

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ УКРАИНЫ
ХАРЬКОВСКИЙ НАЦИОНАЛЬНЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ

**PREPARATION, PURIFICATION AND PROPERTIES OF
COLLOIDAL SOLUTIONS. COAGULATION OF COLLOIDAL
SOLUTIONS. COLLOIDAL PROTECTION**

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

**ОДЕРЖАННЯ, ОЧИСТКА ТА ВЛАСТИВОСТІ КОЛОЇДНИХ РОЗЧИНІВ.
КОАГУЛЯЦІЯ
КОЛОЇДНИХ РОЗЧИНІВ.
КОЛОЇДНИЙ ЗАХИСТ**

Методичні вказівки для самостійної роботи студентів I
з дисципліни «Медична хімія»

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Preparation, purification and properties of colloidal solutions. Coagulation of colloidal solutions: methodical instructions for 1st year students' self-work in Medical Chemistry / compiled by A.O. Syrovaya, S.V. Andreeva, M.O. Vodolzhenko et al. – Kharkiv: KhNMU, 2017. – 28 p.

Compiled by:

A.O. Syrovaya,
S.V. Andreeva,
M.O. Vodolzhenko,
V.O. Makarov,
V.N. Petyunina,
T.S. Tishakova,
O.L. Levashova,
S.N. Kozub,
L.V. Lukianova,
E.V. Savelieva,
N.N. Chalenko

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Укладачі:

Г.О. Сирова,
С.В. Андрєєва,
М.О. Водолаженко,
В.О. Макаров,
В.М. Петюніна,
Т.С. Тішакова,
О.Л. Левашова,
С.М. Козуб,
Л.В. Лук'янова,
О.В. Савельєва,
Н.М. Чаленко

Subject “Preparation, purification and properties of colloidal solutions. Coagulation of colloidal solutions. Colloidal protection.”

1. Number of hours 4

2. Material and methodological support.

Multimedia tutorials (presentations, scientific films)

Tables:

1. Colloidal solutions;
2. The formation of micelles in colloidal solution;
3. Electrokinetic potential;
4. Types of disperse systems;
5. Electro-kinetic phenomena of colloidal solutions and their application;
6. The optical properties of colloidal solutions.

Educational literature:

1. Medical chemistry: textbook / V.O. Kalibabchuk, V.I. Halynska, L.I. Hryshchenko et al. – Kyiv : AUS Medicine Publishing, 2017. – 224 p.

2. Fundamentals of medical chemistry: manual for students' self-work / A.O. Syrovaya, E.R. Grabovetskaya, L.G. Shapoval. – Kharkiv: KhNMU, 2015. – 196 p.

3. Medical chemistry. Adapted concise course: manual for students' self-work / A.O. Syrovaya, E.R. Grabovetskaya, L.G. Shapoval. - Kharkiv: KhNMU, 2013. – 160 p.

4. Medical chemistry: workbook for self-work of first-year students of medical and dentistry faculties / compiled by A. O. Syrovaya, V. N. Petunina, V. A. Makarov et al. – Kharkiv : KhNMU, 2017. – 72 p.

5. Preparation, purification and properties of colloidal solutions. Coagulation of colloidal solutions. Colloidal protection. – Methodical instructions for 1st year students' self-work in Medical Chemistry / completed by A.O. Syrovaya, S.V. Andreeva, M.A. Vodolazhenko et. al. – Kharkiv: KhNMU, 2017. – 16 p.

6. Individual tasks for students' self-control of knowledge in Medical Chemistry / A.O. Syrovaya, L.G. Shapoval, et al. – Kharkiv: KhNMU, 2014. –50 p.

7. Text of lecture.

Laboratory glassware and reagents for demonstration experiment and laboratory work (stand rods with burettes, pipettes, solutions iron (III) chloride ($C(\text{FeCl}_3) = 0,005 \text{ mol/L}$), potassium hexacyanoferrate (II) ($C(\text{K}_4[\text{Fe}(\text{CN})_6]) = 0,005 \text{ mol/L}$), potassium hexacyanoferrate (III) ($C(1/3\text{K}_3[\text{Fe}(\text{CN})_6]) = 0,01 \text{ mol/L}$), potassium chloride ($C(\text{KCl}) = 1 \text{ mol/L}$), potassium chromate ($C(1/2\text{K}_2\text{CrO}_4) = 0,1 \text{ mol/L}$).

3. Substantiation of the subject. Micelle formation takes place in living organisms. Micelles form water insoluble solid particles. For example, blood content of calcium carbonates and phosphates greatly exceeds their solubility in water because part of these substances present in the blood in the form of hydrophilic sols (colloidal particles). Cholesterol and other substances slightly soluble in water also present in biological liquids in the form of sol. Blood protective substances such as proteins, polysaccharides stabilize these substances in colloidal state. Reduction of the protective function related to aging or pathological processes leads to coagulation of calcium phosphates, carbonates, cholesterol and other substances followed by sedimentation on the surface of blood vessels (atherosclerosis, calcification), salt formation in the urinary tract, kidney (urolithiasis) etc. Drugs solutions such as Collargolum, protargola are hydrophilic sols of silver protected by protein. Moreover, aerosols, pastes, ointments, and suspensions are commonly used in medical practice. Therefore, knowledge of methods of preparation, purification, and structure of dispersion systems, as well as the coagulation sols theory are necessary for the practical medicine and biomedical research.

4. The purpose of the subject:

- general: be able to use the knowledge of the physicochemical properties of colloidal solutions and coagulation features of colloidal solutions in biological and medical practice;

- specific: to analyze principles of the formation and purification of colloidal-dispersed systems, to know physicochemical bases of hemodialysis, to use knowledge of physical and chemical properties of the colloidal solution for the evaluation of properties of biological liquids, drugs, and the influence of electrolytes; to determine the coagulation threshold, the rate of coagulation and sedimentation,

know physicochemical principles of colloidal solutions stabilization (“colloidal protection”).

