Laboratory of the department

Lesson plan and organizational structure:

1. Classification of solutions.

2. Natural high-molecular compounds.

3. Structural organization of biopolymers.

4. Comparative characteristics of solutions of HMC, true and colloidal solutions.

5. Swelling and dissolution of polymers.

6. Properties of solutions of HMC.

7. Ionic state of biopolymers in aqueous solutions. Isoelectric state of proteins.

8. Teasing. Properties of gels.

9. Abnormal viscosity of solutions of the polymers. Blood viscosity.

10. Donnan's membrane equilibrium.

The student should be able to and know:

1. Classification of polymer solutions.

2. Peculiarities of dissolution of polymers.

3. Peculiarities of the structure of the molecules of HMC, anomalous properties of polymer solutions.

4. Swelling. What characterizes the degree and speed of swelling.

- 5. What is the effect of different electrolytes on the degree of swelling
- 6. Limited and unlimited swelling.
- 7. According to what principle are ions arranged in lyotropic series?
- 8. Thermodynamic functions during involuntary dissolution of the HMC
- 9. To characterize the types of viscosity of solutions of the polymers

10. Swelling pressure. Pozdniak's equation.

11. Isoelectric point of gelatin. Isoelectric state of a protein molecule.

- 12. The concept of syneresis. Its biological significance.
- 13. Methods of determining IET protein
- 14. What methods can be used to determine the molecular weight of a polymer?

Lesson content

The modern era is often called the age of atoms and polymers. The penetration of synthetic fibers, plastics, elastomers into all spheres of human activity led to the rapid development of modern chemistry of high molecular weight compounds (HMC).

High molecular compounds include compounds with a molecular weight of about $10^4 - 10^6$ and higher. They can be both of natural origin (proteins, nucleic acids, polysaccharides, natural rubber, etc.) and synthetic, obtained in the processes of polymerization or polycondensation (polymers, synthetic fibers, etc.)

Classification of the Navy

By origin, polymers are classified as:

- natural (biopolymers) - proteins, carbohydrates, nucleic acids, etc.

- synthetic - polyethylene, polypropylene, synthetic fibers - nylon, polyacrylic, etc. They are widely used in medicine, in particular in surgical practice as equivalents of various organs and tissues, bones, joints; as substitutes for blood, blood plasma; when designing devices for an artificial kidney, liver, and heart.

- artificial - rubber, gutta-percha, cellulose acetate.

According to the method of receipt:

- polymerization - polyethylene (-CH₂-CH₂-)_n.

- condensation - for example, a protein is a condensation biopolymer, because the interaction of the carboxyl and amino groups creates a peptide bond with the release of a water molecule.

By chemical composition:

- homopolymers;

- copolymers.

By spatial structure:

- linear - (rubber, cellulose)

- branched - (starch fraction - amylopectin, some synthetic fibers).

- mesh or spatial - (glycogen, globular and fibrillar proteins).

From the point of view of interaction with biological environments, synthetic materials used in medicine can be divided into two groups: bioresorbable and biocompatible. Bioresorbable materials are able to perform the functions of lost tissues for some time, then they are gradually dispersed and removed from the body. For the prosthetics of internal organs, biocompatible materials are used, which remain in the human body until the end of his life. Being in constant contact with blood, they must be hemocompatible and thromboresistant.

IUD molecules, like colloidal particles, consist of many thousands of atoms. This explains the similarity of some properties of IUDs and colloidal solutions, but there are also significant differences.

High molecular compounds are characterized by such important specific properties as high plasticity and elasticity. Practically all important properties of the Navy are related to their structure (linear, branched and spatial).

<u>Linear</u> polymers are built from long chains of monomers. Branched polymers have chains with side branches. This is how starch and glycogen molecules are built. Spatial polymers are a three-dimensional network, which is formed when a segment of chains is connected by chemical bonds.

The specific properties of polymers are due mainly to two features:

1. The existence of two types of bonds - covalent (valent) and intermolecular, which hold macromolecular chains close to each other;

2. Rotation of fragments (links) of the carbon chain along σ bonds. Due to rotation along the σ -bond, the chain takes different conformations (globules, balls, stretched forms). Polymers with flexible macromolecules are easily deformed and return to their original state after removing the load, that is, they have elastic properties. The flexibility of polymer chains depends on many factors, including the structure of the chain, the nature of substituents, their number and distribution along the chain, and the number of links in the chain. In addition, the flexibility of the polymer is affected by temperature, environment, and the nature of the solvent.

Natural high molecular weight compounds

The most important polymers found in a living organism are proteins, polysaccharides, and nucleic acids.

Protein molecules are formed by polycondensation of α -amino acids, connected by peptide bonds. There are about 5 million different proteins in the human body, which differ in the sequence of amino acid combinations, as well as the spatial structure of the chains.

Polysaccharides are formed by polycondensation of monosaccharides, mainly glucose and some of its derivatives. In the liver and muscles there is animal starch - glycogen, the monomer of which is α -glucose. An important role in the body is played by heteropolysaccharides of connective tissue (hyaluronic acid, heparin, chondroitin sulfate), formed from the remains of various glucose derivatives.

Nucleic acids are polymers of nucleotides, which in turn consist of a nucleic base (uracil, thymine, cytosine, adenine, guanine), one of two monosaccharides - ribose or deoxyribose, and phosphoric acid. If ribose is part of the polymer molecules, ribonucleic acids (RNA) are formed, and if deoxyribose is deoxyribonucleic acids (DNA).

Comparative characteristics of the solutions, true and colloidal solutions

Solutions of HMC, as well as solutions of low molecular weight compounds (MMC), belong to true solutions, since the dissolved substance is in the form of molecules and ions (for electrolytes). In this regard, solutions of HMC are homogeneous, thermodynamically stable systems, although their physical and chemical properties are close to typical colloidal solutions. Unlike colloidal systems, which are lyophobic, solutions of biopolymers are lyophilic.

Solutions of HMC are formed involuntarily - without the need to add a third component - a stabilizer.

IUD solutions and colloid solutions have some features in common:

- a kind of thermal motion similar to Brownian motion;
- low diffusion rates;

 \triangleright

➤ - macromolecules do not pass through animal and plant membranes, as they do not dialyze;

- small value of osmotic pressure;

slower flow of all kinds of physical and chemical processes;

- increased desire to form various molecular complexes;

 \succ - the ability to coagulate and peptize under the influence of external factors.

precipitated during centrifugation;

diffuse light well;

 \succ the phenomenon of electrophoresis is observed for solutions of IMC - electrolytes;

However, the Navy's solutions have their own specific properties. Owing to the large molecular weight, HMCs are non-volatile and incapable of distillation. Their molecules are relatively easily split under the influence of various factors, which leads to a change in the properties of the polymer:

- they swell and through the swelling stage form true solutions. The latter made it possible to classify lyophilic colloids as true solutions;

- solutions of HMC have high viscosity and can easily gelatinize;

- with a change in temperature, pressure and concentration, reversible processes are carried out in them;

- a high degree of stability of solutions without the introduction of a stabilizer.

The ease of dissolution of most biopolymers and the stability of solutions is due to the presence of a large number of lyophilic groups in their structure (hydrophilicity is due to affinity for water). They can be dissociating ionogenic groups:

-COOH, -COONa, -NH₃OH, -NH₃Cl

or non-dissociating polar groups:

Polar groups attract water molecules, which form a continuous or almost continuous water shell near the macromolecules of the IUD. It was established that one carboxyl group holds four water molecules. Less polar substituents, such as -OH, $-NH_2$ – three water molecules.

The hydrophilicity of such natural biopolymers as proteins, polysaccharides, phosphatides is due mainly to peptide (-NH-C=O) and ester bonds, as well as carboxyl,

carbonyl, alcohol and amino groups. Peptide bonds are most important for protein hydration, due to which 2/3 of all hydration water is bound.

IVM solutions differ from HMS solutions:

- \checkmark by the dissolution mechanism;
- ✓ lower osmotic pressure (under conditions of isomolarity);
- ✓ abnormally high viscosity;
- \checkmark under certain conditions form jelly;

 \checkmark the slow attainment of equilibrium due to the low rate of diffusion of macromolecules.

Properties of the rheologies of the solutions of the Navy

The viscosity of solutions of HMC is much higher than that of true solutions and sols of the same concentration.

Anomalous viscosity is a characteristic feature of HMC solutions, due to the cohesive forces of structured systems.

The viscosity increases in proportion to the asymmetry of the molecules, the increase in the molecular weight of the HMC, if the chemical structure is the same (in the homologous series), it depends on the concentration and fluidity.

In 1922, Bingham introduced the term "plastic flow" because, during flow, the structural grids are destroyed as a result of the different velocities of the layers in the flow. The more structured the system, the more viscosity.

Types of viscosity of solutions of HMC

For Navy solutions, the following are distinguished:

1. Relative viscosity:

$\eta_{\text{relative}} = \eta / \eta_0 = 1 + \beta \nu$

where η - solution viscosity; η_0 - solvent viscosity; ν - volume fraction of the polymer; β is a coefficient depending on the shape of the particles.

2. Specific viscosity

$\eta_{\text{question}} = \eta - \eta_0 / \eta_0$

Staudinger derived the formula for the specific viscosity of dilute solutions of rigid rod-shaped IUDs:

$\eta_{ ext{question}} = ext{KM}_{ ext{S}}$

where: M is the molecular weight of the polymer; C is the mass concentration of the polymer; K is the constant of the polymer homologous series

3. Reduced viscosity

$\eta_{\text{question}}/\text{C} = \text{KM}$

The resulting viscosity does not depend on the shape of the molecules.

4. Characteristic viscosity

$[\eta] = \lim[\eta_{\text{question}}/C]C \rightarrow 0$

This is the reduced viscosity at a concentration tending to zero. Determined graphically by extrapolation to zero concentration or can be calculated using the Mark-Kuhn-Hauwink equation:

$[\eta] = KM_B$

where v is a coefficient depending on the shape of the molecule.

This coefficient for flexible molecules has an insignificant value, and for rigid molecules it tends to unity. By viscosity, the molecular weight of the polymer can be found by the viscometric method.

Optical properties of solutions of HMC

Solutions of HMC scatter light, the Tyndall effect is observed, although to a lesser extent than with sols.

In addition to light scattering, IMC solutions can also selectively absorb light, like true solutions.

Some solutions are characterized by optical anisotropy. This phenomenon is observed in solutions with elongated, deformable molecules.

