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OBTAINING AND PROPERTICS POLYMERMETALCOMPLEX ON THE BASE CARBOXYMETHYLCELLULOSE AND SELENIUM

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ПОЛУЧЕНИЕ И СВОЙСТВА ПОЛИМЕР МЕТАЛЛОКОМПЛЕКСОВ НА ОСНОВ КАРБОКСИМЕТИЛЦЕЛЛЮЛОЗЫ И НАНОЧАСТИЦ СЕЛЕНА

КАРБОКСИМЕТИЛЦЕЛЛЮЛОЗА ВА СЕЛЕН НАНОЗАРРАЛАРИ АСОСИДА ПОЛИМЕРМЕТАЛЛОКОМПЛЕКСЛАР ОЛИШ ВА УЛАРНИНГ ХОССАЛАРИ

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Abstract. In this study, technical sodium carboxymethylcellulose (Na-CMC) with degree of substitution (DS) = 0.62-0.90 and a degree of polymerization (DP) = 200-600 were washed in 70% ethyl alcohol and a 2% fraction of purified Na-CMC was centrifugation at a speed of 6000 rpm for 20 minutes. A 0.1 M solution of SeO_2 was added to the centrifuged Na-CMC solution at 60 ⁰ C and mixed mechanically. Samples of gels, films and powders containing a solution of Na-CMC containing stabilized selenium nanoparticles synthesized by chemical reduction were taken and their physicochemical properties were studied. The size and shape of selenium nanoparticles present in the structure of Na-CMC were determined by X-ray diffraction analysis (XRD), UV spectroscopy, and atomic force microscopy (AFM) methods. Physico-chemical studies have shown that with increasing selenium oxide concentrations in CMC solutions, an increase in the size of spherical selenium nanoparticles to 9–42 nm was observed. In X-ray diffraction analysis (XRD) studies, it was observed that the crystals of selenium nanoparticles formed differential oscillations at 31.5 °, 48.5 °, 63.1 °, 64.6 °, 67 °, and 69 °. Biomedical properties of this drug were studied in collaboration with scientists of the Tashkent Medical Academy, and that the synthesized drug exhibited low toxicity to the organism was studied in experimental animals.

Keywords: sodium - carboxymethylcellulose, selenium nanoparticles, spherical selenium nanoparticles, selenium oxide, ascorbic acid, chemical reduction, X-ray structural analysis, medical-biological.

Аннотация. В данном исследовании, техническая натрий-карбоксиметилцеллюлоза (Na-КМЦ) со степенью замещения (СЗ) - 0,85 и степенью полимеризации (СП) - 600 промывалась 70% этиловым спиртом, и растворенная фракция 2% раствора, очищенного Na-КМЦ полностью отделилась, центрифугировали при 6000 мин/об на 20 мин. К центрифугированному

раствору Na-КМЦ при 60°С добавляли 0,1 М раствор SeO_2 и перемешивали в механической мешалка. Исследаваны физико-химические свойства образцов гелей, пленок и порошков, содержащих раствор Na-КМЦ со стабилизированными наночастицами селена, синтезированными методом химического восстановления. Размер и форма наночастиц селена, присутствующих в структуре Na-КМЦ, были определены методами рентгеновского дифракционного анализа, УФ-спектроскопии и атомно силовой микроскопии (АСМ). Физико-химические исследования показали, что с увеличением концентрации оксида селена в растворах КМЦ наблюдается увеличение размеров сферических наночастиц селена до 9–42 нм. В исследованиях рентгеновского дифракционного анализа было обнаружено, что кристаллы наночастиц селена образуют дифференциальные колебания при 31,5 °, 48,5 °, 63,1 °, 64,6 °, 67 ° и 69 °. Медико-биологические данного свойства этого препарата изучались совместно с учеными Ташкентской медицинской академии и устоновлено не токсичность синтезированного препарата для организма.