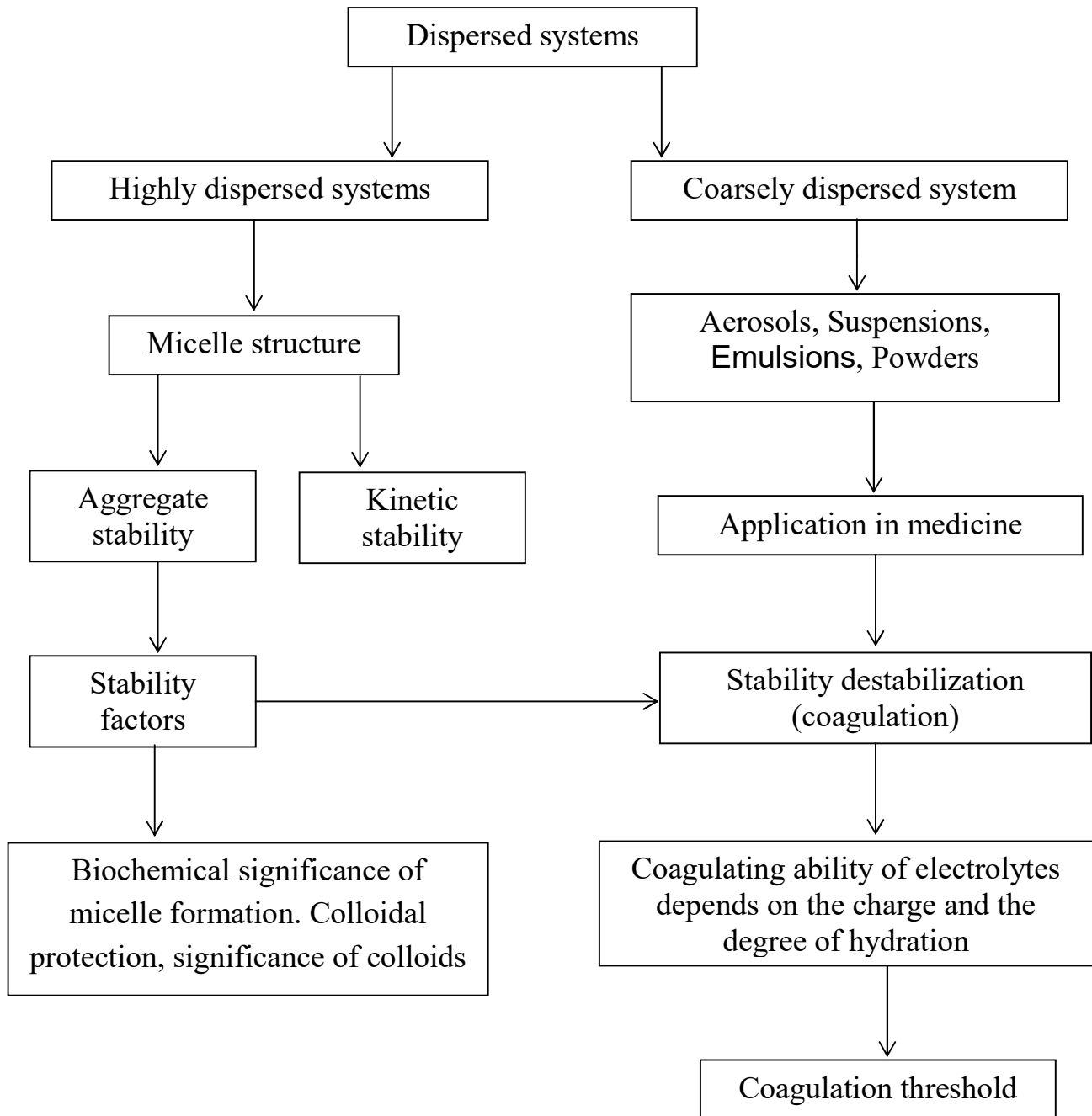
To know: dispersed systems and their classification, methods of colloidal solution formation, purification, dialysis, electrodialysis, ultrafiltration, molecular-kinetic properties of colloidal systems (Brownian motion, diffusion, osmotic pressure); optical properties of colloidal systems; ultramicroscopy; structure of colloidal particles; electrokinetic potential of colloidal particles, electrophoresis, its medical use and biomedical researches; Helmholtz-Smoluchowski equation; kinetic and of aggregative stability of liozols, stability factors, mechanism of coagulation action of electrolytes; coagulation threshold, its determination; Schulze-Hardy rule, coagulation processes in the purification of drinking water and wastewater, colloidal protection, its biological role; coarsely dispersed system (aerosols, suspensions, emulsions, etc.), preparation and properties, medicinal use, semi-colloids.

To be able to: obtain a colloidal solution and purify it from the impurities of low molecular weight compounds, be able to distinguish true solution and colloidal solution based on different molecular-kinetic and optical properties.

Practical skills:

- to make formulas of micelles and explain the reason for their stability,
- to determine which electrolyte ion will provide the coagulation effect on a sol,
- to compare the coagulation power of electrolytes,
- to calculate coagulation threshold of electrolyte in accordance to Hardy-Schulze rule,
- to indicate the direction of particle motion during electrophoresis.

5. Graph structure of the subject.



6. Plan of students' work.

| № | Stages | Time (min.) | Training and visual aids | Location |
|----|--|-------------|---|------------|
| 1. | Motivational characteristics and plan of the subject. Answers to the students' questions | 20 | Text book (work book) | Class room |
| 2. | Control of students' knowledge baseline | 20 | Tests | |
| 3. | Students' individual work with methodical literature, solving of educational tasks | 50 | Methodical instruction for students, lecture notes, text book for students' self-work, reference data, tables. | |
| 4. | Laboratory work | 45 | Methodical instruction for students, lecture notes, text book for students' self-work, reference data, posters. Manuals, reference materials, tables. | |
| 5. | Control of knowledge | 30 | | |
| 6. | Analysis and conclusions | 10 | | |
| 7. | Home task | 5 | | |

7. Tasks for self-work:

- list of questions to be study:

1. The concept of dispersed systems. Classification of dispersed systems: a) by the degree of dispersion (colloidal solutions, coarsely dispersed system); b) by the state of aggregation of the dispersed phase and dispersion medium (sprays, lyosols, solyosols); c) depending on the type of interphase interactions (hydrophobic and hydrophilic).

2. Colloidal solutions and their significance.

3. Methods of colloidal solutions preparation (dispersion: mechanical grinding, ultrasonic dispersion, Bredig's arc method, peptization method, etc.) Condensing methods: physical and chemical (solvent exchange method, chemical reaction involving formation of hardly soluble substances, etc.).

4. The structure of colloidal particles.

5. Methods of purification of colloidal solutions (dialysis, electrodialysis, ultracentrifugation, compensatory dialysis, vivi dialysis, ultrafiltration, etc.).

