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Production and application of selenium nanoparticles to prevent ionizing radiation-induced oxidative stress

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Abstract. The technology of obtaining selenium nanoparticles using laser ablation is presented. Selenium nanoparticles in water and aqueous solutions form stable colloids. For the obtained nanoparticles, the evolution in size and in mass has been established; optical properties have been characterized. The nanoparticles were studied using a transmission electron microscope, a modulation-interference microscope and a Bruker X-ray diffractometer. It has been previously shown that selenium containing preparations can prevent oxidative stress caused by ionizing radiation. In this work, it was shown that the nanoparticles obtained by us are also able to prevent oxidative stress caused by ionizing radiation and protect animals from radiation-induced death. In laboratory mice, it was established that selenium nanoparticles at a concentration of up to 10 mg / kg do not cause acute toxic effects. It is shown that the most effective concentration of selenium nanoparticles is a concentration of 5 mg / kg. The optimal administration time is 5 hours before exposure to ionizing radiation. Also set the dose reduction factor, it was 1.2.

1 Introduction

The search for substances for the prevention of radiation injuries remains one of the urgent problems of radiobiology [1]. Despite the fact that the anti-radiation efficacy of a huge number of compounds has been investigated to date, the available means of radiation protection do not fully satisfy the requirements imposed on them. In particular, on such important characteristics as efficiency, duration of action, portability, ease of use [2,3]. One of the promising areas of development of radioprotectors is based on the use of agents with antioxidant effects, in particular among organic and inorganic selenium compounds [4]. It should be noted that the first radioprotective effect of selenium compounds was found as

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early as 1964 [5]. It is established that selenium is not only manifested radioprotective properties, but can also modulate the protective effects of other radioprotectors [6]. It has been shown that selenium in the form of organoselenium compounds exhibits radioprotective properties only at moderate concentrations, and at higher concentrations, organoselenium compounds can be cytotoxic [7]. It is important to note that selenium compounds exhibit both radioprotective (have an effect when administered prior to exposure to ionizing radiation) and mitigatoric (have an effect upon administration after exposure to ionizing radiation, but before the first clinical signs of radiation sickness appear) properties. Organizational compounds of selenium are considered to be promising as the basis for the development of new radiation protective facilities [4].

The chemical properties of selenium are in many respects similar to those of sulfur, but the ability of some selenium derivatives to deactivate free radicals and peroxides is much higher than that of similar sulfur compounds [8]. Antioxidant and protective activity of selenium is shown in a large number of studies; selenium compounds protect biomolecules from oxidative stress [9-11]. Selenium is also included in the active center of a number of enzymes, including glutathione peroxidase [12]. This enzyme, localized in the cytoplasm, plasma membrane and mitochondrial matrix, utilizes both organic and inorganic peroxides of free fatty acids, nucleotides, nucleic acids, proteins. Selenium atoms are also found in proteins that neutralize peroxynitrite, a product of the interaction of nitric oxide and superoxide anion [13]. It is important to note that selenium plays an important role in carcinogenesis [14]. Traditional selenium supplements usually have a low degree of absorption and high toxicity (about 50-100 mg / kg) [4]. Therefore, it is extremely important to develop innovative systems as carriers of selenium compounds that would increase the bioavailability of this element and allow its controlled release in the body. Nanoscale selenium has aroused great interest as a food additive, especially in people with selenium deficiency, and also as a therapeutic agent without significant side effects in medicine [15]. In this paper, the question of the prospects for using selenium nanoparticles as a radioprotective agent is investigated.

2 Methods

2.1 Production and characterization of selenium nanoparticles

Selenium nanoparticles were obtained by laser ablation of a solid polycrystalline Se target in flowing water reactor [17]. For this purpose, a copper vapor laser was used as the laser source with laser pulse duration of 15 ns and repetition rate of 15 kHz. Cu vapor laser emits two laser lines in the visible at 510.6 nm and 578.2 nm at total average power of laser radiation of 8 Watts. Size distribution of obtained nanoparticles was measured using disk measuring centrifuge DC24000 (CPS Instruments). Morphology of Se nanoparticles was characterized by Transmission Electron Microscopy (TEM) at accelerating voltage of 100 kV. Crystallographic structure of laser-generated Se nanoparticles was acquired with the help of X-ray diffractometer Bruker AXS P4. Extinction spectra of colloidal solutions of Se nanoparticles were characterized with the help of fiber-optic spectrometer (OceanOptics).