Ключевые слова: натрий-карбоксиметилцеллюлоза, наночастицы селена, сферические наночастицы селена, оксид селена, аскорбиновая кислота, химическое восстановление, рентгеноструктурный анализ, медико-биологический

Аннотация. Мазкур ишда алмашиниш даражаси (АД)– 0,85 ва полимерланиш даражаси (ПД) – 600 бўлган техник натрий – карбоксиметилцеллюлоза (Na-КМЦ) 70 % ли этил спиртида ювилди ва тозаланган Na- КМЦ нинг 2 % ли эритмаси эриган фракцияси тўлиқ ажратиб олиш учун 20 мин давомида 6000 айл/мин билан центрафуга қилинди. Цинтрафуга қилинган Na-КМЦ эритмасига 0.1 М ли SeO_2 эритмаси 60^{o} С да қўшилди ва механик мешалкада аралаштирилди. Кимёвий қайтарилиш усулида синтез қилинган таркибида барқарорлаштирилган селен нанозарралари тутган Na- КМЦ эритмасидан гел, плёнка ва кукун намуналари олинди ва уларнинг физик-кимёвий хоссалари ўрганилди. Na-КМЦ структурасида мавжуд селен нанозарраларининг ўлчам ва шакллари рентгеноструктуравий анализ, УФ-спектроскопия ва атом куч микроскопик (АКМ) методлар орқали аниқланди. Физик-кимёвий кимёвий тадқиқодлар шуни кўрсатадики, КМЦ эритмаларида селен оксиди концентрациясининг ошиши билан сферик селен нанозарраларининг ўлчами 9-42 нм гача бўлиши тажриба асосида аниқланди. Рентгеноструктуравий анализ тадқиқодларида селен нанозарраларининг кристаллари 31.5°, 48.5°, 63.1°, 64.6°, 67° ва 69° градусларда дифармацион тебранишларни ҳосил қилганлиги аниқланди. Мазкур препаратнинг тиббий-биологик хусусиятлари Тошкент Тиббиёт Академияси илмий ходимлари билан ҳамкорликда ўрганилди ва синтез қилинган припарат организм учун зарарсиз эканлиги кўрсатиб берилди.

Калит сўзлар: натрий – карбоксиметилцеллюлоза, селен нанозарралари, сферик селен нанозарралар, селен оксиди, аскарбин кислотаси, кимёвий қайтарилиш, рентгеноструктуравий анализ, тиббий-биологик.

Introduction.

Among the scientific and technological progress achieved by the world scientific community is the creation of a new generation of nanostructured polymer preparations and materials for practical medicine. The search for new, effective and nanostructured, antitumor drugs remains one of the leading directions in creating more advanced methods of treating patients with malignant neoplasms [1,2].

The relevance of this study is also determined by the urgent need for public health in new highly effective and low-toxic drugs that have an antitumor effect based on selenium nanoparticles. Due to the high prevalence of oncological diseases, there is a high demand of the domestic chemical and pharmaceutical industry for the production of new drugs using nanochemistry, nanopharmacology and nanotechnology.

In recent ears, there has been increasing interest in the trace element selenium, which is part of the body's antioxidant defense system. In recent ears, there has been increasing interest in the trace element selenium, which is part of the body's antioxidant defense system. Nanoparticles of selenium, unlike antibiotics, are able to have a prolonged effect [3].

Selenium is of exceptional interest as chemical element with a unique biologically active substance with antioxidant, anti-inflammatory, anti-carcinogenic, anti-mutagenic and detoxifying, as well as antitumor activity [4]. Achievements of modern science allow us to develop and use the most advanced technologies, including nanotechnology, to obtain new drugs. The introduction of nanomaterials in clinical medicine requires knowledge of the potential risks and possible side effects associated with their use [5].

The successful introduction of new nanostructured drugs into clinical practice implies the presence of proven safety in their use. To carry out this mentioned one, a certain procedure for conducting research at various levels should be followed, the most important of which is the safety assessment at the stage of preclinical experimental studies. The more thoroughly the toxicity of the studied nanopreparations in animals is studied, the less adverse reactions can occur during clinical trials [6,7].

From the medical and biological point of view, the present study was a preclinical study of the safety of selenium nanoparticles stabilized on biodegradable polymer substrates of natural origin. The purpose of this work is to study the possibilities and methods for producing stabilized selenium nanoparticles in the structure of the polymer matrix – carboxymethcellulose sodium salt and study their structure, physico-chemical, biomedical properties

Experimental part. In this work, selenium (Se^0) nanoparticles obtained by reducing selenium (IV) oxide with ascorbic acid were selected as the object of research. As stabilizer, purified sodium carboxymethylcellulose (Na-CMC) was used, with a degree of substitution (DS) = 0.62-0.90 and a degree of polymerization (DP) = 200-600, obtained from cotton cellulose [8]. Aqueous solutions of SeO_2 were used to form selenium nanoparticles in the solution structure of purified Na-CMC.