Double refraction is given by solutions of polymers due to the fact that the optical axes of individual links of macromolecules are located in space at different angles and as a result of the difference in the refractive indices of the solvent and the IMC.

Photoelastic anisotropy, which occurs as a result of deformation of polymer particles, is the most characteristic of VMS solutions.

Debye proposed a method for determining the molecular weight of a polymer by measuring turbidity:

τ =HMC

where H is a coefficient depending on the refractive indices of the solvent and solution, the wavelength of the incident light, and the osmotic pressure.

The molecular weight of polymers can be determined graphically.

Molecular-kinetic properties of solutions of HMC

Diffusion speed is low in the polymer's solutions. Polymer solutions sediment only during ultracentrifugation. Equilibrium is established for a long time.

In contrast to sols, the osmotic pressure of IMS solutions is high, since flexible molecules behave as several short ones. Van't Hoff's equation is valid for dilute solutions of VMS.

As the concentration of the solution increases, deviations from the Van't-Hoff equation are observed, and Haller's equation must be used:

$\pi = CPT/M + BK2$,

where B is a constant that depends on the nature of the solvent and the polymer.

This is an accurate method. It can be used to determine the molecular weight of IUDs.

Questions to check the final level of knowledge:

1. What is the dependence of HMC dissolution on the structure of their molecules?

2. What is the relationship between the stability of HMC solutions and the features of their storage?

3. Define and characterize the polymers.

4. Give the classification of the polymers.

5. The influence of the structure of the HMC molecule on the process of dissolution of substances.

6. List the factors that cause a violation of the stability of IUD solutions.

7. Name the features of preparing solutions of limited swelling IUDs.

8. Describe colloidal solutions. List their properties.

9. Classification of polymer solutions.

10. Swelling. What characterizes the degree and speed of swelling?

11. What is the effect of different electrolytes on the degree of swelling?

12. What is meant by limited and unlimited swelling?

13. According to what principle are ions arranged in lyotropic series?

14. How do the thermodynamic functions change during the involuntary dissolution of the IUD?

15. What is swelling pressure? Pozdniakov's equation?

16. Isoelectric point of gelatin. Isoelectric state of a protein molecule.

17. What is syneresis? Its biological significance.

18. What methods can be used to determine the molecular weight of a polymer?

19. What methods are used to determine the number average molecular weight? Average molecular weight?

20. Analyze the Staudinger equation. How to determine the characteristic viscosity of a polymer solution?

21. How does the salting out mechanism of polymers differ from the coagulation mechanism of colloidal solutions?

literature

Main:

1. Medicinal chemistry: a textbook for universities / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others; under the editorship of Prof. V.O. Kalibabchuk - K. VSV "Medicine", 2013 - 328p.

2. Kharchenko S. V. Medical chemistry. – Poltava: Poltava Litterator, 2014. – 212 p. (p. 190 - 198).

3. Gubsky Yu.Sh. Biological chemistry. Kyiv-Ternopil: Ukrmedknyga, 2000

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Practical lesson No. 9

<u>Topic</u>: Polymers for medical and biological applications: structure and functions. Medical and pharmaceutical application of polymeric materials

Actuality of theme

The use of synthetic polymers in medicine is due to the unique complex of their physico-chemical and physico-mechanical characteristics, the possibility of modification within wide limits. In some cases, synthetic polymers are indispensable materials specifically for medicine, when without special polymer compositions it is impossible to solve this or that specific problem by other known methods.

- **Goal**: to study the general characteristics of biomaterials, their classification, to have an idea of the contact between polymer materials and tissues of a living organism, to form students' systematic knowledge of the physicochemical properties of biopolymers, to know polymers used in surgery, dentistry, therapy, and medical applications.
- **Basic concepts:** biopolymers; polymers in surgery, traumatology, orthopedics; polymer coatings, medical fibers, prolongation, polymers as blood substitutes, the structure of biopolymers.

Equipment:

Laboratory of the department

Lesson plan and organizational structure:

1. Classification of polymeric materials (by purpose, origin, source, use, structure, ability to be implanted in bone tissue).

- 2. Biocompatibility of polymers
- 3. General basics of the interaction of biological tissues and biological fluids
- 4. Useful polymers for biomedical applications
- 5. Cleaning, sterilization and disinfection of polymers and polymer products

from them.

- 6. Polymers in surgery, traumatology, orthopedics.
- 7. Polymer coatings for affected areas of the skin
- 8. Medical fibers
- 9. Polymers are drug carriers.
- 10. Prolongation. Prolonging substances
- 11. Polymers as blood substitutes. Groups of blood substitutes. Indications for

use

The student should be able to and know:

1. Polymers used in medical practice.

2. Classification of polymer materials.

3. Sterilization, cleaning and disinfection of polymer materials.

4. Polymers used in reconstructive surgery, cardiovascular surgery, traumatology and orthopedics, ophthalmology

- 5. Polymer devices for targeted drug delivery
- 6. Polymer suture materials and polymer adhesives for medical purposes
- 7. Concepts of "prolongers", "blood and plasma substitutes"
- 8. Basic requirements for materials for medical and biological use
- 9. Methods of determining biological compatibility of polymers.

Lesson content

The beginning of the use of polymer materials in medicine can be considered 1788, when the famous Russian doctor A.M. Shumlyansky used rubber. Frankel (1895) was the first to use the artificial polymer celluloid to close skull defects (alloplasty).

Biomaterials, natural and synthetic materials intended for the creation of products, devices and preparations used in medicine, biotechnology, agriculture, cosmetology, etc., and which are used to ensure and optimize the vital activity of humans, animals, plants, and microorganisms. Biomaterials function in direct contact with living tissues and cellular objects.

The largest areas of application of biomaterials are the production of medical implants, including those intended for introduction into the cardiovascular (endoprostheses of blood vessels, valves and the whole heart, etc.) and bone (endoprostheses of joints and bone fragments, fastening parts, glues and cements), ophthalmic implants, suture materials, etc.; drugs with different types of biological activity; materials for separation and purification of biological liquid tissues and environments; polymer systems for cultivating and growing cell and tissue cultures.

Depending on the field of application, biomaterials can be used to create highstrength products, elastic and gel systems, as well as water-soluble drugs.

Classification of biopolymer materials

1. Classification of biomaterials by purpose

All polymer materials used in medicine are divided into 3 groups according to their purpose.

I group- polymeric materials intended for introduction into cavities, tissues and blood, in particular for long-term or permanent stay in the body. These polymers are used in surgery, transplantology, transfusion of blood and blood substitutes, pharmacology.

In turn, they can be divided into several subgroups:

1) internal prostheses, fillings, artificial organs;

2) fabric glues;

3) suture and dressing material;

4) plasma and blood substitutes, detoxifiers, interferonogens, antidotes;

5) medicinal preparations made on the basis of polymers, in particular ionites;

6) polymers used in the technology of dosage forms (protective films, capsules and microcapsules, auxiliary substances, etc.).

2nd group- polymer materials that come into contact with the tissues of the body, as well as with substances that enter it, which are not introduced into the body for a long time, namely:

1) containers for packaging and storage of medicines, blood, blood and plasma substitutes;

2) polymers used in dentistry (except fillings);

3) contact lenses;

4) surgical instruments, syringes;

5) nodes and details of medical devices and devices, in particular semipermeable membranes.

3rd group- polymeric materials that are not intended for introduction and do not come into contact with substances introduced into the body. Products from polymer

materials of this group are most widely represented in medical everyday life, since all products that are not included in the first two groups belong to the 3rd group.

In the sense of hygienic characteristics, the greatest attention should be paid to polymer products of the 1st group. As mentioned, polymer materials of this group are intended for implantation in the human body for different periods.

Polymer materials for prosthetics of internal organs are subject to very strict requirements. The most important of them are the long-term preservation of the main physico-chemical and mechanical properties under the influence of the enzymatic system of a living organism, as well as biological inertness, which causes easy adaptation of the organism to the implant.

Group 2 materials, as well as implantable polymers, must have the following properties.

1. The composition of the polymer material should not include substances with toxic and cumulative properties, specific (carcinogenic, mutagenic, allergenic, etc.) effect on the body.

2. Products made of polymeric materials of the 2nd group during contact with body environments should not change the organoleptic and physicochemical properties of these environments.

3. Polymeric materials should not emit chemicals included in the formulation of the material in excess of permissible migration amounts (DKM).

4. Polymeric materials should not stimulate the growth of microorganisms.

5. Physico-chemical, organoleptic, and mechanical properties of the product, as well as its appearance, should not change during use with the environment of the body.

In ophthalmology, contact lenses are made from polymer materials of the 2nd group.

Polymers of the 3rd group, which are not introduced into the body and do not come into contact with substances introduced into the body, are subject to the same requirements as those for household materials.

2. Classification of biomaterials by origin and sources of production:

- \checkmark automaterials (from the body's own tissues);
- ✓ allomaterials (from body tissues of one biological species);
- \checkmark xenomaterials (from body tissues of another biological species);
- ✓ heteromaterials (foreign materials).

3. Classification of biomaterials by use:

• without violation of tissue integrity - catheters, stents;

• with a violation of tissue integrity - a large part of implants, surgical suture material.

4. Classification of biomaterials by structure:

- ➤ solid;
- liquid (injectable).

5. Classification of biomaterials implanted in bone tissue: biotolerant, bioinert and bioactive.

<u>Biotolerant</u>materials are incorporated into bone through the mechanisms of distant osteogenesis. At the same time, they separate from the bone tissue and sprout a massive fibrous layer. As an example of such substances can be methacrylates or vitalium, PMA, vitamins.

<u>Bioinert</u>the materials practically do not interact with the surrounding tissues, do not cause the formation of a pronounced fibrous layer and stimulation of osteogenesis. At the same time, the bone can be formed in the immediate vicinity of the surface of the implant. An example of such compounds can be metal ceramics made of titanium oxide, vanadium, zirconium and aluminum. Bioinert materials, as a rule, have a protective layer on their surface that prevents the exit of ions from the implant and the penetration of aggressive molecules from the surrounding biological fluid into it

By bioactive materials (BAM) we mean biomaterials intended for linking them with biological systems in order to increase the effectiveness of treatment, education or replacement of any tissue or organ in the performance of certain functions of the body.