6. The properties of colloidal solutions - molecular-kinetic: (Brownian motion, diffusion, osmosis, diffusion-sedimentation equilibrium); Optical: (light scattering, Tyndall effect, light absorption); Methods for Biomedical Research (nephelometry, work of ultramicroscope and electron microscope).

7. Electro kinetic properties (electrophoresis, electroosmosis, flow potential, sedimentation potential) of colloids. Electrophoretic studies in medicine.

8. Kinetic and aggregative stability. Coagulation of dispersed systems. Factors affecting the stability of colloidal solutions.

9. Colloidal protection. Colloidal solutions of surfactants. The biological importance of the colloidal protection.

10. Application of dispersed systems (colloidal solutions, aerosols, suspensions, emulsions) in medicine.

1. Dispersed system (definition and components).

Substances in true solutions exist in molecular or ionic state, particles size does not exceed 10^{-9} m, with no physically distinctive boundary between the solute particles and the solvent, so true solutions are homogeneous system. The interphase boundary appears with an increase of particle size in the solution and formation of the dispersed (heterogeneous) system.

Dispersed system is a heterogeneous (non uniform) system consisting of two or more components with highly developed surface boundary. A solvent is usually a dispersion medium, a substance - a dispersed phase. The substance is uniformly distributed in the dispersion medium and has a fixed degree of dispersion.

2. Classification of dispersed system.

I. The dispersed systems are classified into groups by the degree of dispersion (particle size):

- colloidal solutions (highly dispersed systems, particles size $10^{-9} - 10^{-7}$ m);

- coarsely dispersed system (particles size $10^{-7} - 10^{-4}$ m).

II. According to the aggregate state of the dispersed phase and the dispersion medium system are classified:

1. Aerosols are system with a gas dispersion medium, i.e. dispersed systems consisting of solid or liquid particles disperse in a gaseous medium (usually air). Aerosols which dispersed phase consists of liquid droplets are called mists, and in the case of solid phase - smock or dust. Aerosols are formed by mechanical grinding and dispersion of solids and liquids, burning, spraying with a pulverizer and others.

L/G (phase/medium) – fog, cloud.

S/G – smoke, haze, dust-laden air.

2. Lyosols are systems with liquid dispersion medium:

a) emulsions (L/L) (immiscible liquids represent dispersed phase and dispersion medium, for example, oil or water).

O/W (phase/medium) (1st type emulsions or direct emulsions) – water-oil layer of normal and dry human skin, cosmetic milk, modern cosmetic creams, including medical cosmetics and nutrients - milk, low-fat sour cream, etc.);

W/O (2nd type emulsions or invert emulsions) – water-oil layer of fatty human skin, cream, crude oil, etc.

б) Colloidal solutions, suspensions (S/L) (dispersion medium is a liquid, dispersed phase is a solid substance that slightly or insoluble in the liquid). Colloidal solutions - dispersed systems in which phase particles have ultramicroscopic (colloidal) degree of grinding (1 - 100 nm). Suspensions have larger particles size compared to colloids. For example, cement, enamel paint, suspension of bentonite clay in water are suspensions. Under natural conditions formation of suspensions occurs during the soil of hard- rocks dispersion under the action of the ocean waves and others.

3. Solyosols – system with the solid dispersion medium:

S/S – solid sols, minerals;

L/S – soil capillary system;

G/S – foam.

III. Depending on the size of the interphase interactions dispersed systems are divided into:

Hydrophilic – solute and solvent are hydrophilic substances (CaCO_3 and H_2O). Hydrophilic systems characterize by high intermolecular interactions and small surface tension. Such systems are thermodynamically stable, because solvent molecules form highly developed hydration shell.

Hydrophobic – sulfur (hydrophobic substance) and water (hydrophilic solvent). Intermolecular interactions in hydrophobic systems are small. They characterize by large surface tension, resulting a thermodynamically unstable system. Stabilizers (HMW, SAS) are used to increase the stability of hydrophobic colloidal solutions (instant coffee).

Colloidal solutions (sol) have the greatest significance from all mentioned above solutions. Colloidal solutions include solid dispersed phase and liquid dispersed medium. Cells, genes, viruses are colloidal particles. Biological liquids – blood, lymph, and urine are colloidal systems. Colloidal state of various tissues of living organisms causes a variety of properties (gel state, elasticity, swelling et al.). In addition, colloidal substances are able to bind large amounts of water (connective tissue) and adsorption of various substances is very important for metabolism and digestion processes.

3. Methods of preparation of colloidal solutions

Colloidal systems are formed under the following conditions:

1) the presence of 2 phases; 2) the size of the substance should correspond to the size of colloidal particles; 3) utilization of stabilizers.

In the case of hydrophilic colloidal system, stabilizers are ions of electrolytes, which form an ionic hydration shell on a surface of dispersed phase, and keep colloidal particles in suspension.

HMW solutions (SAS) are used as stabilizers of hydrophobic colloidal systems.

Considering that colloidal solutions occupy an intermediate position between coarse dispersion and true solutions for their preparation can be used two groups of methods: 1) dispersion: grinding larger particles to the desired degree of dispersion,

or 2) condensation: association of molecules or ions into aggregate units having size of colloidal particles.

Disperse methods. Dispersed phase is crushed to the size of colloidal particles and transferred in the dispersion medium, if necessary, the stabilizer is added (SAS). The following methods of grinding of substances are available:

- mechanical grinding in colloid mills (paint);
- electrical dispersion Bredig's arc methods;

- peptization method. Peptization is a process of converting a freshly formed precipitate into colloidal sol by shaking it with the dispersion medium in the presence of a small amount of suitable electrolyte. The electrolyte added is known as peptizing agent. Also peptization can be carried out by creating an electric double layer around the particles and formation of hydration shell on colloidal particles. For example, freshly formed precipitates of $\text{Al}(\text{OH})_3$ will change into a colloid by adding a solution of AlCl_3 ;

- ultrasonic dispersion ($10^5 - 10^6$ Hz);

- dissolution (spontaneous dispersion). This method is used to obtain HMW solution from a solid polymer by dispersing it in a suitable solvent. For example, the dissolution of starch, gelatin, milk or agar-agar in water. Spontaneous dispersion method leads to the formation of a two-phase stable colloidal system.