For the formation of selenium nanoparticles, 2-4% aqueous solutions of purified samples of Na-CMC of various DS and DP were chosen after removal of the gel fraction by centrifugation at a speed of 6000 rpm for 20 minutes. Calculated amounts of 0.1-0.01 M aqueous solutions of SeO_2 were added to Na-CMC solutions freed from the gel fraction with stirring, and stirring was continued until a homogeneous $Se^{4+}CMC^-$ solution was obtained.

Chemical reduction of selenium ions in the structure of $Se^{4+}CMC^-$ to selenium nanoparticles was carried out at 50°C by adding various amounts of 0.1 M aqueous solution of ascorbic acid. To obtain dispersions of selenium nanoparticles, ultrasonic dispersion of the solution on a dispersant of the brand USDN-1, U-4.2 was used in the course of the reduction reaction.

The average size of selenium nanoparticles (Se^0) on the polymer matrix, the coefficient of variation was determined by mathematical analysis, corresponding microphotographs in the MathCad program. The morphology of the surface layers of nanometallopolymers in films cast from Na-CMC, Se^+CMC^- and Se^0CMC solutions was studied using an ASM-5500 atomic force microscope (Germany).

Biomedical-biological studies were performed on healthy sexually mature animals that were quarantined for at least 12-14 days. Toxicological studies of two compounds of the preparation of Selenium nanoparticles (the first - 0.6635% - "A"), (the second - 0.1327% - "B"), was carried out in the accredited testing laboratory of the Ministry of Scientific Research and Technology of TMA on the basis of normative and methodological documents of the State system of the Republic Uzbekistan, taking into account of the requirements of the European Convention for the Protection of Vertebrate Animals used for experimental research or for other scientific purposes (ETS№123, Strasbourg, 1986), the requirements of the National Guide for the Maintenance and Use of Laboratory Animals.

We used sexually mature mice of both sexes (n = 192, weighing 20-24 g), sexually mature white rats of both sexes (n=180, weighing 115-125 g).

Assessment of acute toxicity was carried out by a single intravenous, intraperitoneal, enteral administration in doses: from 500 to 4500 mg/kg. All test doses of the drug were prepared before administration on a physiological solution of sodium chloride. The general condition of laboratory animals was monitored hourly during the first day, and once a day in the next 13 days of the experiment (total observation period of 14 days). Before the start of the study and throughout the experiment (acute experiment) after the administration of the studied drug, clinical signs of possible intoxication were recorded: the general condition of the animals, feed and water consumption, changes in body weight, their behavior, the intensity and nature of motor activity, coordination of movements, reaction to external irritants, the frequency and depth of respiratory movements, the condition of the coat and skin, the color of the mucous membranes, the position of the tail, the amount and type of fecal mass. During the whole experiment, all laboratory animals were kept under standard vivarium conditions and were on a full laboratory diet with free access to water. The mean lethal dose of the studied polymer derivatives of selenium was calculated by the probit analysis method using the Biostat 2009 software package.

Research results and discussion

Amorphous and crystalline structures are inherent in selenium. At present, amorphous nanoselen having a red color has been identified, as well as three crystalline forms of nanoselen: trigonal, α-, β-, γ-monoclinic and rhombohedral. Amorphous selenium is an inorganic polymer with covalently linked chains [9].

The methods of nanoparticle formation used in the scientific literature include: chemical reduction of selenium ions in polymer matrices, which allows controlling the sizes of nanoclusters and nanoparticles. Physical methods for controlling size include sonication of solutions, x-ray irradiation, ultraviolet irradiation, the use of high frequency currents, etc. [10]

To obtain nanoparticles from selenium ions, purified samples of Na-CMC were selected, with DP = 200-600, DS = 0.62-0.90. The obtained solutions of purified samples of Na-CMC were used as a polymer substrate in the preparation of selenium nanoparticles.