A very important property of bioactive polymers is their ability to biodegrade. Ideally, such polymers live in the human body exactly as long as it is necessary to achieve a therapeutic effect, and then disappear, without accumulating in the body and completely disappearing, like other products of vital activity. Orthopedic fixation and suturing of wounds were the first motives for the introduction of biodegradable polymers into medical practice.

Since the 1990s, vascular stents made of biodegradable polymers have been used. Biodegradable polymers are used for drug delivery. For many applications, hydrolytically degradable synthetic polymers are preferred, which have great advantages for use as implants or carriers that gradually release drugs into the bloodstream, as this biodegradation varies little from one individual patient to another or from the location of the implant in the body. In contrast, enzyme-catalyzed degradation of biopolymers is extremely specific. A similar biodegradation pathway is widely used in tissue bioengineering or to replace supracellular matrices. Regarding

the body's immune response to biopolymers and the limited reproducibility of their properties in the process of obtaining from one act of excretion to another, which causes a change in their properties, synthetic polymers have an indisputable advantage.

Biocompatibility of polymers

It is clear that the basis for any applications of polymers are their properties. For medical applications, the defining property is their biocompatibility. The term "biocompatibility" itself is not so easy to precisely formulate, since this term is associated with the specific features of using the material for specific applications. Biocompatibility is related to the specific interaction of the polymer material with biotissues of a living organism, its specific enzymes and biological fluids, including blood, and, ultimately, with the ability of products or devices made of this material to be adopted in the body of the recipient. At the same time, in some cases active interaction of the material with biotissues is required, in other cases its maximum inertness is required. The effect of a living organism on the material introduced into it can be very different and cause its decomposition, absorption or simply inclusion in living tissue. At the same time, the material can affect living tissues, causing inflammation, fouling, etc. Although in each case it is necessary to specifically investigate the process of the interaction between a living organism and a polymer, the nature of this interaction can be divided into three general categories: polymer stability, interaction of the polymer with biological fluids, and compatibility with blood.

Biocompatibility- the ability to perform a certain function for the required time without harming the surrounding tissues and the body as a whole; such materials are called biocompatible or biocompatible. The exception is biomaterials that are components of drugs with biocidal or inhibitory activity.

The field of application of biocompatible polymers is extremely wide. Reinforced and non-reinforced elastic sheet materials are made from them for defective organ walls or entire hollow organs, such as tracheas and esophagus. The use of connecting elements in the form of sheets or thin films that can gradually dissolve in the body, applied to the resected areas of internal organs, ensures the necessary tightness of the wound surface, reduces or completely eliminates the risk of adhesions. Important features of such connecting elements are minimal injury and deformation of the tissues adjacent to them, which creates good prerequisites for the restoration of organ functions.

In combination with a bioinert base, biocompatible polymers are used in the creation of artificial vessels. Various connecting elements have been created from biocompatible polymers, which make it possible to solve the problem of connecting segments of hollow organs (vessels, intestines, esophagus) and connecting them with prostheses in a fundamentally new way. Connecting elements in the form of pins will

make it possible to replace metal pins that are used to fix bone fragments that require repeated surgical operations to remove these pins.

The use of biocompatible foaming compositions for filling residual cavities in the body is promising during lung operations, for filling fistulas, empyema cavities, caverns and in a number of other cases. Such compositions in the form of liquids are introduced into the cavity using a syringe, bronchoscope or another method, and then foamed and solidified. Radiopaque additives or special drugs are added to the filler polymer. Fibers from biocompatible polymers are used as absorbable sutures. Biocompatible materials also include promising polymer adhesives for use in surgery. Interest in adhesives in medicine is growing steadily. A positive feature of cyanoacrylate adhesives, used for joining soft tissues of the body, is the ability to gradually dissolve in tissues, characteristic of all biocompatible materials. Adhesives can be used both individually and in combination with connecting elements made of biocompatible polymers.

Biocompatible polymers are used not only in restorative surgery. On their basis, new highly effective means for the treatment of eye diseases have been created in the form of polymer films that contain drugs and are placed in the conjunctival cavity of the eye. Medicinal films, being an application on the mucous surface of the oral cavity, have an effective local effect, which ensures their successful use during the treatment of dental diseases. The same films make it possible to deliver drugs directly into the bloodstream, bypassing the negative impact of the gastrointestinal tract environment, which is typical during oral administration of drugs. This unique property of medicinal films was implemented in the creation of anti-ischemic nitrate-containing agents - trinitrolong and dinitrosorbilong, which in terms of therapeutic effectiveness are significantly superior to known agents of a similar purpose, a unique buccal form of acetylsalicylic acid - ascolong, a number of cytostatics and other drugs.

Biocompatible polymers are successfully used as the basis of therapeutic ointments, materials for the shells of microencapsulated drugs, extenders of drugs in solutions, etc.

The range of new products-materials and effective medicines based on synthetic polymers for medical purposes, presented in this Catalog, is constantly replenished and expanded. We work for the future, because we are convinced that the high efficiency of medical polymer products is an objective prerequisite for the further accelerated development of this field of practical health care.

An important property of biomaterials in contact with blood is hemocompatibility, that is, the ability not to exert negative effects on blood. In a number of cases, products made of biomaterials must be easily subjected to biodegradation, which is accompanied by a decrease in size and mass in the process of functioning under the influence of the components of the surrounding biological

environment, in particular as a result of biodestruction, which leads, under these conditions, to the breaking of chemical bonds in the biomaterial molecule.

For the production of biomaterials, metals (for example, tantalum) and alloys, ceramic materials (for example, based on Al_2O_3 , ZrO_2), biositals (CaO - MgO - SiO₂ - P2O5), materials based on hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$, carbon materials. Most of the assortment of biomaterials consists of polymers (so-called biomedical polymers, polymers for medical and biological purposes), as well as composites based on them.

The most important biomedical polymers are polyolefins, mainly polyethylene and polypropylene, polyethylene terephthalate, capable of biodegradation of polyesters based on hydroxycarboxylic acids (for example, glycolic and lactic), which have increased hemocompatibility, segmented polyurethanes, polymers and copolymers of ethers of methacrylic, acrylic and cyanoacrylate acids, polymers and copolymers of N-vinylpyrrolidone, natural polymers - cellulose derivatives, as well as dextrans, heparin, chondroitin sulfates, chitosan, starch, collagen and products of their transformations.

<u>Biomaterials can be conditionally divided into two groups</u>: transplants and implants. A special place is occupied by biomaterials built from cells or are their carriers.

The first group- these are organs and tissues transplanted from the patient himself or his close relatives (for example, a kidney, a piece of bone, skin). In this case, the problem of material compatibility either does not arise, or, on the contrary, the organ is rejected, but with a successful result, it fully ensures the necessary functioning. However, the impossibility of predicting the results of transplantation, as well as the more than limited number of transplants impose their limitations on this type of biomaterials.

*The second group*there are "inanimate" materials that are not directly related to the body: polymers, ceramic blocks, coral skeletons, etc. In the case of implants, the problem of genetic incompatibility of the material does not arise, here the question arises of its basic toxicity or biocompatibility. Implants can be made in any number to ensure the necessary demand, which is their undoubted advantage, however, they are unable to fully restore the functions of the replacement organ.

According to the method of origin, biomaterials are divided into materials of natural and synthetic origin, intended for contact with the environment of a living organism and used for the manufacture of medical products and devices. Films, sponges, gels, microspheres and other forms can be created from biomaterials, which are convenient for use in a specific case of their clinical application.

Biocompatible is a material that has the ability to produce an appropriate host response when it is used specifically. This definition was formulated at a working group meeting held in Amsterdam (Williams, 1987). The authors emphasize that biocompatibility is not the complete absence of toxicity or other negative properties, but the requirement that the material behaves adequately when implanted, which allows the task to be performed. V.I. Sevastyanov (1999), analyzing the available information, singles out the following main properties of biocompatible materials:

- biomaterials should not cause a local inflammatory reaction;
- biomaterials should not have a toxic or allergic effect on the body;
- biomaterials must not have a carcinogenic effect;
- biomaterials should not provoke the development of infection;
- biomaterials must retain their functional properties during the expected service life.

Biocompatible materials and devices act or function harmoniously and harmoniously when in the body or in contact with biological fluids, without causing disease or painful reactions. It should be emphasized that no biomaterial, probably with the exception of what will be obtained with the help of genetic engineering and cloning, cannot be completely biocompatible.

Therefore, the actual existing practice allows us to speak only about the existence of biocompatible and safe biomaterials. They can be in the body for a long period of time, sufficient to perform its function, without causing the development of negative reactions in it.

The process of decomposition of non-viable materials in contact with living tissues, cells and biological (bodily) fluids is called biodegradation (BD). The mechanism of biodegradation can be very diverse - from corrosion of metals, phagocytosis of calcium phosphates and collagen, to chemical replacement of corals with hydroxyapatite.

Biodegradable materials and devices can be partially or completely dissolved, absorbed by macrophages, included in metabolic and biochemical processes and/or replaced by living tissue.

Control materials for the final stage of the lesson. Questions to check the final level of knowledge:

- 1. What are biomaterials, biocompatibility?
- 3. Name the main areas of use of biomaterials.
- 4. What are the requirements for biomaterials?
- 5. What are implants, transplants?
- 6. Main classes of polymers
- 7. Biodegradable polymers
- 8. Ways of synthesis of polymers
- 9. Causes of toxicity of polymers
- 10. Polymers used for the manufacture of vascular prostheses
- 11. Polymers, drug carriers

12. Influence of polymer composition on its stability

13. Effect of material on tissue compatibility

14. Sealing materials

15. What are the requirements for polymers recommended for use in medicine?

16. What are the directions of research in the development of medical polymers?

17. How are polymers classified by the nature of interaction with a living organism?

18. What are the methods of sterilizing polymers?

19. What is thermal sterilization of polymer materials and products?

20. What is the chemical sterilization of polymer materials and products?

literature

Main:

1. Technology of production and processing of polymers for medical and biological purposes: teaching. manual / V. L. Avramenko, L. P. Pidgorna, H. M. Cherkashina, O. V. Bliznyuk. – Kharkiv: Publishing House and Printing House "Technological Center", 2018. - 356 p.

