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Evaluation of the Anticancer Potential of Selenium Nanoparticles

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Abstract

The use of selenium nanoparticles in pharmaceutical research is well-documented in the scientific literature, particularly regarding their therapeutic potential in treating a variety of conditions such as hepatitis C, cancer, thyroid disorders, cardiovascular diseases, asthma, and more. This research investigated the effect of selenium nanoparticles on cancer tumor development. The study involved five groups of white laboratory mice: group 1, a healthy control group, group 2, a negative control group, which consisted of mice infected with EPNT-5 cancer cells, group 3, which received selenium nanoparticles after being infected, group 4, which was treated with both selenium nanoparticles and immunoglobulin imG, and group 5, which received only immunoglobulin imG after infection. The experiment monitored both the progression of the disease and the behavior of the mice. At the end of the 4 weeks, blood samples were taken for general and biochemical testing, and the internal organ masses of the mice were also evaluated.

Keywords: Immunoglobulin ImG, Cancer, Selenium nanoparticles, EPNT-5

Introduction

Selenium deficiency can lead to a variety of diseases in animals, humans, and birds [1]. In birds and animals, these include white muscle disease, toxic liver dystrophy, encephalomalacia, exudative diathesis, depression, retained placenta, and pancreatic fibrosis [2-4]. Selenium plays a vital role in enzyme activity, redox reactions, vitamin metabolism, and immune defense, while also providing antioxidant protection for the body [5-8].

Considered an essential trace element for both animals and humans, selenium has been widely studied for its therapeutic potential in conditions such as cancer, hepatitis C, diabetes, cerebrovascular insufficiency, Alzheimer's disease, heavy metal poisoning, thyroid disorders, cardiovascular diseases, asthma, and more [9-13]. Research is also exploring selenium compounds as growth promoters, antioxidants, and agents that restore liver and brain enzyme function [14, 15]. It has been confirmed that selenium nanoparticles can exert their effects over a longer period compared to traditional antibiotics [16-18].

At the cellular level, selenium nanoparticles interact with biological systems by introducing excess energy, thus enhancing the processes in plants, and are classified as bioactive substances [19-21]. It is well established that low selenium levels in the body increase the risk of developing cancer [22-24]. Studies show that in regions with higher selenium content in the soil, the rates of colorectal, lung, and cervical cancers are significantly lower [25]. Consuming selenium in moderate amounts is crucial for maintaining a balance in the expression of both selenium-dependent and selenium-independent microsomal enzymes, which play a key role in the

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biotransformation of xenobiotics. Selenium is essential as a gene protector, preventing DNA damage caused by peroxidation products and metals, and regulating their systemic elimination within the body [26].

The use of nanoparticles in pharmaceutical development has been extensively discussed in the literature. Selenium nanoparticles, in particular, have demonstrated potent antitumor activity and can be combined with other agents in cancer chemotherapy [27]. Research confirms several mechanisms underlying their antitumor effects, including the inhibition of cancer cell growth through cell cycle arrest, induction of apoptosis, and activation of autophagy [28, 29]. Beyond their direct anticancer properties, selenium nanoparticles exhibit enhanced selectivity, distinguishing between normal and cancerous cells more effectively. This research explores the impact of selenium nanoparticles on cancer tumor development.

Materials and Methods

This study involved five separate groups of laboratory mice, each group containing five individuals, aged 1.5 to 2 months, with normal weight and size. The purpose was to assess the effects of cancer cell inoculation (EPNT-5) in these animals.

Group 1: This group acted as the healthy control, with untreated, normal mice.

Group 2: The cancerous control group, where mice were subcutaneously injected with EPNT-5 cancer cells into their withers.

Group 3: An experimental group receiving a single intraperitoneal dose of nano-selenium solution (0.75 mg/ml), immediately following the cancer cell inoculation.

Group 4: This group was administered both nano-selenium (0.75 mg/ml) and immunoglobulin imG intraperitoneally, right after receiving the cancer cells (EPNT-5).

Group 5: The final experimental group was given only immunoglobulin imG intraperitoneally, immediately after the cancer cells.