The objects of the study were selenium-containing nanostructures obtained by the reduction of selenium (IV) oxide with ascorbic acid in the presence of a solution of purified Na-CMC. Selenium nanoparticles in Na-CMC solutions were prepared as follows: a solution of selenium (IV) oxide with a constant concentration of selenium of 0.005% was added to a solution of purified Na-CMC with a concentration of 2-4%, and stirred on a mechanical stirrer (1600 rpm) for 30 min., Then, under the influence of an ultrasonic dispersant, various amounts of a reducing agent, ascorbic acid with concentrations of 0.01 M, were introduced into the solution for 20 minutes and stirring was continued. Selenium oxide interacts with ascorbic acid in a ratio of 1:2. As a result of the reaction at a temperature of 50°C, a reddish-orange amorphous nanoselen forms.

When recovering selenium (IV) oxide in the presence of an aqueous solution of carboxymethylcellulose, a coloration of the colloidal solution from ellowish-orange to red was observed, which determines the formation of selenium nanoparticles depending on their size. The reduction of selenium oxide SeO_2 (IV) with ascorbic acid $C_6H_8O_6$ in aqueous solutions of Na-CMC proceeds according to reaction equation and leading to the formation of null-valent selenium (Se^0) and dehydroascarboxylic acid. (1) [11].

(1) $$\mathbf{SeO_2+2C_6H_8O_6 = Se^0+2C_6H_6O_6 +2H_2O}$$

In the formation of selenium nanoparticles, ascorbic acid acts as a reducing agent, oxidizing to dehydroascarboxylic acid according to the following mechanism:

The uniformity of the formed nanoparticles in size is achieved due to the fact that Na-CMC macromolecules, enveloping selenium nanoparticles, create a charged shell around them, preventing their agglomeration due to electrostatic repulsion (Fig. 1).

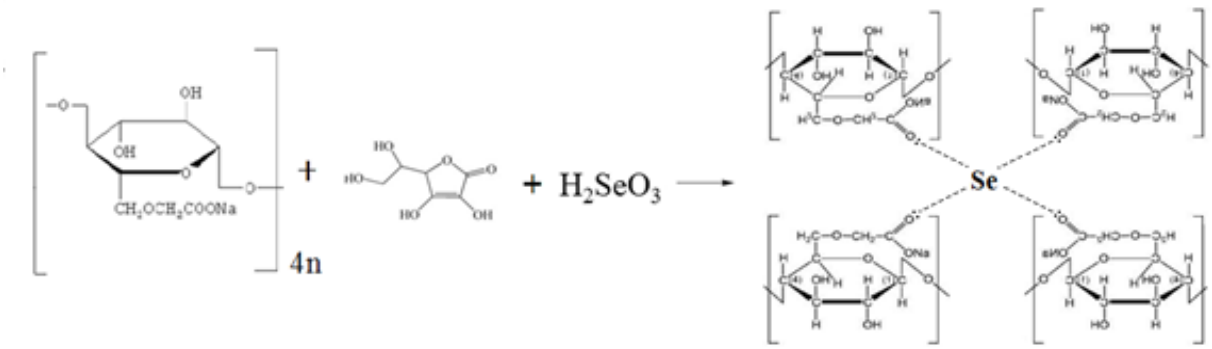
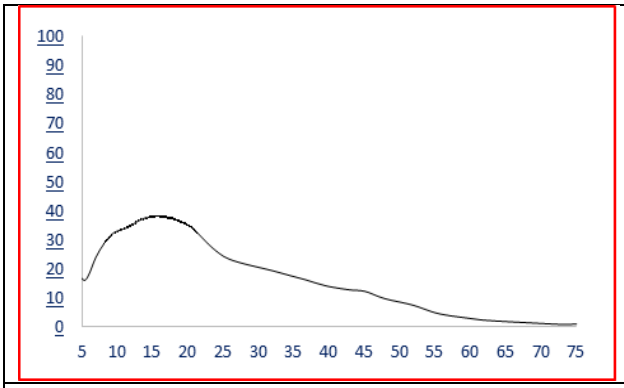