2. Pharmacology: textbook / I.V. Nekoval, T.V. Kazanyuk — 4th ed., corrected. — K.: VSV "Medicine", 2011.— 520 p.

3. Zyman Z.Z.Calcium-phosphate biomaterials: study guide / Z. Z. Ziman. – Kharkiv: V. N. Karazin KhNU, 2018. – 288 p.

4. Pharmaceutical and medical-biological aspects of drugs / I.M. Pertsev, O.Kh. Piminov, M.M. Slobodyanuk and others; Under the editorship I.M. Pepper — Vinnytsia, 2007;

5.Biopolymers and Biomaterials /Edited By<u>Aneesa Padinjakkara,Aparna</u> <u>Thankappan,Fernando Gomes Souza, Jr.,Sabu Thomas</u>. //Apple Academic Press. -2019. - 386 Pages

6. Biopolymers for Medical Applications Edited ByJuan M. Ruso, Paula V. Messina. //CRC Press. - 2021. - 372

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8. Biomedical materials: from history to the present: study guide / H. V. Berladir, T. P. Govorun, O. M. Oleshko. – Sumy: Sumy State University, 2022. – 223 p.

Practical lesson No. 10

Topic: Chemical quality control of drinks

- <u>**Goal:**</u> to acquaint students with the problems of the dangerous action of the components of modern drinks, to reveal the influence of natural components that have a bad effect on the human body, to reveal the concepts of toxicants, food poisoning, xenobiotics, to consider the impact of alcoholic and energy drinks on people's health.
- **Basic concepts:** carbonated water, xenobiotics, antialimentary factors, antivitamins, inhibitors, tannins, "heme" iron, glycosidic bond, coenzyme, toxicant, intoxication.

Equipment: Laboratory of the department

Plan:

- 1. Human health and beverage safety issues.
- 2. Natural components of food raw materials that have a negative effect on the human body.
- 3. Social toxicants.
- 4. Mineral waters.
- 5. The influence of drinks on taking medicines.

The student should know:

• normative documentation of the quality of beverages;

• chemical composition, properties, general principles of methods of production and storage of beverages in accordance with modern requirements for ensuring their quality and food safety;

• the main dangerous components of drinks and mechanisms for eliminating their consequences.

The student should be able to:

• analyze the state of the soft drinks market;

• high requirements for the hygienic properties of water and other raw materials and semi-products;

• to determine the organoleptic parameters of samples of carbonated soft drinks.

Content of the practical lesson

1. <u>Natural components of food raw materials that have a negative effect on the</u>

<u>human body</u>

Xenobiotics- foreign chemical substances and biological agents that enter the human body with food or in other ways, do not perform any of the functions of nutrition and, under certain conditions, adversely affect health.

Alimentary (food) toxicology studies patterns of the body's interaction with harmful chemical substances included in food, with the aim of preventing acute and chronic poisoning, remote effects and allergies.

In addition to foreign compounds that contaminate food products, so-called contaminants - pollutants and natural toxicants, it is necessary to take into account the effect of anti-alimentary factors of food. According to Academician O.O. Pokrovsky, anti-alimentary factors include compounds that do not have general toxicity, but have the ability to selectively impair or block the assimilation of nutrients. This term applies only to substances of natural origin that are components of natural food products. The list of anti-alimentary factors of nutrition is quite extensive. Let's consider some of them.

1.1. Inhibitors of digestive enzymes

Protein substances that block the activity of digestive enzymes (pepsin, trypsin, chymotrypsin, amylase) belong to this group. Protein inhibitors were found in the seeds of legumes (soy, beans, etc.), cereals (wheat, barley, etc.), in potatoes, egg whites, and other products of plant and animal origin.

<u>Mechanism of action of these compounds consists in the formation of stable</u> "enzyme-inhibitor" complexes, suppression of the activity of the main digestive enzymes and thus, reduction of digestibility of protein substances and other macronutrients.

Currently, protein inhibitors are quite well studied and characterized in detail: their primary structure has been deciphered, the structure of the active centers of inhibitors has been studied, the mechanism of action of inhibitors has been studied, etc.

Thus, potatoes contain a whole set of chymotrypsin and trypsin inhibitors, which differ in their physicochemical properties: molecular weight, features of amino acid composition, isoelectric points, thermal and pH stability, etc. In addition to potatoes, protein inhibitors have been found in other nightshades, namely tomatoes, eggplants, and tobacco.

These protein inhibitors of vegetable origin are characterized by high thermal stability, which is generally not characteristic of substances of a protein nature. That is why the use of these substances, without negative effects on the human body, is possible only after appropriate heat treatment.

1.2. Cyanogenic glycosides

Cyanogenic glycosides are glycosides of some cyanogenic aldehydes and ketones, which release hydrocyanic acid during enzymatic or acid hydrolysis, which causes damage to the nervous system.

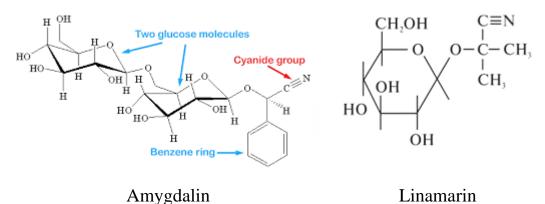
Hydrocyanic acid disrupts redox processes in tissues, which leads to impaired tissue respiration and the development of tissue-type hypoxia. CN- has the property to easily connect with Fe3+ of the oxidized form of cytochrome oxidase instead of an electron. At the same time, inactivation of cytochrome oxidase occurs, which leads to suppression of tissue respiration by 90-95%, although the oxygen content in the blood is increased. In addition, it is assumed that there is a direct effect of poison molecules on the central nervous system (respiratory and vascular centers). This is associated with rapid forms of poisoning from a large dose of toxicant, in which inhibition of cytochrome oxidase is not detected.

Such processes can occur during food preparation or in the case of long-term storage. The release of enzymes that cleave the O-glycosidic bond in the plant product causes the formation of a monosaccharide molecule and its subsequent breakdown to yield an aldehyde or ketone and highly toxic hydrocyanic acid:

glycosidase
$$CH_3$$

 $C_6H_{11}O_6 - C - CN \longrightarrow C_6H_{12}O_6 + HO - C - CH_3$
glycoside CH_3
 $C_6H_{12}O_6 + HO - C - CH_3$

Here are some representatives of cyanogenic glycosides: limarin (contained in white beans), amygdalin (gerolo - almond kernels (up to 8%), peaches, plums, apricots (from 4 to 6%), linamarin (a component of flax seeds), dhurin (includes to the composition of sorghum grain), etc.



2.3 Antivitamins

Antivitamins- substances capable of blocking the action of natural vitamins. Antivitamins belong to two groups compounds:

1) compounds that are chemical analogues of vitamins, with the replacement of any functionally important group by an inactive radical;

2) compounds that in one way or another specifically inactivate vitamins, for example, by means of their modification, or limit their biological activity.

2. <u>Mineral waters</u>

Mineral waters- these are waters that contain in a soluble state more than 1 g/dm3 of mineral salts or at least 0.25 g/dm3 of gaseous products. According to Standart 17403-72, water is classified according to mineralization (salt content). Mostly mineral table water is consumed, although it is also possible to prepare artificial water, which is characterized by the process of dissolving the corresponding mineral salts in drinking water.

If we analyze the drinking water standards of the World Health Organization and most of the world's leading countries, none of them have strict requirements for the minimum or optimal salt content in water.

Norms of the national and European standard of general salt water:

- Ukraine: minimum 100 mg/l, maximum 1000 mg/l (DSanPiN);
- EU: up to 1000 mg/l.

Natural mineral waters— natural underground mineral waters of objects (deposits), characterized by a certain and stable physicochemical composition, the content of biologically active components and compounds in accordance with the conditions established for each object (deposit), which are used without additional processing, which can affect the chemical composition and microbiological properties.Natural mineral waters are an aqueous solution of physiologically active salts and some gases (carbon dioxide, hydrogen sulfide, etc.) that formed underground.

Mineral waters are divided into natural canteens, medicinal-canteens and mixed-type medicinal canteens.

Natural table mineral waters include waters with a mineralization of 1.0 g/dm3, which do not contain microcomponents that have a therapeutic effect. Mineral-table mineral waters include waters with mineralization from 1.0 to 1.5 g/dm3 of the following groups: bicarbonate-sodium, bicarbonate-chloride, chloride-hydrocarbonate sodium. Medicinal and table waters of a mixed composition are obtained by mixing natural waters of different mineralization in a certain ratio. Such waters are used medicinally as prescribed by a doctor and as table drinks in an unsystematic manner.

More than 500 sources of various mineral waters have been discovered on the territory of Ukraine, mainly within the Ukrainian Carpathians (Naftusya, Svalyava, Polyana Kvasova, etc.), the Ukrainian Shield (Khmilnyk,<u>Myronivka</u>etc.), the Dnipro-Donetsk Basin (<u>Myrhorod</u>).The Carpathian hydrogeological zone and the Carpathian artesian basin are considered the most promising regions.

Such mineral components of water as hydrocarbons, sulfates, chlorides, calcium, magnesium, sodium, potassium and iodine improve metabolism, stimulate the activity of the gastrointestinal tract, cleanse the liver, and activate the work of the kidneys.

All types of mineral waters must be filtered, treated with ultraviolet rays, and saturated with carbon dioxide before bottling or other hygienically clean containers. Mineral water is bottled in such a way that the average filling of 10 bottles corresponds to their nominal capacity with a deviation of $\pm 3\%$. Bottles filled with water are hermetically sealed with crown caps and they are subject to inspection, which involves checking the transparency of the water, the absence of foreign impurities in it, the cleanliness of the inner and outer surface, the completeness of the filling and the tightness of their closure.

Glass bottles, PET polymer bottles with non-alcoholic drinks are placed on cardboard bases and covered with a thermo-matching film. It is also possible to use a heat-matched film of increased strength without a cardboard base.

Bottles and cans with non-alcoholic carbonated drinks are marked by pasting a label on each of them, which contains the following information in the national language: the name of the drink, its type and group; the name of the country of manufacture; o the name of the manufacturing enterprise or the place of packaging, its address; trademark, logo; designation of standards; capacity, 1 (dm3); production date (date, month, year); expiration date; storage conditions; the composition of the drink (indicating the list of raw materials); the inscription "artificially mineralized"; mineralization, g/l; chemical composition (for artificially mineralized waters); energy value; nutritional value; bar code.

The influence of drinks on taking medicines

The instructions for taking any medication contain instructions that will prevent serious harm to health, reduce or neutralize the effect of the drug. Sometimes the interaction of medicine and drink can turn out to be poisonous for the human body. That is why it should be understood that their effectiveness directly depends on the drink with which we drink the medicine.