2.2 Biological tests

Males of SHK mice used in the experiments. The animals were kept in a commercial mouse chow and tap water [19]. The work was performed in compliance with the principles of the Helsinki Declaration on the Humane Attitude towards Animals, the principles of humanity set forth in the European Community Directive (2010/63 / EU), in GOST R 53434-2009

"National Standard of the Russian Federation. Principles of good laboratory practice". The experimental animals were irradiated at the dose of 5-9 Gy with a short-focused X-ray generator Wolf T-160 (Womed GmbH, St Gangloff, Germany). The radiation source in this system is an X-ray tube with a voltage of 80 kV, a current amperage of 15mA, a half-value layer – 1 mm of aluminum, and a field radius of 50 mm. Immediately prior to the experiment selenium nanoparticles were dissolved at 37°C in isotonic glucose solution. Colloidal solution of selenium nanoparticles (0.2 ml) was injected intraperitoneal (i.p.) to mice prior irradiation. Control mice were injected i.p. with isotonic glucose solution. Mice were inspected daily and the number of survived animals were recorded throughout the postirradiation period [20].

3 Results

Colloidal solution of Se nanoparticles is reddish in appearance (see Fig. 1(a)). However, absorption spectrum of this solution has no distinct maxima in the visible. Transmission electron microscope (TEM) image of Se nanoparticles confirms that their average size of is about 50 nm (Fig. 1(b)). Laser-generated Se nanoparticles are amorphous, as it has been shown by X-ray diffractometry, though the initial Se target has polycrystalline structure. Absence of crystallographic lattice of laser-generated Se nanoparticles may be assigned to fast quenching of hot Se nanodrops in liquid environment.

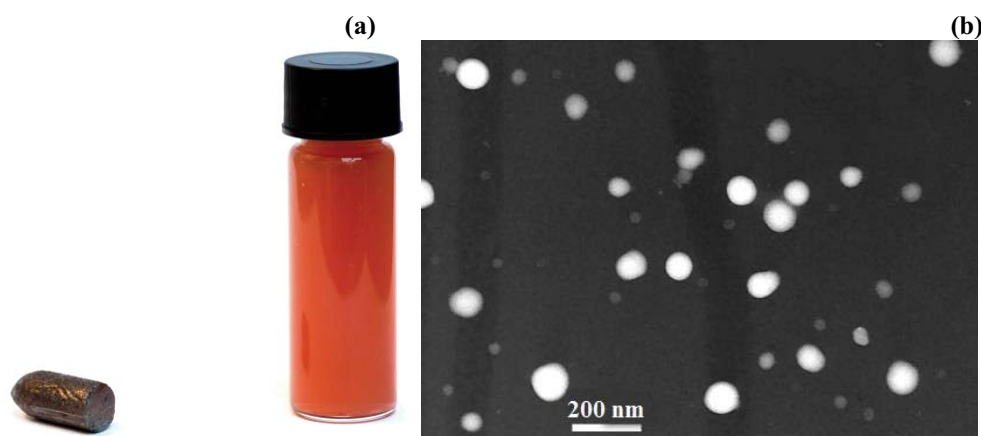


Fig. 1. (a): General view of the Se target (left) and aqueous colloidal solution of Se nanoparticles (right). (b): TEM view of Se nanoparticles. Scale bar denotes 200 nm.

The survival rate of SHK mice was studied after a single injection of selenium nanoparticles at different time intervals before exposure to X-rays at a lethal dose of 7 Gy (Fig. 2). It was shown that mice that did not receive selenium nanoparticles have a median survival of 6 days, the maximum survival time of 13 days. Mice treated with selenium nanoparticles 15 minutes before exposure to ionizing radiation have a slightly higher median survival of 8 days and a maximum survival time of 16 days. Mice treated with selenium nanoparticles 1 hour before exposure to ionizing radiation also do not live up to 30 days, their median survival is 10 days and the maximum survival time is 25 days. With the introduction of selenium nanoparticles to mice more than 3 hours before exposure to ionizing radiation, survivors can be observed by 30 days. For example, with the introduction of nanoparticles 3 hours before irradiation to 30 days, about 10% of animals remain alive. With the introduction of 5 hours in the living remains about 20% of animals, and with the introduction of 1 day before exposure to radiation, almost half.

The survival rate of SHK mice was studied with a single injection of selenium nanoparticles in different concentrations 24 hours before exposure to X-ray radiation at a lethal dose of 7 Gy (Fig. 3). It was shown that even at selenium nanoparticle concentrations of about 1 mg/kg, a radioprotective effect is observed. Under such experimental conditions, by 30 days, about 10% of individuals remain alive. When increasing the concentration of selenium nanoparticles to 5 mg/kg, about half of the individuals survive a dose of 7 Gy. With an increase in the concentration of selenium nanoparticles to 10 mg/kg, the effectiveness of radioprotection decreases, no more than 30% of animals remain alive by 30 days. In separate experiments, we investigated the acute toxicity of selenium nanoparticles. It is established that at concentrations up to 10 mg/kg no damage of the skin is observed, the consumption of water and food does not change.