All procedures complied with the “Rules of Laboratory Practice in the Russian Federation” (Order No. 708n, Ministry of Health of the Russian Federation, August 23, 2010), and were performed following the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes.

The focus of this study was primarily on investigating the potential antitumor effects of selenium nanoparticles, with the added consideration of immunoglobulin imG’s influence.

Animals were thoroughly examined through clinical assessments, microbiological testing, and laboratory analysis throughout the study.

Cancer cell preparation and inoculation (EPNT-5)

Under strict safety protocols, the cell suspension was centrifuged at 2500 rpm for 5 minutes. Afterward, the supernatant was carefully removed, leaving behind 2 ml of solution. The sediment was resuspended without forming bubbles. The resulting suspension, with a concentration of 10^-7, was drawn into a syringe and injected subcutaneously into the animals. For groups that did not receive immunoglobulin imG, each animal was injected with 100 µl as per the standard procedure [30]. For the immunoglobulin imG groups, each animal received 200 µl.

Premedication protocol

Before the immunoglobulin imG injection, animals underwent premedication. Prednisolone was given intramuscularly at 10 µl per animal. In addition, dipyrone (analgin) and diphenhydramine (dimedrol) solutions were combined in 1 insulin syringe, with each drug injected intramuscularly at 20 µl per animal. All procedures were performed with necessary precautions to ensure safety.

Introduction of immunoglobulin imG

Immunoglobulin imG is delivered via intraperitoneal injection. The solution has a concentration of 50 mg/ml, and the administered volume is one hundred µl per animal, corresponding to a dose of 400 mcg per kg of body weight.

Synthesis of selenium nanoparticles from dichlorodiacetophenonyl selenide

To synthesize the selenium nanoparticles, five hundred ml of isopropyl alcohol is measured in a glass flask. Then, 57.72 g of polyvinylpyrrolidone is added, and the mixture is heated and stirred at 50 °C. Once well-mixed, 28.86 g of dichlorodiacetophenonyl selenide is incorporated, and the stirring continues at 1000 rpm for 40 minutes. After this process, distilled water is added to bring the total volume up to 2000 ml. The solution is then frozen and freeze-dried. The resulting selenium nanoparticles are measured to be between 1 to 2 nm in size [31].

Preparation and administration of selenium nanoparticle solution

For the preparation of the selenium nanoparticle solution, 0.0175 grams of selenium nanoparticles are mixed into ten ml of distilled water. A 100 µl volume of this solution is intraperitoneally injected into each mouse, corresponding to a dose of 7 mg/kg body weight [32].

Equipment used

The following equipment was utilized throughout the study: a magnetic stirrer, freeze-drying apparatus, pipette dispenser, and laboratory centrifuge (Sigma-202MK, Refrigerated, USA). A veterinary-grade automatic hematology analyzer (MicroCC-20 Plus), which differentiates leukocytes into three populations and produces histograms, was also used. Additionally, analytical instruments such as an Explorer Pro EP214C balance (Ohaus, Switzerland) and VK-300 electronic scales (CJSC Massa-K, Russia) were employed, along with other essential devices.

Results and Discussion

During the treatment, the animals did not show any noticeable signs of discomfort or distress [33]. For the initial 14 days, no significant changes were observed. However, on the fifteenth day, abnormalities appeared in groups 2, 3, and 4, while group 5 remained unaffected.

The most significant lesions were found in group 2, where the sizes of the formations ranged from 0.4 cm to 1.6 cm. These formations were round, with distinct and smooth edges **(Figure 1)**.

Figure 1. Neoplasms in group 2 mice; day 15

In group 3, the occurrence of formations was considerably lower compared to group 2 (control). The lesions observed were round with well-defined edges, ranging in size from 4 to 8 mm.

Group 4 exhibited a slightly higher occurrence of lesions than group 3, with the neoplasms showing a variety of shapes. Most of the formations measured between 7 and 10 mm in size, although in some cases, they grew as large as 2 cm in diameter. These neoplasms were more heterogeneous in appearance compared to the other groups. By day 18, the development of these lesions was uniform and proportional.

Additionally, one mouse in group 5 developed a neoplasm during the study.