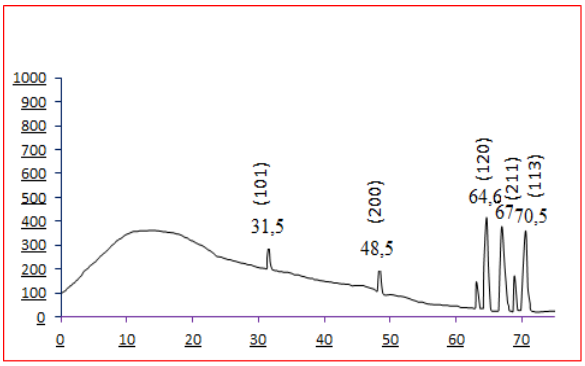
Fig. 1. Estimated stabilization mechanism and pattern of selenium nanoparticle formation.

Studies on the formation and stabilization of selenium nanoparticles in polymer solutions of CMC were carried out and their properties were studied. Using the methods of X-ray diffractometer analysis and atomic force microscopy, the size, shape, and structure of selenium nanoparticles were studied.

X-ray diffractometer analysis show that sodium-carboxymethyl cellulose was analyzed in a calibrated device when operating using Cu Ka (1.54059 A) irradiation and in the Mathcad program, an amorphous gala was observed at 2θ = 10⁰ , 17.5⁰ , 23⁰ , 30⁰ , 43⁰ degrees. The crystallite nature of chemically prepared nanoselenium was examined by XRD. The obtained nanoselenium was highly crystalline and all diffraction peaks have been well indexed as 31.5°, 48.5°, 63.1°, 64.6°, 67°, 69° and 70.5° which correspond to 101, 110, 111, 200, 201, 120, 211 and 113 crystal planes respectively.



a. Results of x-ray structural analysis of Na-CMC



b. the results of x-ray diffractometer analysis of Na-CMC containing Se^0 nanoparticles (100: 40 ml 0.01 M)

Fig. 2. X – ray diffraction analisis results of CMC containing selenium nanoparticles

The internal intensity of the peaks in the crystalline state of selenium nanoparticles, the distance in pixels and pitch was based on Mathcad Professional software and used the Sherrer equation, the crystalline nature of selenium nanoparticles is antique (Table 1)

$$L= 0.94\lambda/\beta\cos\theta$$

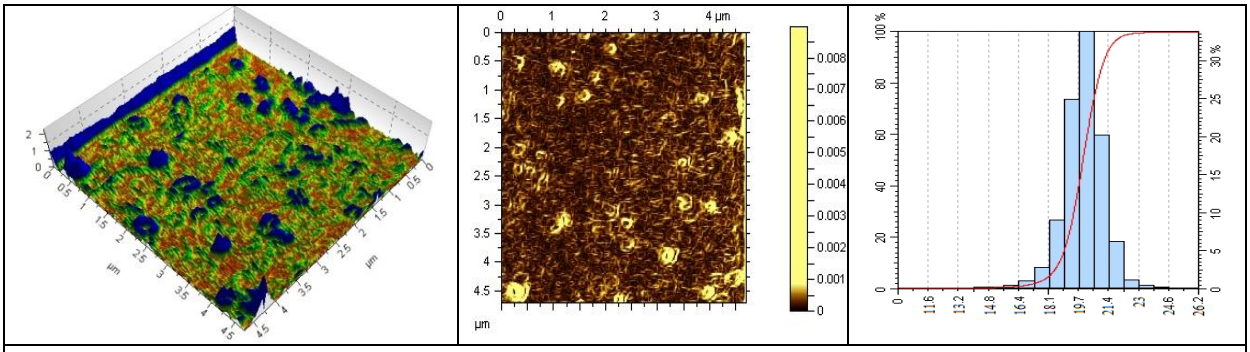
Table 1

Results of crystalline nature of CMC, contained Selenium nanoparticles.