A third substance usually is used as the stabilizer in dispersion methods.

Condensation methods are based on the association of particles from the size of molecules to the size of colloidal particles. Condensation methods can be physical (formation of fog, clouds, smoke) and chemical (formation of colloidal particles as a result of various chemical reactions). The condensation methods of colloidal solutions formation:

- by exchange of solvent (changing the solvent in a solution in which soluble dispersed phase). For example, during dilution of alcohol tinctures of valerian and others with water colloidal solutions of drugs are formed. Solute molecules that were in alcoholic tinctures, during dilution with water are condensed into large colloidal particles. Active substances are less soluble in water than in ethanol;

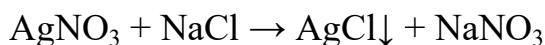
- reactions that result in formation of hardly soluble substances.

For the formation of colloidal solution in a one component dilute solution a small volume of concentrated solution of the second component is added with vigorous stirring. The role of stabilizer, in this case, plays the component that was taken in excess.

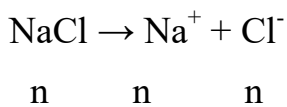
4. Structure of colloidal particles

Unlike true solutions containing molecules and ions, the structural unit of colloidal solutions is micelle. Micelle, which forms the dispersed phase of sol, consists of a nucleus with electrical double layer. The nucleus has a crystalline structure. Electrical double layer consists of adsorbed and diffuse layers. An ionic electrical double layer appears due to the selective adsorption of ions completing the crystal lattice of the solid phase.

For example, hardly soluble substance of silver chloride is formed, if you add sodium chloride solution to silver nitrate solution:

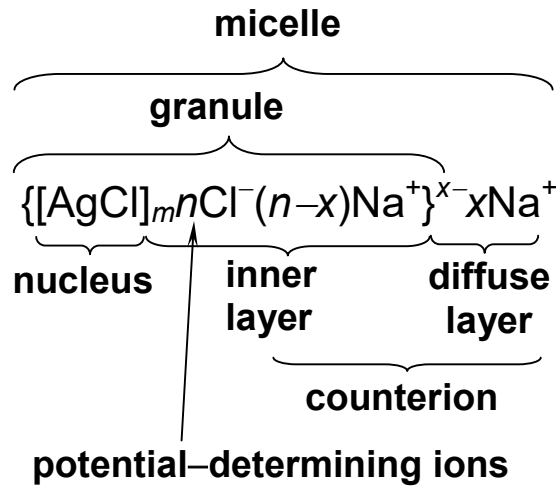


NaCl is a stabilizer that present in excess. NaCl dissociates:

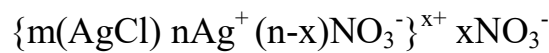


The hardly soluble AgCl form the nucleus of micelle. According to Peskov-Fajans rule, the stabilizer's ions are adsorbed on the nucleus (ions identical to the crystalline nucleus or isomorphic them), particles of the nucleus adsorb Cl^- ions and become negatively charged. These ions are called potential-determining ions because they determine the charge of the granule. Then part of counterions of opposite charge (in this case, sodium ions $(n - x) \text{Na}^+$) tends to adsorb to the particles to form an adsorbed (inner) layer. Part of remaining counterions, $x\text{Na}^+$ is located in the diffuse layer.

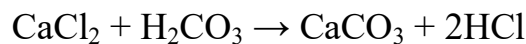
Micelles has a negative charge (negative sol):



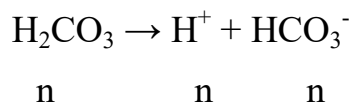
If a solution of silver nitrate is added to a solution of sodium chloride, and the stabilizer in this case is silver nitrate, a positively charge micelles forms (positive sol):



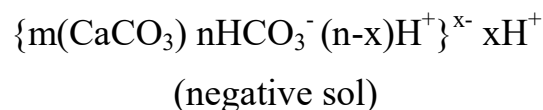
For blood plasma and other biological liquids we can write the structure of the micelle of calcium carbonate colloidal solution, based on the reaction:



Carbonic acid in plasma exists in partially ionized form



Thus, the micelle has the following structure:



The charge of the granule determines the value of zeta potential (ξ) (electrokinetic potential), which appears at the border of adsorbed and diffuse layers. The value of zeta potential is the difference between the total number of potential determining ion charge and number of charges of counterions present in the adsorbed layer. The value of zeta potential indicates the stability of the colloidal system. Electrokinetic potential cannot be measured.

5. Methods of purification of colloidal solutions

Colloidal solutions need to be purified from the impurities (ions, low molecular weight substances) that reduce the system stability. The following methods are used for this purpose: dialysis, electrodialysis, ultracentrifugation, compensation dialysis and vivi-dialysis.

Dialysis is a separation technique that relies on the selective diffusion of component of a solution across a semi-permeable membrane to separate them based on size. Low-molecular weight substances or ions present in biological liquids can be washed away, while colloidal particles that are larger than the membrane' pores are retaining in the solution. Typically, cellophane, parchment, nitrocellulose, or acetylcellulose are used as semi-permeable membrane. This method is widely used for the purification of colloidal dispersions and solutions of low-molecular weight compounds. This is a very slow process that can be quickened by applying an electric field.

Electrodialysis — process, during which ions are transported through semi permeable membrane, under the influence of an electric potential. The device consists of three parts separated by two semipermeable membranes. Colloidal solution is placed in the middle chamber, clean solvent - in the side chambers with immersed electrodes operated at a constant voltage. Thus, this process accelerates movements of ions and purification process of colloidal solution goes much faster.

The essence of *compensation dialysis* is that the analyte in the dialyzer washed with solvents having different concentration.

Vivi-dialysis is similar to compensation dialysis. It uses to determine low molecular weight substances content in the blood. To do this, a cut vessel attached to tubes with semipermeable material and immersed in a vessel with physiological solution or water. The presence of glucose and amino acids in the blood was established using this method.

The “artificial kidney” machine works according to the principle of compensating dialysis. It is used for treatment of acute renal failure, poisoning, toxicity, severe burns, and others. In this analysis the blood under pressure flows through a narrow gap between two semipermeable membranes, washed by physiological solutions. Toxic products are drawn out of the blood. Cleaning the blood (hemodialysis) uses dialysis to remove impurities and waste products from the bloodstream (urea, uric acid, an excess of potassium, chlorine, etc.) during 4-hours treatment.