After the experiment, it was essential to assess changes in the blood and internal organs of the animals. Mice were euthanized by decapitation, and their organs were carefully removed and weighed. The relative weight of each organ concerning the total body mass was also calculated **(Table 1)**. Notably, the livers of mice in group 4 appeared paler compared to the livers of animals in the other groups. A full blood count and biochemical analysis were conducted **(Tables 2 and 3)**.

Table 1. Mass of organs of laboratory mice

Indicator	Group 1	Group 2	Group 3	Group 4	Group 5
Mouse weight	29.04 ± 1.47	25.07 ± 9.92	28.78 ± 2.95	26.87 ± 1.86	27.77 ± 2.82
Heart weight	0.134 ± 0.03	0.103 ± 0.03	0.128 ± 0.03	0.113 ± 0.03	0.113 ± 0.03
Heart (%)	0.459 ± 0.1	0.427 ± 0.08	0.445 ± 0.09	0.421 ± 0.08	0.406 ± 0.05
Liver weight	1.16 ± 0.21	1.44 ± 0.51	1.28 ± 0.16	1.38 ± 0.05	1.3 ± 0.2
Liver (%)	4 ± 0.62	5.8 ± 0.46	4.45 ± 0.35	5.15 ± 0.52	4.66 ± 0.34
Kidney weight	0.284 ± 0.07	0.307 ± 0.11	0.328 ± 0.1	0.347 ± 0.04	0.347 ± 0.12
Percent of kidneys	0.974 ± 0.23	1.241 ± 0.11	1.13 ± 0.29	1.295 ± 0.19	1.233 ± 0.3
Spleen weight	0.084 ± 0.02	0.217 ± 0.12	0.106 ± 0.05	0.187 ± 0.08	0.11 ± 0.02
Spleen (%)	0.289 ± 0.05	1.05 ± 0.88	0.367 ± 0.15	0.7 ± 0.31	0.4 ± 0.06

Table 2. A general blood test of laboratory mice

Indicator	Group 1	Group 2	Group 3	Group 4	Group 5
White blood cells ($x10^9$/L)	1.26 ± 0.61	4.37 ± 3.53	1.02 ± 0.35	2.17 ± 0.8	11.9 ± 9.73
Lymphocytes ($x10^9$/L)	0.96 ± 0.52	2.37 ± 1.46	0.78 ± 0.29	1.23 ± 0.46	11.63 ± 9.45
Content of monocytes, basophils, and eosinophils (MID) ($x10^9$/L)	0.28 ± 0.11	1.6 ± 1.58	0.2 ± 0.11	0.57 ± 0.17	0.23 ± 0.24
Granulocytes ($x10^9$/L)	0.02 ± 0.04	0.37 ± 0.52	0.04 ± 0.05	0.1 ± 0.01	0.03 ± 0.06
Lymphocytes (%)	0.71 ± 0.08	0.58 ± 0.1	0.75 ± 0.1	0.66 ± 0.05	0.98 ± 0.01
Content of monocytes, basophils, and eosinophils (MID) (%)	0.23 ± 0.08	0.34 ± 0.06	0.17 ± 0.07	0.28 ± 0.04	0.02 ± 0.01
Granulocytes (%)	0.05 ± 0.02	0.08 ± 0.04	0.09 ± 0.05	0.06 ± 0.01	0 ± 0
Red blood cells ($x10^{12}$/L)	6.17 ± 1.36	7.72 ± 2.27	5.62 ± 0.93	5.18 ± 0.74	4.97 ± 0.86
Hemoglobin (g/L)	92.6 ± 20.49	120 ± 32.74	87.2 ± 14.51	87 ± 7.92	75 ± 15.9
Mean corpuscular hemoglobin concentration (g/L)	361.2 ± 12.93	369 ± 25.74	385.2 ± 20.38	378 ± 4.28	383 ± 10.45
Mean concentration hemoglobin (pg)	15.04 ± 0.51	15.7 ± 0.88	15.52 ± 0.63	16.1 ± 0.97	15.1 ± 0.69
Mean corpuscular volume (fl)	41.66 ± 1.48	42.53 ± 1.01	40.36 ± 1.23	43.5 ± 2.75	39.5 ± 1.42
Red cell distribution width (RDW-CV) (%)	0.16 ± 0.01	0.15 ± 0.01	0.18 ± 0.02	0.15 ± 0.01	0.14 ± 0.01
Red cell distribution width (RDW-SD) (fl)	33.06 ± 3.54	31.77 ± 2.73	35.44 ± 2.7	32 ± 4.02	27.43 ± 0.94
Hematocrit (%)	0.26 ± 0.02	0.33 ± 0.1	0.23 ± 0.04	0.23 ± 0.02	0.2 ± 0.04
Platelets ($x10^9$/L)	371.2 ± 166.4	403.67 ± 86.8	580 ± 344.92	308.33 ± 70.8	378 ± 88.23
Mean platelet volume (fl)	7.18 ± 2.67	6.3 ± 1.13	7 ± 2.89	5.83 ± 0.35	5.2 ± 0.2
Relative width of platelet distribution by volume (PDW) (fl)	7.96 ± 5.47	6.5 ± 3.53	4.14 ± 0.52	4.03 ± 0.24	4 ± 0.49
Thrombocrit (%)	0.216 ± 0.05	0.0025 ± 0	0.01 ± 0.01	0.0017 ± 0	0.002 ± 0
Percentage of large platelets (P-LCR) (%)	0.15 ± 0.2	0.112 ± 0.11	0.14 ± 0.21	0.047 ± 0.03	0.008 ± 0.01