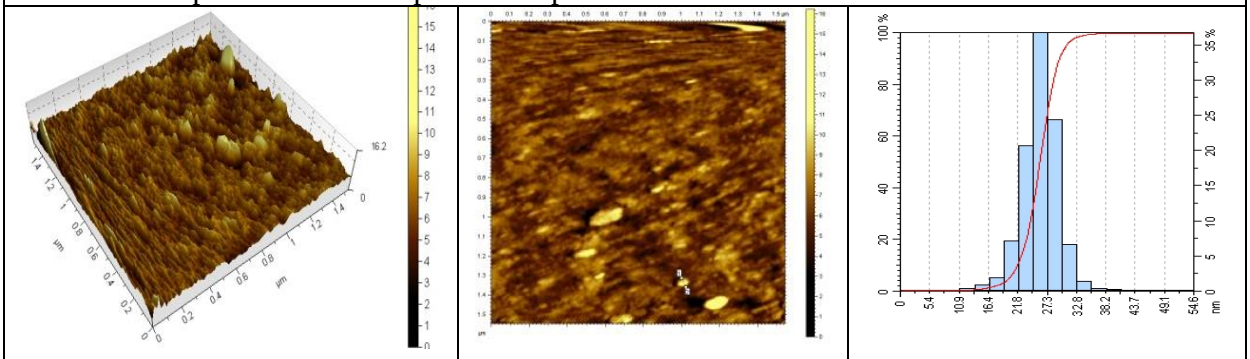
№	Semples	θ(°) angle of rotation	β the half-height width of the peaks	d(Å) distance between planes	L (Å) crystal size	degree of crystallization (%)
2	Na-CMC films containing 0.0226% selenium nanoparticles	31,5	$8,727x10^{-4}$	2,84	$8,261x10^{3}$	26,1 %
		48,5	$8,727x10^{-4}$	1,877	$8,72x10^{3}$	
		63,1	$8,727x10^{-5}$	1,473	$9,33x10^{3}$	
		64,6	$1,396x10^{-3}$	1,443	$5,879x10^{3}$	
		67	$2,182x10^{-3}$	1,397	$3,814x10^{3}$	
		69	$8,727x10^{-4}$	1,361	$9,647x10^{3}$	
		70,5	$8,727x10^{-4}$	1,336	$9,736x10^{3}$	

The surface topography of thin CMC films containing stabilized selenium nanoparticles obtained from Se^{0}CMC aqueous solutions was studied by atomic force microscopy AFM-5500 (Germany). The measurements were carried out in contact mode in atmospheric conditions using NSG 01 silicon contilivers. The data obtained are presented in Fig. 3.

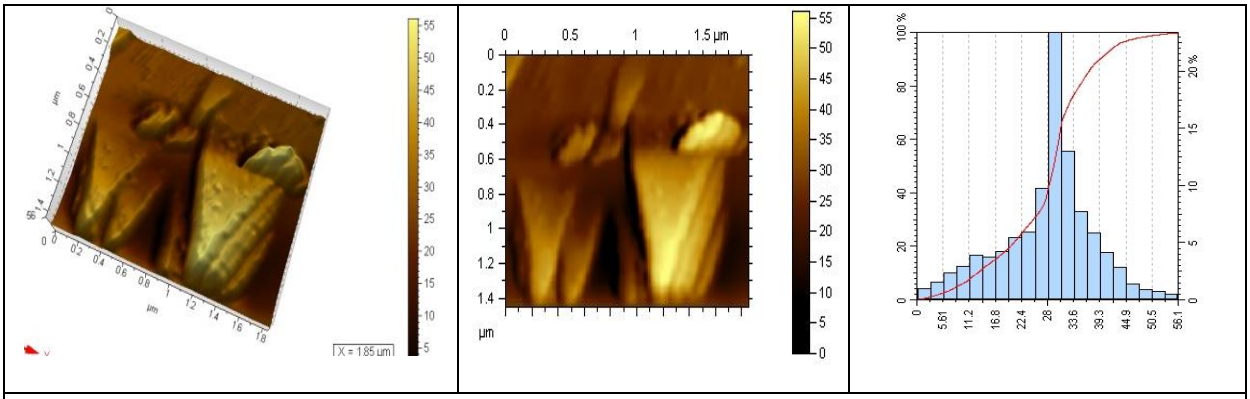
It can be seen from micrographs that at low SeO_2 concentrations spherical monodisperse selenium nanoparticles are formed (Fig. 3-a) with sizes of 2-14 nm. With an increase in the concentration of selenium oxide in CMC solutions, an increase in the size of spherical nanoparticles to 9-42 nm is observed. (Fig. 3-b).