In most of the instructions, there are instructions: the drug should be taken before or after meals. If there are no instructions, take the medicine on an empty stomach.

It should be remembered:

- to take on an empty stomach is to take in 20-40 minutes. before the first meal;
- before meals in 20-30 minutes. before eating;
- during a meal, or immediately after a meal at the end of a meal or immediately after a meal;
- after eating after 30-40 minutes. after eating.

It is known that the most appropriate drink for our body is water. Water is an excellent solvent and has the least effect on the active ingredient. The recommended volume of liquid is from 100 ml.

You should not drink the medicine with milk, because the effectiveness of drugs similar in structure to proteins - cardiac glycosides, caffeine, anti-ulcer drugs -

decreases. Enzymes (pancreatin, etc.) should not be drunk with milk. It is not recommended to combine antibiotics with dairy products. Milk contains a lot of calcium, magnesium and iron ions. They can bind to antibiotic molecules and reduce their availability to the body. Therefore, it is highly not recommended to drink antibiotics with milk.

Note that milk softens the aggressive effect of some substances on the mucous membrane of our stomach. Therefore, it is even useful to drink painkillers and antipyretics with milk. Fat-soluble vitamins (A, D, E, K) also benefit from the combination with milk. However, sometimes in the annotation to the drug (for example, for dysbacteriosis), the manufacturer indicates: "To be taken with a small amount of liquid, excluding milk."

Why should you not drink medicine with tea? Tea contains tannin, catechin and caffeine, which form insoluble compounds with nitrogen-containing agents. Tannin can form insoluble compounds and simply cause some drugs to precipitate (papaverine, codeine, euphylline, cardiac glycosides, etc.). Also, tea can enter into "conflicts" with drugs for the nervous system. Tonic drinks based on catechin and caffeine can inhibit the absorption of hormones and some ophthalmic drugs. Of course, serious side effects from the interaction of tea components and drugs have not been found, but this does not mean that they are absent.

*Grapefruit juice*you can not drink together with cholesterol-lowering drugs, antidepressants, anticonvulsants, antiallergens, hormones and many other drugs.

Taking this juice together with medication does not manifest itself at first. When the concentration of active substances in the body reaches a critical level, symptoms of overdose and side effects begin to appear: ventricular tachycardia, changes in muscle tissue, symptoms of kidney failure, capillary hemorrhages (purpura).

Separately, it should be said about the simultaneous intake of drugs and alcohol. Practice shows that it is with such a combination that the most serious complications arise. For example, in the case of long-term use of non-steroidal drugs and alcoholic beverages, damage to the mucous membrane of the stomach occurs and an ulcer may form. As you know, alcohol hits the liver the hardest. Ethyl alcohol contained in alcohol affects the permeability of cell membranes. Due to this, the effect of all drugs, as well as their side effects, increases. But you should not think that this method will help to reduce the dosage of expensive drugs: the load on the liver increases faster than the intended action and very quickly reaches dangerous limits, causing signs of overdose.

Antibiotics when taken simultaneously with alcohol not only lose half of their medicinal properties, but can also form chemical compounds harmful to the body.

By the way, beer (especially non-alcoholic) also contains substances that negatively affect the work of the liver and its release of enzymes. Due to this, drugs are

processed much more slowly, which increases the risk of improper concentration of the medicinal substance in the body. This is especially true of antibiotics.

It is absolutely impossible to mix alcohol with painkillers: this can lead to gastric bleeding. It is also forbidden to combine alcohol with antidepressants.

Ethyl alcohol can weaken or strengthen the effect of drugs up to the development of side effects, causing nausea, fever, vomiting, headache, liver dysfunction, ulcer and stomach bleeding, blood coagulation disorders, changes in blood pressure, etc.

Summing up

Questions for self-control:

- 1. What is food safety;
- 2. Define the nutritional and biological value of food products;
- 3. What substances are called anti-alimentary factors of nutrition?
- 4. What is the mechanism of action of digestive enzyme inhibitors?
- 5. How is the destruction of digestive enzyme inhibitors in food raw materials?
- 6. What substances belong to antivitamins, give examples;
- 7. Describe the ingredients that reduce the assimilation of mineral substances;

8. Features of technological processing of plant raw materials to reduce the amount of demineralizing substances;

9. Explain the term "heavy metals";

- 10. Explain the negative effects of alcohol on the human body;
- 11. How and with what should the medicine be taken?
- 12. Interaction of drugs and alcohol

List of recommended literature

<u>Main:</u>

1. Bondar, O.I. Fundamentals of biological safety (ecological component): academic. manual / O. I. Bondar, L. P. Novoselska, T. G. Ivashchenko; under general ed. H. G. Shmatkova; State Environmental Academy of Postgraduate Education and Management. – Kherson: D. S. Gryn, 2016. – 372 p.

2. Gagara, V. F. Rational nutrition of different categories of the population: education. manual / V.F. Gagara; Zaporizhzhia National Technical University. – Zaporizhzhia: ZNTU, 2016. – 183 p.

3. Goyko, I. Yu. Physiology and nutrition hygiene: teaching. manual / I. Yu. Goyko, A. O. Bashta; National University of Food Technologies. - Kyiv: NUHT, 2018. - 192 p.

Practical lesson No. 11

<u>Topic</u>: Food products, their quality.

- <u>Actuality of theme</u>: Nutrition, together with other environmental conditions, ensures optimal development of the human body, its physical and mental capacity, sufficiently high resistance to negative factors that affect a person, supports its immunobiological properties, increases resistance to infectious diseases and exposure to toxic substances. Physiological features of the human body must be considered taking into account its interaction with the environment. In this case, a more complete picture of the sources of danger to human health and life is possible. Such interaction is carried out through the exchange of substances and energy.
- <u>The purpose of the lesson</u>: the student must be able to analyze the body's reaction to the influence of harmful substances in food products and the possibility of reducing the amount of these substances, deepening and consolidating the theoretical knowledge and practical skills necessary for determining the safety of food and its importance in the safety of life.
- **Basic concepts:** biopolymers; polymers in surgery, traumatology, orthopedics; polymer coatings, medical fibers, prolongation, polymers as blood substitutes, the structure of biopolymers.

Equipment: Laboratory of the department

Lesson plan and organizational structure:

- 1. Use of food additives in Ukraine. Regulation. Regulations.
- 2. The main goals of introducing HD into food products.
- 3. E-codification of food additives.
- 4. Biologically active additives. Effect on the human body.
- 5. The impact of nutrition on human activity.
- 6. Food safety as a component of safe human activity.
- 7. Principles of safe (rational) nutrition.
- 8. Quality levels of food products.
- 9. Ways of entry of harmful substances (xenobiotics) into food products.
- 10. Food additives as possible contaminants.
- 11. Contamination of products with radionuclides.

The student should be able to and know:

1. Concepts of "food supplements", "dietary supplements", "xenobiotics".

2. Classification of food additives.

3. Positive and negative consequences of using food and biologically active additives.

4. Paths of entry of harmful substances into food.

5. Pollution by radionuclides.

6. The impact of nutrition on human activity.

7.Food additives as possible contaminants.

Lesson content

Use of food additives in Ukraine. Regulation. Regulations

Today, hundreds of food additives are used in the food industry in order to obtain new products or to achieve certain technological goals. In most European countries, more than 540 known food additives (FD) are used, in the USA their number, including appropriate mixtures, exceeds 1,500, in Russia - 450, in Ukraine until 2014, 300 HD were allowed.

The reasons that led to the widespread use of HD

- transportation of products over considerable distances;

- increasing consumer demands for modern food products;

- creation of new types of food products (dietary, healthy).

In Ukrainian legislation, the sphere of use of food additives is regulated in accordance with the Law of Ukraine "On Basic Principles and Requirements for the Safety and Quality of Food Products" of the new edition dated 01.20.18, and state control over the production and use of food additives is entrusted to the State Sanitary and Epidemiological Service and the Ministry of Health of Ukraine. Departmental control over the use of food additives is carried out by the technological service of the enterprise and the production service of the laboratory.

According to Art. 30 "...the use of only those food additives included in the State Register of Food Additives...1" is allowed.

The State Register of Food Additives is maintained by the Ministry of Health. The State Register of Food Additives, in particular, specifies their maximum permissible levels and the food products in which they are used.

Food additives recognized by the European Union as safe for human consumption are automatically included in the State Register of Food Additives and, accordingly, their use in the production of food products and food products in circulation is allowed Definition of "food additive"

The law "On basic principles and requirements for the safety and quality of food products" provides the following definition of food safety:

dietary supplement- any substance that is not normally considered a food product or its component, but is added to a food product for a technological purpose in the production process, and which as a result becomes an integral part of the product (the term does not include pollutants, pesticides or substances added to food products to improve their nutritional properties).

Food additives can remain in food products in their entirety or in the form of substances that are formed after the chemical interaction of additives with food components.

Food additives do not include dietary supplements (or dietary supplements) - substances that increase the nutritional value of the product.

Dietary supplement- a food product consumed in small defined quantities in addition to the usual food diet, which is a concentrated source of nutrients, including proteins, fats, carbohydrates, vitamins, minerals (this list is not exclusive), and is made in the form of tablets, capsules, dragees, powders, liquids or other forms.

Nutritional value/food value- all the main natural components of a food product, including carbohydrates, proteins, fats, vitamins, minerals and salts.

Auxiliary materials for processing- any materials... that are not consumed as food by themselves, but are used during the production or processing of a food product or its components to achieve a certain production goal, the result of which is the presence of residues or the formation of derivatives in the final food product.

The main goals of introducing HD into food products

1) improvement or facilitation of the technological process related to the manufacture, packaging, transportation and storage of food products (FP);

2) preservation of food products (increasing the resistance of CP to various types of spoilage);

3) improvement and preservation of organoleptic properties of CP and increase of their stability during storage;

4) production of special or dietary products.

The use of HD is not allowed

1) to mask technological defects, spoilage of raw materials and the finished product; 2) to reduce the nutritional value of the product (by replacing the nutritional components with carrageenan, KMC, sweeteners, etc.);

3) in cases where the required effect from the use of HD can be achieved with the help of technological methods - technically and economically expedient

The Codex Alimentarius Commission, depending on the technological functions, divided food additives into 23 functional classes for labeling.