Ultrafiltration is a type of the membrane filtration in which separation through semipermeable membrane is forced by pressure or concentration gradient.

The components of dispersed system can be separated by ultracentrifugation. The

centrifuge, which through rapid spinning, imposes high centrifugal forces on components of the solution, and causes separations on the basis of differences in weight.

6. The properties of colloidal solutions

- molecular-kinetic;
- optical;
- electro kinetic.

Comparative characteristics of physical and chemical properties of disperse systems and true solutions

| Coarse dispersions ($d > 10^{-7}$ m) | Colloidal dispersions ($d 10^{-7} - 10^{-9}$ m) | True solutions ($d < 10^{-9}$ m) |
|--|---|---|
| Micro-heterogeneous | Ultramicro-heterogeneous | Homogeneous |
| Formed of insoluble substances | Formed of insoluble substances | Formed of soluble substances |
| Opaque | Opaque | Transparent |
| Kinetically unstable | Kinetically stable, aggregately unstable | Kinetically and aggregately stable |
| Do not diffuse | Diffuse slowly | Fast diffusion |
| Do not pass through the filter paper | Pass through a filter paper, do not pass through the ultra-filter | Pass through a filter paper and ultra-filter |
| Do not pass through the semipermeable membrane | Do not pass through the semipermeable membrane | Pass through the semipermeable membrane |
| Visible in the optical microscope | Invisible in the optical microscope, visible in ultra-microscope | Invisible in the optical and ultra-microscope |

Molecular-kinetic properties

Molecular-kinetic properties, such as a Brownian motion, diffusion, and osmosis are common to true and colloidal solutions. The difference is that colloids characterize by lower values of these properties, due to the larger size.

Osmotic pressure is directly proportional to the concentration for true and colloidal solutions. Besides that, the magnitude of the osmotic pressure is not stable, due to the volatility of colloidal solutions and their dispersed particles have a tendency to aggregation.

Brownian motion is the chaotic motion of particles in microheterogeneous

systems resulting from the thermal motion of the particles of dispersed phase and dispersion medium.

Specific properties such as sedimentation-diffusion equilibrium are typical for colloidal solutions.

Dispersed phase particles in colloidal solutions settle under the gravity forces. Sedimentation time depends on the particle size. Sedimentation-diffusion equilibrium is the state attained when the force of gravity and diffusion forces act in the opposite direction, balancing one another. This equilibrium can be disturbed by the influence of centrifugal forces, resulting in sedimentation process. This principle is used in centrifuges. Centrifugation is used for separation of proteins, separation of blood cells components, separation of cell organelles from the tissue homogenates, etc.

Optical properties of colloidal solutions

Colloidal solutions are optically heterogeneous (have different size, shape and particles structure), so colloidal solutions have the ability to:

- scatter light (opalescent effect due to light diffraction);
- Tyndall effect – the appearance of cone at a side lighting of the colloidal solution on a dark background. This effect caused by the size of colloidal particles. Since the size of colloidal particles larger compared to the wavelength of light in the visible region, a beam of light falling on the surface of particles whose dimensions are larger than the wavelength of the beam repelled from causing a diffraction (light scattering).
- light absorption. The colourless colloids absorb only in the ultraviolet part of the spectrum, and the absorption in the visible spectrum is usually very weak. Selective light absorption is a function of dispersity. Highly dispersed sols absorb the green part of the spectrum (they have red color). With increasing the particle size the color of sol becomes blue.

The important biomedical researches methods are based on the light scattering by colloidal particles. The concentration of protein in the urine determines by the turbidimeter. The turbidity is proportional to the suspended solid concentration. This technique measures the transmitted and scattered light intensity due to scattering and absorption effect of colloidal particles. Ultra-microscope (observation of particles on a

dark background with side lighting) and electron microscope enable to determine the concentration and the dispersity of particles in a biological matrix.

An electron microscope uses an “electron beam” to produce the image of the object and magnification is obtained by “electromagnetic fields”; unlike light or optical microscopes, in which “light waves” are used to produce the image and magnification is obtained by a system of “optical lenses”.

7. Electrokinetic properties of colloidal solutions

Electrokinetic phenomena are processes occurring in heterogeneous system with a relative movement of two phases involving electric field (F.F. Reuss). The reason of electrokinetic phenomena is the existence of the electrical double layer in the interface of solid phase and liquid medium as well as granules motion with respect to the diffusion layer.

There are four types of electrokinetic phenomena - electrophoresis, electroosmosis, flow potential and sedimentation potential (settling).

Electrophoresis — the motion of dispersed particles with respect to liquid medium under the influence of the electric field. Electrophoresis is used to separate amino acids, proteins, enzymes, antibodies etc. This method is used for isolation and investigation of protein fractions of plasma. Blood electrophoretograms of healthy people are the same, but in pathological state they look specific for each disease and are used to make a diagnosis. Important information of electrochemical properties of biological systems was obtained using this method. It was established that all biological surfaces are charged negatively. The electrophoresis phenomenon observed during the leukocytes migration to the inflammation source. Because the tissue that were destroyed during inflammation, due to the formation of acidic products, have a positive charge, and the surface of leukocytes is charged negatively.

Electroosmosis — the motion of liquid medium with respect to solid phase under the influence of the electric field.

Flow potential — the potential difference between points on the current of the dispersion medium with respect to stationary phase. This is an inverse phenomenon to electroosmosis.

Sedimentation potential — the motion of dispersed particles under influence of gravity or centrifugation forces in a medium that generate an electric field. The potential difference between points at different heights of the moving dispersed phase. This phenomenon is reversible to electrophoresis.

Electrophoretic velocity is calculated using the Helmholtz-Smoluchowski equation:

$$U = \frac{\varepsilon \xi E}{4\pi\eta l}, \text{ where}$$

η - the dynamic viscosity of the liquid (**kg / m·s**); L – the distance between the electrodes; **H – electrophoretic mobility**, m/s; ε - dielectric permeability of the liquid (for water $9 \cdot 10^{-9}$), F/m; U – potential difference, V.