a. Spherical monodisperse nanoparticles of selenium with sizes of 2-14 nm



b. Spherical monodispersed nanoparticles of selenium with a size of 9-42 nm.



c Trigonal nanoparticles of selenium with a size of 12-60 nm and a thickness of 4-28 nm.

a. Na- CMC:SeO_2 (0,08:2 • 10^{-5} mol) 0,12% SeO_2.
b. Na- CMC:SeO_2 (0,08:5 • 10^{-5} mol) 0,3% SeO_2.
c. Na- CMC:SeO_2 (0,08:3 • 10^{-4} mol) 1,7% SeO_2.

Fig. 3. AFM images and histograms of the size distribution of selenium nanoparticles on Se^0CMC films.

With a further increase in the concentration of selenium oxide in CMC solutions, the formed spherical nanoparticles of selenium acquire trigonal shapes and their sizes reach 4–28 nm in thickness and 12–60 nm in length (Fig. 3-c).

Biomedical tests of semi-finished samples containing stabilized nanoparticles of selenium were carried out in the laboratory of the Tashkent Medical Academy of the Ministry of Health of the Republic of Uzbekistan

The results of experimental studies in mice showed that the average lethal dose (LD_{50}) for intravenous administration of the drug "A" was 729.85 (649.33÷810.37) mg/kg, with an intraperitoneal dose of 750.01 (675,71÷824.31) mg/kg, and at enteric dose - 1405.31 (1283.29÷1527.02) mg/kg. In rats, when administered intravenously, LD_{50} was 697.82 (589.20÷806.44) mg/kg, intraperitoneal-797.81 (689.22÷906.48) mg/kg, enteral-1602.98 (1437.91÷1768.68) mg/kg.

When studying the acute toxicity of another drug "B", the following results were obtained: in LD_{50} mice, intraperitoneal administration was 950.91 (772.79÷1129.03) mg/kg, and in case of enteral administration, 2005.36 (1734.19÷2276), 53) mg/kg. In rats with intraperitoneal administration, it amounted to 3175.52 (2972.67÷3378.37) mg/kg, and for enteric administration - 3750.03 (3481.95÷4015.38) mg/kg. Analysis of the results of toxicological studies indicates that the studied drugs are low toxic, however, the LD_{50} value differs depending on the type of animals and the route of administration of the drug. So, the value of the preparation "A" containing 0.6635% selenium nanoparticles with intravenous administration equals 729.85 mg/kg, and with intraperitoneal administration 750.01 mg/kg, while with enteral administration the value of this figure almost doubles and is 1405.31 mg/kg. It can be seen that the drug exhibits a higher toxicity with parenteral administration, which is probably due to the high bioavailability of the drug, especially when administered intravenously. The low toxicity of the drug during enteral administration is possibly associated with low absorption through the mucous membrane of the digestive system or biodegradation of the drug by digestive juice enzymes or microflora of the gastrointestinal tract. As can be seen from the data in table 2, this assumption can be fully attributed to the second drug ("B" - containing 0.1327% nano particles of selenium).

The published tables show that the LD_{50} value of this drug, regardless of the route of administration, is slightly higher than that of drug "A". So with intraperitoneal administration, if the

LD_{50} value of drug "A" is 750.01 mg / kg, then for drug "B" it is 950.91 mg/kg. The same picture is observed with the enteral administration of drugs: 1405.31 and 2005.36 mg/kg, respectively. The lower toxicity of compound "B" is associated with more than four times lower content of selenium in the preparation (Table 2).

Table 2.

Values of the average lethal dose of selenium nanoparticles stabilized on biodegradable polymer substrates of natural origin