REGULATION EC No. 1333/2008 on food additives identifies 26 functional classes

1. "sweeteners" are substances used to give a sweet taste to food products or in table sweeteners;

2. "dyes" are substances that add or restore the color of a food product;

3. "preservatives" are substances that extend the shelf life of food products, protecting them from spoilage caused by microorganisms, and/or that prevent the growth of pathogenic microorganisms;

4. "antioxidants" are substances that extend the shelf life of food products, protecting them from deterioration caused by oxidation, for example, from the rancidity of fats and discoloration;

5. "carriers" are substances used to dissolve, dilute, disperse or otherwise physically change a food additive or flavoring, food enzyme, nutrient and/or other substance added for nutritional or physiological purposes to a food product, without changing its functions (and not providing any technological action) to facilitate its processing, consumption or use;

6. "acids" are substances that increase the acidity of a food product and/or give it a sour taste;

7. "acidity regulators" are substances that change or control the acidity or alkalinity of a food product;

8. "anti-caking agents" are substances that reduce the tendency of individual food product particles to stick together; 9. "anti-foaming agents" are substances that prevent or reduce the formation of foam;

10. "fillers" are substances that increase the volume of a food product without significantly increasing its energy value;

11. "emulsifiers" are substances that enable the formation or maintenance of a homogeneous mixture of two or more immiscible phases in a food product, such as, for example, oil and water;

12. "emulsifying salts" are substances that transform the proteins contained in cheese into a dispersed form and thus ensure a uniform distribution of fats and other components;

13. "thickeners" are substances that make or keep the tissues of fruits and vegetables dense or fresh or interact with gelling agents to obtain or thicken jelly;

14. "taste and aroma enhancers" are substances that enhance the natural taste and/or aroma of a food product;

15. "foaming agents" are substances that enable uniform dispersion of the gas phase in a liquid or solid food product;

16. "gelling agents" are substances that give the food product its consistency due to the formation of jelly;

17. "glazing agents" (including lubricants) are substances that, when applied to the external surface of a food product, give it a shiny appearance or form a protective layer;

18. "moisturizers" are substances that prevent drying of the food product by neutralizing the action of atmospheric air with low humidity, or contribute to the dissolution of the powder in an aqueous medium;

19. "modified starch" is a substance obtained as a result of one or more chemical treatments of edible starch, which may have been subjected to mechanical or enzymatic treatment and may have been diluted or bleached by acid or alkaline treatment;

20. "packaging gases" are gases, other than air, which are introduced into the container before, during or after placing the food product in this container;

21. "extruders" are gases, other than air, which push the product out of the container;

22. "raising agents" are substances or combinations of substances that release gas and thus increase the volume of dough or liquid dough;

23. "complex formers" are substances that form chemical complexes with metal ions;

24. "stabilizers" are substances that make it possible to maintain the physical and chemical state of the food product; stabilizers include substances that contribute to the maintenance of a homogeneous dispersion of two or more immiscible substances in a food product, substances that stabilize, preserve or intensify the color of a food product, and substances that increase the binding capacity of a food product, including the formation of cross-links between proteins , contributing to the binding of parts of the food product into a reconstituted food product;

25. "thickeners" are substances that increase the viscosity of a food product;

26. "flour processing agents" are substances, other than emulsifiers, added to flour or dough to improve its baking qualities.

E-codification of food additives

To harmonize their use, the European Council developed a system of digital codification of food additives with the letter "E" (from the word Europe), abbreviated as the E-numbering system. It is included in the Codex Alimentarius.

All components that are permitted for use by the Codex Alimentarius are included in the INS (International Numeral System) list and have their own number.

Digital codification involves the grouping of food additives by technological purpose. The numbering of food additives starts with the number 100. E replace the long names of food additives.

Codes are used only in combination with the names of functional classes of additives (for example, preservative E211).

It is allowed to indicate the additive as an individual substance and as a representative of the functional class in combination with the E number. For example: 1) sodium benzoate or 2) preservative E211.

According to the European digital codification, food additives are divided as follows:

E 100...E 182 – dyes;

E 200...E 299 – preservatives;

E 300...E 399 - antioxidants (antioxidants);

E 400...E 449 – consistency stabilizers;

E 450...E 499 – emulsifiers;

E 500...E 599 – acidity regulators, leavening agents;

E 600...E 699 – taste and aroma enhancers;

E 700...E 800 – spare indices for other possible information;

E 900 and further – glazing agents, sweeteners, flour processing agents, propellants, coolants.

E1000-E1521 - sealants, enzymes, humectants, modified starches

Roman numerals after E-numbers specify differences in the specification of additives of the same group and are not a mandatory part of the number and designation:

 $E339 - Sodium \ phosphates$

E339 (I) - monosubstituted sodium orthophosphate

E339 (II) - Disubstituted sodium orthophosphate

E339 (III) - trisubstituted sodium orthophosphate

Letters after the number(a, b, c, d, e, f, etc.) is a classification unit:

E 160 - Carotenes E160a - Extracts of natural carotenoids

E160b – Annatto extracts (bixin, norbixin)

E160c – Paprika oil resins (capsanthin, capsarubin)

E160d - Lycopene

In some cases, after the name of the food additive or the index that replaces it, its concentration may be indicated.

The presence of food additives in products must be indicated on the consumer packaging, label, jar, package and in the recipe.

Control materials for the final stage of the lesson.

Questions to check the final level of knowledge:

- 1. The impact of nutrition on human life.
- 2. Requirements for the quality and safety of food products.
- 3. Ways of entry of harmful substances into food products.

- 4. The concept of the formation of toxic substances in the process of food preparation
- 5. Food additives as possible contaminants
- 6. Methods of reducing the amount of pollutants in food products.

literature

Main:

1. Nutritional supplements:Texts of lectures for students of specialty 181 "Food technologies" / Compiler: Humenyuk O.L. – Chernihiv: ChNTU, 2019. – 177 p.

2. Chemistry of surfactants in the food and cosmetic industry. Methodological recommendations for laboratory work for students of the Faculty of Chemistry. / Compilers: Yurchenko O.M., Kormosh Z.O. – Lutsk: Tower Printing. – 2017. - 68 p.

3. Basics of nutrition: a textbook / M.I. Kruchanytsia, I.S. Mironyuk, N.V. Rozumikova, V.V. Kruchanytsia, V.V. Brych, V.P. Quiche Uzhhorod: Publishing House of UzhNU "Hoverla", 2019. 252 p.

4. Safety of food products: anti-alimentary factors, xenobiotics, food additives: study guide / L.V. Krychkovska, A.P. Belinska, V.V. Ananieva and others. - Kharkiv: NTU "KhPI", 2017. - 98 p.

5. Velisek J. The Chemistry of Food. – Wiley-Blackwell, 2014. – 1124

Practical lesson 12

- **Topic:** Sorption of biologically active substances at the boundary of phase separation. Adsorbents in modern medicine. Sorbents for food poisoning. Chromatography.
- **Goal:** giving students an idea about the main onesphysico-chemical processes occurring in the surface layer, the concept of adsorption on solid sorbents. To master the basics of chromatographic methods of analysis and adsorption therapy. Acquaintance with the most important fields of use of sorbents in medicine and pharmacy.
- **Basic concepts:** adsorption, adsorbent, adsorbate, chemical adsorption, physical adsorption, limiting adsorption, adsorption of electrolytes, ion exchange and selective adsorption, cations and anions, chromatography, chromatographic

methods.

Equipment: Laboratory of the department

Plan:

<u>1. Organizational measures</u>(greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).

2. Control of the reference level of knowledge:

The student should know and be able to:

- use scales and chemical utensils correctly;
- determine the concentration of a substance by the titrimetric method;
- determine graphically and calculate the amount of adsorption.

• to study the basics of physical and chemical processes occurring in the surface layer;

• learn how to calculate the amount of adsorption, build graphic regularities of the above parameters from concentration;

• physical and chemical bases of adsorption therapy (hemosorption, plasma sorption, lymphosorption, enterosorption, application therapy); immunosorbents.

• learn how to operate with formulas and use them to solve situational problems on the subject of the lesson;

• to acquire practical skills of experimental work on determining the amount of adsorption using solid sorbents.

- learn to assess the reliability of the results obtained;
- learn the test material on the lesson topic.

3. <u>Requirements for students' theoretical readiness to perform practical</u> <u>classes:</u>

PLAN:

- 1. Adsorption, adsorbent, adsorbate.
- 2. Physical and chemical adsorption
- 3. Specific adsorption.
- 4. Description of experimental data. Langmuir equation
- 5. Adsorption at the solid-solution interface
- 6. Molecular adsorption
- 7. Adsorption of strong electrolytes
- 8. Ionites in medicine and biology
- 9. Ion exchange in biological systems

Adsorption at a stationary phase interface means the accumulation of one substance on the surface of another.

A solid substance on the surface of which another substance accumulates is called an adsorbent, and the absorbed substance is called an adsorbate or adsorptive.

In terms of energy, the areas of the surface of a solid body with the largest local supply of Gibbs surface energy are called active centers, where adsorption primarily occurs.

Adsorption can be considered as the interaction of adsorbate molecules with the active centers of the adsorbent surface. This interaction can be different, as a result of which physical and chemical adsorption are distinguished.

<u>Physical adsorption proceeds involuntarily, reversible and not very specific.</u> As the temperature increases, physical adsorption decreases.

<u>During chemical adsorption (chemosorption)</u>a chemical bond is formed between the adsorbent and the adsorbate and each loses its individuality. Chemosorption is similar to a chemical reaction and is usually accompanied by the formation of compounds at the phase interface.

Chemosorption is characterized by the specificity of the interaction and is often irreversible. During chemical adsorption, instead of the adsorbed substance, another compound can be desorbed.

Usually, the adsorption process is reversed. Some particles can detach from the surface of the adsorbent and go into the surrounding space. This process is called desorption.

Subsequently, both processes bring the system to a state of adsorption equilibrium: adsorption \rightleftharpoons desorption.

The depth of adsorption is characterized by specific adsorption -

Most often, the specific adsorption on the surface of a solid substance is expressed in moles per 1 kg (or mmol per 1 m) of adsorbent, since measuring the surface area of any adsorbent is a rather time-consuming operation:

P = n / m, mol / kg,

where n is the amount of adsorbate, mol; m is the mass of the adsorbent, kg.

Adsorption depends on the nature of the adsorbent and adsorbate, on temperature, on the specific surface area of the adsorbent, on the pressure of the adsorbate (for adsorption of gases), on the nature of the solvent and the concentration of the adsorbate in the solution (for adsorption from solutions).