Hence, calculate the value of zeta potential:

$$\xi = \frac{4\pi\eta LH}{\varepsilon U},$$

8. Stability and coagulation of dispersed systems (according to Peskov)

From a pharmaceutical point of view the most important property of colloidal solutions is a high degree of lability. Different kinds of the external effects such as increase or decrease in temperature, shaking, mixing, radiation, addition of some chemical substances and so on may cause the coagulation of colloidal solutions. Coagulation is the process of growing and aggregating of the primary particles resulting in the phase sedimentation. Sometimes during coagulation sol is transformed into transparent gel. Even the most careful storage cannot prevent sol from aging processes followed by coagulation or gelatination.

There are two types of stability of dispersed systems - aggregative and kinetic.

Kinetic stability is the ability of the dispersed phase to be in the suspension without undergoing sedimentation. Highly dispersed systems are stable kinetically and the sediment-diffusion equilibrium is typical for them.

Aggregative stability is the ability of a system to keep the fixed degree of dispersion without being combined into more coarse (large) aggregates. Breaking of the aggregative stability as the result of the primary particles adherence and formation the

more coarse aggregates followed by the dispersed phase sedimentation is called coagulation. The dispersed systems are mostly unstable aggregatively.

Factors of stability of colloidal solutions:

- 1) The presence of the electric charge in the dispersed systems (ξ -potential). The greater the ξ - potential, the higher the stability due to the mutual electrostatic repulsion.
- 2) The solvating (hydrating) effect of counterions of diffuse layer. The more hydrated are the counterions of the diffusive layer, the greater is the thickness of the hydrated shell surrounding the granules and the more stable is the dispersed system. Solvated (hydrated) shells possess elastic properties and result in generation of repulsive forces between the particles.
- 3) Adsorption-structural properties of disperse systems. Hydrophobic particles well adsorb on their surface SAS (HMW) having hydrophilic properties. Adsorption-solvate layers with considerable length and density are formed on the surface of hydrophobic sol. These layers provide high stabilization even at very high concentration of the dispersed phase.

The HMWC's ability to form the adsorption-solvate layers on the surface of the lyophobic particles is called a protective activity. In all biological liquids colloidal solutions are protected.

The most significant factor causing coagulation is an action of electrolytes. Here are the rules of coagulation:

1. All electrolytes cause coagulation of a sol because they reduce the thickness of the double layer and zeta potential value.
2. The coagulation of positively charged soles is caused by anions, and the coagulation of negatively charged soles is caused by cations. Addition of electrolytes causes the formation of the isoelectric state of a micelle:



The critical value of ζ -potential at which the coagulation process begins is ± 30 mV.

3. Every electrolyte is characterized by the threshold concentration (C). Threshold concentration (C) – the minimum concentration measured in millimoles, which have to be added to a liter of the colloid solution to cause its coagulation.

$$C = \frac{C_e \cdot V_e \cdot 1000}{V_{sol} + V_e} \text{ mmol/L}$$

Coagulating power (P) is inversely proportional to the coagulation threshold:

$$P = \frac{1}{Ck}$$

4. The coagulation power of ions depends of the value of their charge. The greater is the ion charge, the greater is its coagulating power (Hardy-Schulze rule).

$P_{Al^{3+}} > P_{Ca^{2+}} > P_{K^{+}}$ lyotropic series

$C_{K^{+}} > C_{Ca^{2+}} > C_{Al^{3+}}$, the lower the ion charge, the higher electrolyte concentration will cause coagulation (the higher is the threshold concentration).

$P_{PO_4^{3-}} > P_{SO_4^{2-}} > P_{Cl^{-}}$

$C_{(k)Cl^{-}} > C_{(k)SO_4^{2-}} > C_{(k)PO_4^{3-}}$

The coagulating power for the ions with the same sign of charge depends on the radius of the solvated ion: the more is the radius, the lower is its coagulating power. The atom and the ion radius in the sub-group of the Periodic table increase downwards. The more is crystallographic radius, the less is the radius of the solvated ion.

$P_{Cs^{+}} > P_{Rb^{+}} > P_{K^{+}} > P_{Na^{+}} > P_{Li^{+}}$

$P_{CNS^{-}} > P_{I^{-}} > P_{Br^{-}} > P_{Cl^{-}}$

Many organic substances have higher coagulating power than inorganic substances. H^{+} and OH^{-} ions have high coagulating power.

The following phenomena can be observed during the coagulation process caused by electrolytes:

Additivity — the coagulating power of electrolytes in a mixture is equal to the sum of the coagulating powers of each electrolyte. Such a phenomenon is quite rare when coagulating ions have the same sign of charge and similar degree of hydration.

Antagonism — the coagulating power of ions in a mixture is less than the power of each ion taken separately.

Synergism — the coagulating power of ions in a mixture increases.

Tolerance. If we add a small portions of electrolyte coagulating agent to the sol every wide interval the coagulation will not occur, though the total amount of the added electrolyte exceeds much the threshold concentration value. It is called a tolerance, as the sol behave like a living organism that can become tolerant to poison inserted in small doses (nicotine, arsenic, morphine, etc.).

The mutual coagulation of soles. When two oppositely charged sols are mixed in equimolar proportions, they mutually neutralize their charges and both coagulate. This process has electrostatic nature. The phenomenon of mutual coagulation widely used for purification of natural and industrial water.

On the water stations $\text{Al}_2(\text{SO}_4)_3$ or FeCl_3 salt are added to sand filters. Positively charged sols of $\text{Al}(\text{OH})_3$ or $\text{Fe}(\text{OH})_3$ are formed after hydrolysis. They cause coagulation of negatively charged soil particles, microflora, and organic impurities.

9. Colloidal protection. Colloidal solutions of surfactants. The biological significance of colloidal protection

Structural-mechanical factor of soles stabilization by the addition of some amount of high-molecular weight compounds is called a colloidal protection. Adsorption of HMC (high-molecular compounds) on the surface of colloidal particles protects them. The sol acquires the properties of lipophilicity and become stable. The process of protecting a lyophobic sol from being coagulated on addition of an electrolyte by adding a lyophilic colloid to it is called protection, and the lyophilic colloid that is used in the process is called a protective colloid. Quantitatively the protective power of protective colloids is expressed in terms of gold number.

The gold number is a number of milligrams of the protective colloid required to prevent the coagulation of 10 ml of a given sol when 1 ml of 10% NaCl is added to it.

In the organism all hydrophobic sols are protected by proteins, polysaccharides, pectins. Healthy people have a fixed amount of protective substances in biological liquids. The protective qualities of proteins and other substances are changing when some kind of pathology or ageing processes take place in an organism resulting in formation of hardly soluble salts. Precipitation of these salts leads to formation of stones in kidneys, liver and ducts of digestive glands.