Table 3. Biochemical blood test of laboratory mice

Indicator	Group 1	Group 2	Group 3	Group 4	Group 5
Alanine aminotransferase	34.52 ± 4.09	44.07 ± 29.72	49.64 ± 8.5	49.27 ± 33.08	42.83 ± 19.97
Aspartate aminotransferase	104.92 ± 16.02	192.24 ± 26.71	128.5 ± 10.74	332.33 ± 155.06	160.03 ± 39.91
Creatinine	58.62 ± 2.92	133.67 ± 17.02	110.72 ± 14.99	49.67 ± 12.76	89 ± 55.57
Urea	6.1 ± 0.2	5.5 ± 1.7	6.38 ± 0.84	5.47 ± 0.69	6.67 ± 0.33
Phosphorus	1.62 ± 0.07	2.8 ± 0.57	1.84 ± 0.54	2.83 ± 0.46	2.23 ± 0.24

From the analysis of the data presented in **Tables 1-3** and the observational results, it can be inferred that the most severe disease progression occurred in groups 2 and 4, suggesting the detrimental effects of tumor growth in these groups.

Conversely, the administration of selenium nanoparticles in group 3 led to a 60% reduction in the likelihood of tumor formation. This finding is consistent with the results reported by Tian *et al.* [34], Stolzoff and Webster [35], and Spyridopoulou *et al.* [36]. Furthermore, the use of Immunoglobulin imG was found to significantly decrease the tumor risk, a result also corroborated by Cervia *et al.* [37].

Conclusion

In the last 20 years, the exploration of nanoparticles for various applications has significantly expanded, particularly in the field of medicine, where nanoparticles of different compositions have been investigated for therapeutic purposes. Research indicates that selenium nanoparticles, in contrast to their crystalline or amorphous counterparts, are more easily absorbed by

cells. Given the increasing incidence of cancer and the ongoing challenge of developing safe and effective treatments, oncology has emerged as a primary focus in pharmaceutical research. Our findings in laboratory animals demonstrate that selenium nanoparticles, sized between 1-2 nm, hold potential as preventative agents against the onset of cancer. From the results of our study, we can draw the following conclusions:

1. Selenium nanoparticles, administered at a dose of 7 mg/kg, decreased the likelihood of EPNT5 tumor development by 60%.
2. The administration of ImG immunoglobulin also contributed to a reduction in tumor formation risk.
3. The combined application of selenium nanoparticles with ImG immunoglobulin did not show any preventative effect against tumor growth.

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Conflict of Interest: None

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Ethics Statement: The study involving laboratory animals was conducted in compliance with the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes.

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