Non-polar adsorbents, for example, carbon black or activated carbon, better adsorb non-polar organic compounds. Polar adsorbates are better adsorbed on the surface of polar adsorbents, such as, for example, silica gel, aluminum oxide, cellulose, etc. At the same mass of adsorbent, adsorption increases with an increase in the specific surface area (ie grinding) of the adsorbent.

A large number of equations have been proposed to describe experimentally obtained data on adsorption on the surface of both a solid substance and a liquid, but the Langmuir and Freundlich equations are more often used.

The general equation of the Langmuir adsorption isotherm:

$$\mathbf{G}=\mathbf{G}_{\infty}\frac{C}{K+C}\,,$$

where G_{∞} -marginal adsorption, observed at the degree of filling of the surface with an adsorbent equal to 1, mol/m2;

K is a constant numerically equal to half of the limit adsorption;

C is the equilibrium concentration of the solution, mol/dm3.

In the case of adsorption of gases and vapors in the equation, the equilibrium concentration of the solution is replaced by the value of the equilibrium partial pressure of the gas or vapor (p):

$$\mathbf{G} = \mathbf{G}_{\infty} \frac{P}{K+P}$$

The mass of the substance per unit surface of the saturated adsorption layer, which is equal to the product of the marginal adsorption Γ_{∞} ·per molar mass (M) of the substance:

$$m = \mathbf{G}_{\infty} \cdot \mathbf{M}$$

QUESTIONS FOR SELF-TRAINING

- 1. Define adsorption, adsorbent, adsorbate.
- 2. Basic characteristics of physical adsorption
- 3. List the signs of chemisorption
- 4. What is specific adsorption?
- 5. Adsorption isotherms and the Langmuir equation, their analysis.

4. Summary of results.

List of recommended literature:

Main:

1. Medical chemistry: a textbook / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others. ; under the editorship V.O. Kalibabchuk. - K.: VSV "Medicine", 2019. - 336 pp. Medical chemistry: textbook / V.P. Muzychenko, D.D. Lutsevich, L.P. Yavorska ; under the editorship B.S. Zimenkovsky. – 3rd ed., corr. - K.: VSV "Medicine", 2018. - 496 p.

2. V. I. Homonai Medical chemistry: a textbook / V. I. Homonai, S. S. Milovych – Vinnytsia: Nova kniga, 2016. – 672 p.

Practical lesson 13

Topic 13: Chemical weapons. Protective equipment and first aid.

- **Goal:** studying the toxicity of substances capable of causing group or mass damage to people; study of methods for diagnosing chemical damage and assessing the functional state of persons exposed to toxicants; creation of means and methods of prevention and minimization of the consequences of chemical exposure; preservation of life, restoration of health and professional capacity of victims.
- **Basic concepts:** military toxicology, combat poison, chemical weapon, biotransformation, "volatile synthesis", detoxification, antidote, focus of chemical damage.

Equipment: Laboratory of the department

<u>Plan</u>:

1, Features of chemical weapons;

2, Ways of entry of poisons into the body;

3, Biotransformation of xenobiotics in a living organism;

4, Poisonous and highly toxic substances (OVTR) of nerve-paralytic action;

5, FOR damage: mechanism of toxic action, diagnosis, detoxification, prevention and treatment of FOR poisoning;

8. Characteristics of the center of chemical damage and the zone of chemical pollution.

The student should know:

- general principles of diagnosis of acute injuries caused by poisonous highly toxic substances, depending on the route of entry of the poison into the body;
- the scope of therapeutic care for those affected by poisonous highly toxic substances;
- the most promising directions in the development of issues of prevention and treatment of the main syndromes of diseases caused by the action of factors of military and occupational hazards.

The student should be able to:

- perform first aid measures for those affected by poisonous substances;
- apply modern means of diagnosis and treatment of poisoning by highly toxic poisons;
- correctly justify the treatment for poisoning with highly toxic poisonous and

poisonous substances in accordance with modern ideas.

Content of the practical lesson

1. Features of chemical weapons

Chemical weapons were first used during the First World War. Germany conducted a massive chlorine attack on April 22, 1915, near the Belgian city of Ypres. As a result, 15,000 soldiers were injured, 5,000 of them died. The Germans at the front released chlorine from almost 6,000 cylinders. 168 tons of chlorine were released within 5-8 minutes.

The use of chlorine for military purposes was proposed by the German chemist Fritz Haber. He is considered the first scientist who subordinated scientific knowledge to military needs. Fritz Haber discovered that chlorine is an extremely poisonous gas that, due to its high density, concentrates low above the ground. He knew that this gas causes swelling of the mucous membranes, coughing, suffocation and eventually death. In addition, the poison was cheap: chlorine is found in waste from the chemical industry.

Since the time when chemical weapons were first used on a large scale, the variety and effectiveness of their new variants have steadily increased. The particular threat posed by chemical weapons today arises from the existence of new and far more toxic chemical compounds than those known a hundred years ago.

The purpose of military toxicology is to improve the system of medical measures and means that ensure the prevention or weakening of the effects of poisonous substances during emergency situations, as well as the preservation of life, restoration of health and professional performance of affected servicemen.

Among the main criteria that make it possible to identify toxicants capable of causing mass damage to people in extreme conditions are:

- the possibility of their use for military purposes;
- high toxicity when acting through respiratory organs, intact skin and mucous membrane of the gastrointestinal tract;
- lack of organoleptic characteristics;
- long duration of infectious action;
- stability during storage;
- large stocks of substances at production facilities and storage bases.

Thus, a combat poisonous substance (BOR) is a chemical compound that has certain toxic and physicochemical properties that, when used in combat, ensure damage to the enemy's manpower, as well as contamination of the air, weapons, military equipment, food, water, etc. . The purpose of using BOR is to destroy the enemy or disable him due to incapacitation and harm to health.

Applied chemistry in medicine

In numerous studies, it was established that toxicity is inherent in the vast majority of chemical substances. An important achievement of toxicology is the proof of the fact that, depending on the effective dose, the characteristics of the organism, and the conditions of interaction between the substance and the organism, almost any substance, even the most necessary for maintaining life (for example, oxygen), can become a poison. The toxicity of substances, of course, is different. Modern science knows both mildly toxic (under normal conditions) and extremely toxic substances that cause death in a dose of a few micrograms.

The lack of basic toxicological knowledge among the population and responsible officials creates, on the one hand, unfounded phobias about non-existent dangers, and on the other hand, ignoring the real threat. Programs in the discipline should be based on fundamental ideas about the phenomenon of toxicity, which is realized during the interaction of chemical substances with biological systems, the methodology of toxicity assessment, the laws of kinetics and transformations of xenobiotics in biological systems, the development of the toxic process at the cellular, tissue, organismal, and population levels of living organisms body

Chemical weapons- the oldest type of weapon of mass destruction (WMD), the impressive action of which is based on the use of BOR.

Chemical weapons- these are highly toxic substances (or poisonous substances - OR), as well as ammunition containing them, or devices used for their distribution, specially designed to cause in small doses to injure people, causing death, temporary incapacity or causing permanent damage to health. harm to humans, animals, plants, and machinery due to chemical exposure

Inhalation poisoning characterized by the fastest entry of poison into the blood. This is explained by the large absorption surface of the pulmonary alveoli (100-150 m2), the small thickness of the alveolar membranes, the intense flow of blood through the pulmonary capillaries, and the lack of conditions for significant deposition of poisons. Absorption of volatile compounds begins already in the upper respiratory tract, but is most fully carried out in the lungs. It occurs according to the law of diffusion according to the concentration gradient. Similarly, volatile non-electrolytes enter the body: hydrocarbons, halogenated hydrocarbons, alcohols, ethers, etc. The speed of arrival is determined by their physical and chemical properties and to a lesser extent by the state of the body.

3. Poisonous and highly toxic substances (OVTR) of nerve-paralytic action

Among the poisonous and highly toxic substances (OVTR) of nerve-paralytic action can be attributed:

1. Organophosphorus compounds (FOC) (sarin, zoman, armine, dichlophos, etc.);

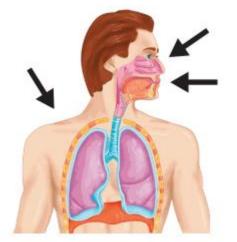
2. Derivatives of carbamic acid (propuxor, aldicarb, dioxacarb, etc.);

- 3. Bicyclophosphates (butylbicyclophosphate, isopropylbicyclophosphate, etc.);
- 4. Hydrazine derivatives (hydrazine, dimethylhydrazine, etc.);
- 5. Complex heterocyclic compounds (tetrodotoxin, saxitoxin, etc.);
- 6. Protein toxins (botulotoxin).

Modern nerve-paralytic poisons differ in their toxic effects. Some substances cause the development of a convulsive syndrome, coma and death from respiratory and cardiac arrest in severe intoxications. Others primarily cause paralysis of voluntary muscles, including respiratory muscles, and death from asphyxiation. Convulsive syndrome is a consequence of the action of substances on the central nervous system (CNS). Paralysis of the muscles is the result of a violation of the conduction of the nerve impulse in the neuromuscular synapses.

ORs of nerve-paralytic action are organophosphorus compounds (FOCs) by their chemical structure. They are distinguished by extremely high toxicity, very fast action, difficulties in detection and resistance. Easily and quickly penetrate through the skin, respiratory organs, gastrointestinal tract.

A turning point in the history of chemical weapons occurred in 1937, when the German



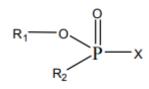
chemist Gerhard Schrader, while working on remedies for agricultural pests, saw that one of his assistants was severely poisoned by vapors of the substance. So, as early as 1938, Schrader discovered sarin, which was named after the first letters of the surnames of his codiscoverers. Also, such well-known poisonous substances from this class as tabun, sarin, zoman were synthesized there, which were tested on monkeys, and therefore on concentration camp prisoners.

The spread of FOS is caused, first of all, by their

widespread use as poison chemicals (insecticides - chlorophos, carbophos, phosphamide, etc.). Many FOS are used in the chemical industry, in particular, as starting and intermediate products of organic synthesis.

The source of poisoning can be contaminated food and water, as well as air containing FOS vapors and aerosols.

According to their chemical structure, FOS are esters of pentavalent phosphorus acids. General appearance of FOS:



where P is a phosphorus atom, R1 and R2 are usually organic radicals, and X is a halogen

*Zone of chemical contamination*OR includes the center of chemical damage and the territory within which the danger of chemical damage is created.