Disbalance of lecithin-cholesterol equilibrium, reduction of protective proteins

properties, leads to the development of atherosclerosis (cholesterol deposits in the walls of arteries).

The phenomenon of colloidal protection is used in manufacturing drug preparations (protargolum, collargolum etc.).

A protected sol does not obey Hardy-Schulze rule and its coagulation can cause the electrolyte quantity that exceeds the threshold value or the reagent that cause the precipitation of HMW.

At low concentrations of surface-active substances (SAS) in water (less than 10^{-3} mol/L) true solutions are formed. Concentrated solutions of surfactant have a colloidal structure due to spontaneous formation of colloidal aggregates in the system. The formation of spherical micelles occurs at concentrations known as the critical micelle concentration (CMC). This dramatically changes physical and chemical properties of surfactant solutions: osmotic pressure, conductivity, turbidity, and surface tension. CMC value usually stays in the range 10^{-4} - 10^{-5} mol/L, for phospholipids and sphingolipids the CMC range is 10^{-8} - 10^{-10} mol/L.

The main feature of micellar surfactant solutions is solubilization (colloidal dissolution, protection). In other words the incorporation of the surfactant component in the inner core of the micelle or on the surface of the micelle is called micellar solubilization. If this other component is sparingly soluble in the solvent alone, solubilization can increase its solubility due to the presence of the association colloid. The solubility of hydrophobic compounds in micellar surfactant solutions highly increases as a result of solubilization. For example, the process of fats assimilation in the organism begins with the solubilization by the combination of lecithin with bile salts and the polar lipids. This mixture possesses an enhanced emulsifying power.

Semi-colloids are solutions having a mixed nature. The dispersed phase may be in dynamic equilibrium of the molecular-ionic form and in the form of colloidal particles in the same solvent.

Soaps, detergents, tannin, dyes are semi-colloids.

Soaps (salts of higher carboxylic acids) and detergents (octadecyl ammonium chloride, duponol etc.) have high surface activity. They represent a long hydrocarbon chains with ionogenic groups at the end. Most commonly, they classified according to the nature of ionogenic group: anionic ($-\text{COO}^-$, $-\text{OSO}_3^-$ etc.) or cationic ($-\text{NH}_3^+$).

Due to intermolecular forces of attraction hydrocarbon chains associates in aqueous environment with the formation of spherical or lamellar micelles.

As a result of micelle formation on the surface of the micelles will be located polar groups that hydrolyze in water, ensuring the stability of the colloidal system.

Alkaline metal soaps in concentrations less than 1% exist as molecular solutions. At concentrations above 1% - in the form of spherical or lamellar micelles in which ionogenic groups directed toward the water.

At concentrations above 7-8% soap solutions lose fluidity and turn into a gel.

Solubilization is an important property of micellar solutions which results from their structure, i.e. penetration of poorly or almost insoluble in this solvent compounds into micelles of lyophilic colloids, leading to a sharp increase in the solubility of these compounds in micellar solutions.

The emulsifying effect of surfactants, cleaning properties of soaps and detergents related with the solubilization process.

Many natural molecules possess surfactant properties, e.g. phospholipids may form bilayer structures, in which their molecules are turned to each other with hydrophobic ends (hydrophobic interactions), and polar – to water molecules. These structures can be not only bilayer but also multi-layer. They may contain water, which is present in the interspace between two bilayer structures – inner and outer. These formations are called liposomes. They are suitable as an object for investigation of the models of cellular membranes. They are used for the directed drugs delivery to the injured organs and tissues.

Proteoliposomes are liposomes containing a protein molecule inside, they widely used in medicine as drugs.

10. Application of disperse systems in medicine

All biological liquids in our organism are colloidal solutions. For example, in blood enzymatic elements form a dispersed phase, and plasma is the dispersion medium. Coagulation processes are characteristic for the dispersed phases of blood. In particular, the red blood cells are normally sediment with a certain rate (ESR). In a variety of pathological states biochemical composition of the blood changes. Red blood cells absorb large molecules of globulins, fibrinogen, become heavy and ESR

increases. Coagulation is very important for the blood clotting process. This process leads to stop the bleeding.

Colloidal solutions are widely used in the modern medicine. In particular, an introduction of colloidal solutions (Plasma Substituents) is more effective than true solutions in order to maintain blood volume (v/v) for the treatment of heavy bleeding. In clinical practice, 5% and 25% of serum human albumin solutions are used, defining more than 80% of colloidal osmotic pressure (oncotic) of plasma and play an important transport function for the antibiotics and ions delivery. In addition, 6% hetastarch solution and dextran-40 solution are used for this purpose.

“Refortan” (Stabizol, Infukoll, Venofundin, Hemohes) - 6% of hydroxyethyl starch solution is used as plasma-substituting colloidal solution for the treatment and the prevention of hypovolemic shock, burns, trauma, surgical interventions.

“Komizol. Gold (^{198}Au) colloidal”- intravenous injection solution is used to scan the liver, as a liver blood flow parameter, regional lymph flow and lymph gland scan, as an anti-tumorous agent introduced into tissues, cavities and lymph vessels.

Aerosols insecticides, fungicides, so-called industrial aerosols (smoke, aerosols containing lead, zinc, silica oxides, etc., manufactured by chemical companies) are destructive to health. The following aerosols are used in medical practice:

“Berotec N” - for the prevention of acute bronchial asthma;

“Lioxasolum” - for the treatment and prevention of the acute radiation damage of skin;

“Camphomen” - for the treatment of inflammatory diseases of the upper respiratory tract, acute rhinitis, pharyngitis, and others.

In medicine water-insoluble drugs are used in the form of suspensions, including:

Suspensions of sulfur in dermatology;

Blue clay suspension, therapeutic mud;

“Zinc-corticotropin suspension” administered intramuscularly as an anticonvulsant in the treatment of atrophy, rheumatism, infectious nonspecific polyarthritis, bronchial asthma, leucosis, neurodermatitis, eczema, and allergic diseases;

“Bactrim suspension” (sulfamethoxazole) is used internally after meals for the treatment of respiratory, urinary tract and the gastrointestinal tract infections;

“Maalox” (oral suspension) contains as active ingredients magnesium hydroxide and aluminum hydroxide, used as antacid agent (in violation of acidity) for the treatment of stomach or duodenal ulcers in the acute phase.