To determine the radioprotective efficacy of selenium nanoparticles, the dose reduction factor (DRF) was calculated. For this, LD_{50/30} was determined in control experiments and with the introduction of selenium nanoparticles (5 mg/kg) 24 hours before exposure to X-ray radiation in the dose range of 5–9 Gy for a 30-day mouse survival test (Fig. 4). It was shown that LD_{50/30} for mice that did not receive selenium nanoparticles was 5.9 Gy; for animals treated with selenium nanoparticles, LD_{50/30} was 7.1 Gy. Thus, the DRF with the introduction of selenium nanoparticles at a concentration of 5 mg/kg 24 hours before exposure to ionizing radiation is 1.2.

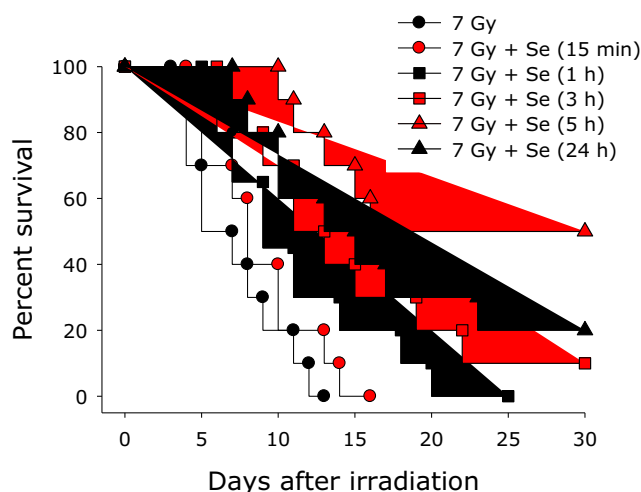


Fig. 2. Kaplan-Meier estimate of 30-day survival of X-irradiated (7 Gy) mice injected i.p. with selenium nanoparticles (~ 5 mg/kg) at different time intervals after exposure.

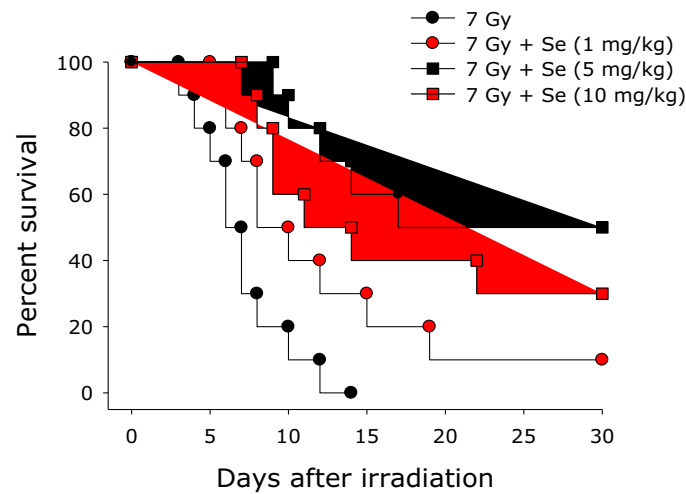


Fig. 3. Kaplan-Meier estimate of 30-day survival of X-irradiated (7 Gy) mice injected i.p. with selenium nanoparticles (24 h) at different concentration.

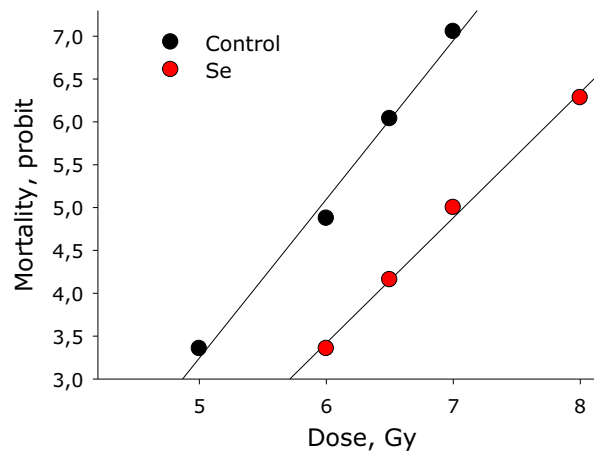


Fig. 4. Radiation dose-response of selenium nanoparticles injected i.p. 24 h prior 5, 6, 7 and 8 Gy, plotted as probit mortality.

4 Conclusion

This paper shows that selenium nanoparticles can be produced using laser ablation. Moreover, the nanoparticles will have one characteristic size and consist of zero valence selenium. The resulting selenium nanoparticles exhibit radioprotective properties. The greatest radioprotective effect is observed when nanoparticles at a concentration of 5 mg/kg are administered to animals 24 hours before exposure to ionizing radiation at a lethal dose. Under these conditions, the dose reduction factor is 1.2. The new scientific results obtained as a result of our studies are in good agreement with the data of various scientific studies that have been obtained by other scientists [21-32].

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