The center of chemical damage is understood as the territory with personnel, military equipment, transport and other objects that were affected by chemical weapons, as a result of which human injuries occurred or may occur. The size and nature of the foci of chemical damage depend on the physico-chemical and toxic properties of poisonous substances (PO), means and methods of their application, meteorological conditions, topography, etc.

In the focus of chemical damage, the following are distinguished:

- the area of contamination, which includes the area of direct application of poisonous substances and part of the zone of spread of contaminated air, where, in addition to the damage to the personnel, a high degree of contamination of the terrain, military equipment, transport, uniforms is achieved;
- the area of spread of contaminated air (primary and secondary cloud of OR), characterized for a certain time by the danger of damage to personnel and the absence or insignificant contamination of the terrain, military equipment, and uniforms.

Centers of chemical contamination, depending on the OR used by the enemy, can be of several types.

Their classification is based on two criteria: the duration of infection of the territory, the objects located on it, and the speed of development of lesions in humans.

There are 4 types of foci:

- 1) the site of damage by fast-acting persistent ORs, which is formed during the use of nerve-paralytic poisons (sarin, zoman and VX gases in an aerosol state);
- 2) the focus of damage by slow-acting resistant ARs, which is formed when using mustard;
- 3) the site of damage by fast-acting unstable toxic compounds formed when hydrocyanic acid is used;
- 4) the focus of damage by slow-acting unstable ORs, which is formed when using phosgene.

Lesions caused by fast-acting ARs, are characterized by an almost instantaneous (in the first minutes, tens of minutes) formation of massive sanitary losses with a violent course of intoxication. In these conditions, self-help and mutual aid measures with the use of personal protective equipment, antidotes and individual anti-chemical packages (IPPs) become crucial.

They are characterized by:

- damage to a significant number of military personnel;
- the probability of a partial failure (injury) of the medical staff of a military unit, unit;

- the occurrence of a significant number of seriously injured people, whose life expectancy, in the absence of timely and effective help, does not exceed 1 hour from the moment of the poisoning clinic;
- the need to provide medical assistance in the cell and at the stages of medical evacuation in the established optimal terms

The rapid course of intoxication, the predominance of severe forms (up to 60-70%), the limited time for providing first medical and qualified medical aid require urgent evacuation of the affected from the cell.

Lesions formed by slow-acting OR, are characterized by the gradual formation of losses (within 4-12 hours or more). At the same time, conditions are created for the deployment of the forces and means of the medical service, the sorting and evacuation of the injured in order to provide timely first, pre-medical, first medical and qualified aid.

Significant differences in the lesions of slow-acting AR are:

- consecutive, within several hours, the appearance of signs of poisoning in the affected; therefore, measures to actively identify affected people among the population are of particular importance;
- short life expectancy of the seriously injured: in the case of a mustard-type, phosgene-type AR injury, etc. - several hours or days.

With the use of persistent ORs for a long time (more than an hour), there is a danger of injury not only directly on the territory of the outbreak, but also beyond it. As a result of desorption of OR from the uniforms and bandages of the injured, contact with them or with infected transport and property, damage to the wounded and medical personnel at the stages of medical evacuation is possible.

Summing up List of recommended literature

<u>Main:</u>

7. Disaster medicine. Military medicine: rec. annotated bibliography show / edited by: N. B. Havrish, V. V. Khivrenko, I. M. Lazorenko, L. M. Dragan. - Kh., 2018. - 36 p.

8. Toxicological chemistry: a textbook / I.V. Nizhenkovska, O.V. Velchynska, M.M. Coachman. — 3rd edition. - K. "Medicine",2020 – 372 p.

9. Essentials of Medical Chemistry and Biochemistry /J. Dostal, H.Paulovand, E.Tandborskand – Brno, 2014- 211

10. Practical Guide for Medical Management of Chemical Warfare Casualties / OPCW Organization for the Prohibition of Chemical Weapons International Cooperation and Assistance Division Assistance and Protection Branch, 2016. - 169

Practical lesson No. 14

<u>Topic</u>: Fundamentals of nanochemistry. Nanotechnology in medicine

- **Goal** imagine the possibilities of nanomedicine, where devices and systems work entirely at the molecular level, distinguish the concepts of nanotechnology, nanochemistry, nanostructure, nanoreactor; have an idea of the importance of the size effect for the properties of nanoparticles; to find out the effect of the size effect with the increase of the surface of nanoparticles; distinguish methods of nanoparticle synthesis and give examples of their production; have an idea about supramolecules, photodynamic therapy, nanorobots and their role in medicine.
- **Basic concepts:** nanotechnology, nanochemistry, nanodiagnostics, nanoparticles, nanomaterials, nanosystems, nanostructure, size effect, nanoreactor.

Equipment: Laboratory of the department

<u>Plan</u>:

<u>1. Organizational measures(greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).</u>

2. Control of the reference level of knowledge:

- Rules for performing laboratory work.
- Methods of experimental data processing.
- Basic laws of chemistry and physics.
- 4. <u>Requirements for students' theoretical readiness to perform practical</u> <u>classes:</u>
 - 1. Basic concepts and terms of nanochemistry.
 - 2. Classification of nanoobjects.
 - 3. Methods of synthesis of nanoparticles.
 - 4. Carbon nanomaterials.
 - 5. Porous nanoobjects.
 - 6. Nanotechnology in medicine.

The main stage of the lesson

First, let's analyze the meaning of the most commonly used prefixes designed to display decimal fractions of a unit:

micro - from the Greek. mikros - small - 10^{-6} m, nano - from the Greek. nanos – dwarf – 10^{-9} m

In fact, the NANOS prefix is designed to display the decimal part of the unit, which corresponds to 10⁻⁹ m. Particles between 1 and 100 nm in size exhibit unusual chemical properties that are difficult to predict and are characterized by excess energy and high chemical activity. With them, reactions can be carried out in a wide range of temperatures, which is impossible for microparticles.

Nanoscience- a system of knowledge based on the description, explanation and prediction of the properties of material objects with nanometric characteristic dimensions or systems of a higher metric level, ordered or self-ordered on the basis of nanosized elements.

Nanoscience- an interdisciplinary field of knowledge, the foundation of which is chemistry, physics, biology. Research in nanoscience becomes the basis for the development of nanotechnology.

Nanotechnology is a set of methods and methods that are used in the study, design, manufacture and use of structures, equipment and systems that include purposeful control and modification of the shape, size, integration and interaction of nanoscale elements (1-100 nm), which are used to obtain objects with new chemical, physical and biological properties.

For example, the size of the elementary cells of a fullerene crystal exceeds 1 nm, and there are nanometer clusters in the composition of ordinary liquid water, but fullerene powder and water are not included in the objects of nanotechnology.

The goals of nanotechnology are the design, production and use of nanoparticles.

Nanochemistry - one of the components of nanoscience, which develops methods of synthesis of nanodispersed substances, prevention of degradation of nanostructures, regulation of chemical transformations of nanometer-sized bodies and their use to improve the quality of life, including treatment methods.

Nanodiagnostics - a set of specialized research methods aimed at studying structural, morphological-topological, mechanical, electrophysical, optical, biological characteristics of nanomaterials and nanosystems, analysis of nanoquantities of substances, measurement of metric parameters with nanoprecision.

Nanoparticles- objects consisting of atoms, ions or molecules and having dimensions smaller than 100 nm.

The dependence of the physical and chemical properties of nanoparticles on their size is called *dimensional effect*.

Size effects –a phenomenon manifested in a qualitative change in properties and reactivity with a change in the number of atoms or molecules in a nanoparticle.

Nanostructure- a set of nanoparticles of a certain size with the presence of functional connections.

Systems with a limited volume in the process of their interaction with other chemical reagents are called *nanoreactors*.

Nanomedicine- science that studies the use of macromolecules and nanoparticles for diagnosis, treatment of diseases, as well as restoration of damaged tissues.

Achievements of nanotechnology in medicine

- A significant increase in the sensitivity threshold of modern diagnostic tools

 magnetic resonance and computer tomography, bringing it to the cellular
 and subcellular levels.
- Contrast agents based on nanoparticles of iron or its oxide.
- ✤ A method of detecting and neutralizing cancer cells using hollow gold nanoparticles.
- The method of detecting malignant tumors using quantum dots that can accumulate in tumors
- Technologies for the delivery of drugs in nanocapsules hollow spheres with a solid wall containing embedded oil or water - have been created
- The use of nanocapsules with a large number of pores on the surface as carriers of antitumor drugs makes it possible to significantly reduce side effects during the pharmacotherapy of malignant neoplasms.
- The use of supramolecular nanoparticles to fight cancer. A particle (supermolecule) assembled from individual molecules with the help of weak non-covalent interactions is called supramolecular.

Scheme of a dendimer – a molecule designed for drug delivery:

- The use of microemulsions as nanoreactors makes it possible to create a unique system of microlattices with various surface properties
- Use of miniemulsions as a nanoreactor. They are kinetically more stable. The time of existence of miniemulsion droplets ranges from several days to months.
- The use of innovative oral hygiene products, the active components of which, thanks to their nano-size, penetrate deeply into all layers of the teeth and gums.
- ✤ Using stem cells to grow new teeth.
- ✤ Application of nanoclusters, silver nanowires, copper in surgical stomatology.

The amount of knowledge in nanoscience is constantly growing, and the share of that knowledge that is transformed into nanotechnology is also increasing, which contributes to the development of chemical disciplines as well.

Tasks for independent control

- 1. Define the terms: nanoparticle, nanostructure, cluster, quantum dot.
- 2. Explain the meaning of the concept of size effect. What does it look like?
- 3. How to explain the different colors of colloidal solutions of gold in water
- 4. How to explain the healing properties of water in contact with silver.
- 5. Name the main methods of obtaining nanoparticles.

- 6. Define the concept of nanomedicine. What is its advantage over traditional medicine?
- 7. Suggest two ways to convert fullerene into a water-soluble form.
- 1. Summary:

List of recommended literature:

Main:

1. Medical chemistry: a textbook / V.O. Kalibabchuk, I.S. Chekman, V.I. Galinska and others. ; under the editorship V.O. Kalibabchuk. - K.: VSV "Medicine", 2019. - 336 pp.

2. Medical chemistry: textbook / V.P. Muzychenko, D.D. Lutsevich, L.P. Yavorska ; under the editorship B.S. Zimenkovsky. – 3rd ed., corr. - K.: VSV "Medicine", 2018. - 496 p.