Pastes (coarsely dispersed system) with a high concentration of the solid dispersed phase (from 25% to 75%) in a liquid dispersion medium are widely used in dentistry and dermatology.

Emulsions are also widely used in medicine, especially:

“Omegaven emulsion” for parenteral nutrition by intravenous injection. It contains highly purified fish oil, egg protein phospholipids as emulsifiers, and water for injection;

“Nutriflex 40/80 Lipid” for parenteral nutrition containing amino acids, electrolytes, olive oil, and dextrose;

“Kabiven central” for parenteral nutrition containing soybean oil, amino acids, dextrose, electrolytes.

From a pharmaceutical perspective, it should be remembered that drugs containing heterogeneous dispersed systems have a short-term stability. Therefore, it is important to adhere the specific storage (in a dry, cool, dark place without overheating or overcooling) and visual quality control of medicinal products containing dispersed systems for their homogeneity before use. At the slightest change in the organoleptic properties of the drug it cannot be used.

- list of laboratory works:

During the classes students perform demonstration experiment “Determination of colloidal particle charge by capillary method” and laboratory experiments

“Determination of coagulation threshold of iron (III) hydroxide sol”.

Demonstration experiment: “Determination of colloidal particle charge by capillary method”

Algorithm of the demonstration experiment

A drop of Berlin blue solutions obtained earlier from ferric chloride (III) solution with $C(\text{FeCl}_3) = 0,005 \text{ mol/L}$ and potassium ferrocyanide (II) solution with $C(\text{K}_4[\text{Fe}(\text{CN})_6]) = 0,005 \text{ mol/L}$ take in the following proportions and place on the filter paper: a) 3 ml of FeCl_3 solution and 1 ml of $\text{K}_4[\text{Fe}(\text{CN})_6]$ solution; б) 3 ml of $\text{K}_4[\text{Fe}(\text{CN})_6]$ solution and 1 ml of FeCl_3 solution.

After the adsorption of the drop a positive sol is adsorbed by the paper and produces a spot colored in the center and having colorless edges; negative sol is not adsorbed by the paper and produces evenly colored spot.

Record the results of the observation. Write the formulae of micelles of sols used in this experiment.

Laboratory work “Determination of coagulation threshold of iron (III) hydroxide sol”.

Algorithm of the laboratory work

1. Fill burettes with following solutions: 1) potassium chloride $C(\text{KCl}) = 1 \text{ mol/L}$; 2) potassium chromate $C(1/2 \text{ K}_2\text{CrO}_4) = 0,1 \text{ mol/L}$; 3) potassium hexacyanoferrate (III) $C(1/3 \text{ K}_3[\text{Fe}(\text{CN})_6]) = 0,01 \text{ mol/L}$.

2. Add 5 ml of iron (III) chloride sol into three test tubes.

3. Add potassium chloride to the first sol dropwise, potassium chromate to the second, and potassium hexacyanoferrate (III) to the third one until the appearance of turbidity (coagulation).

Record the data in the table:

| Electrolyte | C(E) of electrolyte, mol/L | Volume of electrolyte, ml | Coagulating ion | Coagulation threshold, C(x), mmol/L | Coagulating power, P(x), mol/L |
|---------------------------------------|----------------------------|---------------------------|-----------------|-------------------------------------|--------------------------------|
| KCl | 1 mol/L | | | | |
| K ₂ CrO ₄ | 0,1 mol/L | | | | |
| K ₃ [Fe(CN) ₆] | 0,01 mol/L | | | | |

1. Calculation of coagulation threshold:

$$C(1/z) = \frac{C(E) \cdot V(x) \cdot 1000}{V(\text{sol}) + V(x)}$$

2. Calculation of coagulating power of electrolytes:

$$P(x) = 1/C(x) = \quad \quad \text{L/mmol}$$

Conclusions:

- list of practical skills to be mastered.

After studying the subject you must be able to carry out coagulation of sols under the influence of electrolytes, to compare the coagulating power of electrolytes, make

formula micelles and explain the reason for their stability, indicate the direction of particle motion during electrophoresis.

8. Tasks for knowledge control.

1. What kind of charge does sol have if its particles move toward anode?

A. (+);

C. (0);

B. $(-)$;

D.partial (+).

2. What is the structure of AgCl micelle, if its charge defines as negative?

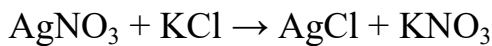
$$\text{A. } \{(\text{AgCl})_m \text{nAg}^+ (\text{n}-\text{x})\text{Cl}\}^0$$

B. $\{(\text{AgCl})_m \text{nCl}^-(\text{n}-\text{x})\text{Ag}^+\}^0$

C. $\{(AgCl)_m n Ag^+ (n-x) NO_3^-\}^{x+} x NO_3^-$

$$\text{D. } \{(\text{AgCl})_m \text{nCl}^-(\text{n}-\text{x})\text{K}^+\}^{\text{x}-} \text{x K}^+$$

3. AgCl sol obtains by the following reaction



What kind of reagent should be taken as a stabilizer, if particles of obtained sol move towards anode in an electric field?

A. KCl

C. KCl , AgNO_3 equal

B. AgNO_3

D.H₂O

Answers: 1 - B; 2 - D; 3 - A.

9. Recommendations for presentation of the results.

Algorithms for solving educational problems of class work and self-work should be recorded in the workbook. Make a protocol of laboratory work, conclusions regarding characteristics of physical and chemical properties of dispersion systems and their use in clinical practice.

10. Suggested readings

V. Kalibabchuk, V. Halinska, L. Hryshenko, S. Hodzynski, T. Ovsyanikova, V. Samarski. Medical chemistry. –Kyiv AUS Medicine Publishing, 2010, –224p.

Навчальне видання

Одержання, очистка та властивості колоїдних розчинів. Коагуляція колоїдних розчинів. Колоїдний захист

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Укладачі:

Г.О. Сирова,
С.В. Андрєєва,
М.О. Водолаженко,
В.О. Макаров,
В.М. Петюніна,
Т.С. Тішакова,
О.Л. Левашова,
С.М. Козуб,
Л.В. Лук'янова,
О.В. Савельєва,
Н.М. Чаленко

Відповідальний за випуск Водолаженко М.О.

Комп'ютерний набір та верстка Водолаженко М.О.