Route of administration	Mice, LD_{50} (mg/kg)	Rats, LD_{50} (mg/kg)
Intravenous "A"	729,85(649,33 ÷ 810,37) 689,85(617,21 ÷ 780,32)	697,82(589,20 ÷ 806,44) 646,82(545,22 ÷ 786,42)
Intraperitoneal "A"	750,01(675,71 ÷ 824,31) 712,61(631,42 ÷ 794,18)	797,81(689,22 ÷ 906,48) 761,41(649,41 ÷ 876,42)
Enteral "A"	1405,31(1283,29 ÷ 1527,02) 1393,31(1264,12 ÷ 1571,13)	1602,98(1437,91 ÷1768,68) 1575,32(1387,54 ÷1712,22)
Intraperitoneal "B"	950,91(772,79 ÷ 1129,03) 918,52(742,45 ÷ 1098,22)	3175,52(2972,67 ÷ 3378,37) 3085,62(2972,67 ÷ 3306,45)
Enteral "B"	2005,36(1734,19 ÷ 2276,53) 1966,31(1664,19 ÷ 2004,43)	3750,03(3481,95 ÷ 4015,38) 3701,03(3433,62 ÷ 3971,76)

Note: *In the numerator, the data obtained in males, and in the denominator in female rats and mice*

Therefore, the studied drugs exhibit toxicological properties that can be attributed to compounds of class IV (low toxicity according to the OESD classification).

As shown, the results of the next series of experiments conducted on male white rats studied drugs show toxicological properties not significantly different from those that we noted in experiments conducted in mice. As can be seen from the data of tables 2, the drug "A" has a lower (twice) toxicity with enteral administration than with parenteral. In contrast to mice in rats, drug B exhibits a distinctly low toxicity both with the enteral and especially with the parenteral route of administration (more than three times). The toxicological properties of the studied drugs in female rats, as can be seen from the data given in tables 2, do not significantly differ from the values of male rats, although the average lethal dose is slightly less. It is likely that female rats, like mice, are more sensitive to the action of preparations of selenium nanoparticles on stabilized substrates of natural origin.

As a result of observation and examination in experimental animals, no signs of intoxication and death of rats were revealed, which may indicate the absence of skin-resorptive action of the preparation of selenium nanoparticles in the polymer composition.

One of the first steps in carrying out the stages of preclinical studies is to establish safety in repeated applications of new compounds [4]. In connection with the experience presented in this series, we studied the subchronic toxicity of the preparation of selenium nanoparticles stabilized on biodegradable polymer substrates of natural origin.

Table 3.

The effect of various doses of selenium nanoparticles stabilized on biodegradable polymer substrates of natural origin on the body weight of animals with repeated injections

Groups of animals	Animal body weight (g.)			
	Control (water)	The drug "A" (30 mg/kg)	The drug "A" (60 mg/kg)	The drug "A" (160 mg/kg)
Initial	119,3±3,2	122,0±3,9	117,2±3,4	120,5±6,1
After 30 days	143,2±5,2*	149,3±4,4*	140,2±2,8*	148,0±7,4*

In the course of studies in a subchronic experiment between animals receiving test drugs and control animals receiving distilled water, statistically significant differences in body weight and its growth were not detected (table 3).

Conclusion

The synthesis of stabilized selenium nanoparticles by chemical reduction of selenium cations with ascorbic acid in Na-CMC solutions was first performed. It was established by optical and atomic force microscopy that the sizes and shapes of selenium nanoparticles vary depending on the conditions of the reduction reaction.

Based on the results of experimental studies, it was found that, depending on the ratios of CMC, SeO_2, ascorbic acid, and reaction conditions, the size and shape of stabilized selenium nanoparticles that form in aqueous solutions during the chemical reduction of Se^{4+} change.

The resulting CMC solutions containing selenium nanoparticles open up prospects for the creation of broad-spectrum drugs based on them, in particular, antitumor drugs that reduce the negative effects of radiation and chemotherapy on the body, and drugs that compensate for the deficiency of selenium in the body.

The medicinal compound created on the basis of selenium nanoparticles stabilized in the CMC structure according to toxicological properties can be classified as class IV compounds (low toxicity according to OECD classification). In this case, the acute toxicity of the drugs does not significantly differ in different species and sex of animals, however, they exhibit higher toxicity with parenteral administration than with enteral.

The studied compounds containing nanoparticles of selenium stabilized in the CMC structure do not have a meso-irritating and skin-resorptive effect.

The drug "A" containing selenium nanoparticles stabilized in the CMC structure does not have toxicity after repeated injections, which is reflected in the results of physiological, hematological and biochemical studies.

Obtained biodegradable materials, contained selenium nanoparticles can be used in medicine as anticancer drug for the treatment cancer disease.

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