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The synthesis of selenium nanoparticle (SeNPs) – Review

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SUMMARY

Selenium is an important dietary micronutrient required for the normal physiology and metabolism of humans and animals. The biological properties of selenium nano particle depend on their size and forms. Selenium nanoparticle (SeNPs) attracts even more attention, thanks to its high bioavailability and much lower toxicity than inorganic and organic forms. In this review, I summarized the information and ways of production of selenium nanoparticle. SeNPs have been produced in chemical, physical, and biological ways. In recent years, biological ways have been especially important in the production of selenium nanoparticles.

Keywords: *nanosize selenium, antidote effect, toxicity, Paramecium caudatum*

INTRODUCTION

More recently, nanoscale matter has been looked at with interest for potential application in nanocomputers, synthesis of advanced materials, energy storage devices, electronic and optical displays, chemical and biosensors as well as biomedical devices. Bionanotechnology is an emerging important technical tool for the development of reliable eco-friendly methodology for the synthesis of materials in nanoscale using biological sources. Nano-sized particles possess unique properties due to their larger surface to volume ratio and higher surface energy. An important feature of nanotechnology concerns the development of experimental procedure for the arrangement of nanoscale materials with special properties (Murrat et al., 2000). For example, interest in SeNPs as a natural trace element nanomaterial for nanomedicine has resulted in a number of studies evaluating their bioactivities, such as anticancer, antimicrobial, and antioxidant properties. In addition, selenium nanoparticles (SeNPs) are promising candidates for development in biomedical applications, because selenium is an essential microelement in mammals and is present in 25 selenoenzymes. Selenium plays an important role in the formation of several important types of selenoproteins such as glutathione peroxidase and thioredoxin reductase (Yu et al., 2005) and provides protection to the body against oxidative stress (Burk and Hill, 1993). The incorporation of selenium into nanoparticles has emerged as a promising approach to harness both the therapeutic benefits of Se and the unique properties of nanoparticles. Selenium supplementation prevents cell damage and plays an important role in the development, fertility, and immune functions of humans and other vertebrates, including fish (Hoffmann and Berry, 2008; Schrauzer and Surai, 2009). However, its deficiency causes many metabolic disorders and diseases such as calf pneumonia, white muscle disease in calves and beef cows, exudative diathesis, and infertility in fish and other vertebrates; thus, a lack of selenium exerts a negative influence on the immune function (Muller et al., 2002; Ekiz et al., 2005). Therefore, this review article focuses on the ways of producing selenium nanoparticles.

The applicability of selenium nanoparticles (SeNPs) is dominated by several significant characteristics such as size, shape, atomic arrangement, structure, and surface charge. The SeNPs can be synthesized chemically (Zhang et al., 2004) or using physical procedures (Quintana et al., 2002) or can even be obtained by biological way – using microorganisms or plant extracts, the so-called green synthesis (Oremland et al., 2004; Shoeibi and Mashreghi, 2017). There are several advantages of nanoparticles as shown in *Figure 1*. SeNPs attract even more attention, thanks to their high bioavailability and much lower toxicity than inorganic and organic forms (Wang et al., 2007). For example, in mice, SeNPs showed much lower toxicity measured by median lethal dose (50%, LD_{50}), liver impairment, and short-term toxicity (Zhang et al., 2008). The biological properties of selenium nanoparticles depend on their size: smaller particles have a greater activity (Torres et al., 2012).

THE CHEMICAL WAYS OF PRODUCING NANO-SIZED ELEMENTAL SELENIUM

In terms of chemical synthesis, SeNPs are usually prepared by reduction of selenious acid solution by ascorbic acid in the presence of polysaccharides such as CS, glucomannan, acacia gum, or carboxymethylcellulose (Zhang et al., 2004). CS is positively charged, biocompatible, non-immunogenic, nontoxic, pH sensitive, and biodegradable, and is therefore a suitable component for oral administration for a wide range of biomedical and nutritional applications (Agnihotri et al., 2004; Saini et al., 2015). It has been extensively examined in the pharmaceutical industry due to its potential in the development of medication delivery systems (Rinaudo, 2006).

Zong-Hong Lin et al., used sulfur dioxide and SDS as reducing agents, and selenious acid was used as a precursor to synthesize senp with a size range of 30–200 nm (Lin et al., 2005). SeNPs are ionic liquid-

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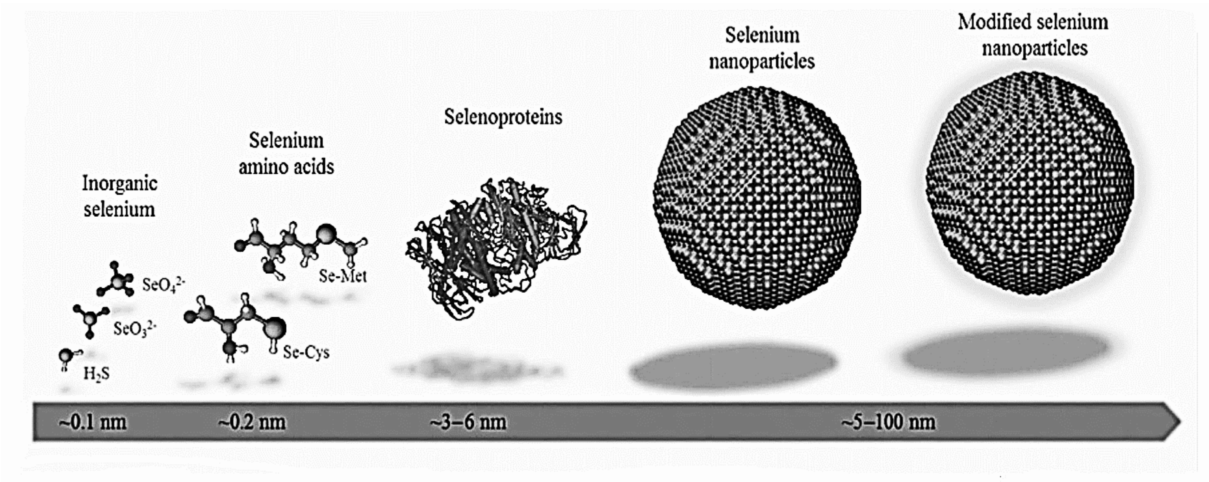
induced synthesis with sodium selenosulfate as selenium precursor, in the presence of polyvinyl alcohol stabilizer, which can produce spherical senps in the size range of 76–150 nm (Langi et al., 2010).

Barnaby et al. synthesized Se nanospheres of larger diameter >500 nm using dithiothreitol and gallic acid as a reducing agent and sodium selenite as an se source (Barnaby et al., 2011). In addition, Barnaby used organic carboxylic acids like acetic acid, oxalic acid, and aromatic acid to synthesize SeNP of spherical shape and size 40–100 nm using sodium selenosulphate as the source of Se (Charu et al., 2011).

Many biocompatible reducing agents have been employed in the synthesis of SeNPs. For example; Ramos and Webster (2012) employed glutathione and NaOH mixture to prepare spherical SeNPs by reducing sodium selenite (Ramos and Webster, 2012).

Figure1: **Function selenium across multiple length scales: from molecular to functionalized nanoparticles; an increase in size is associated with a reduction in cytotoxicity without compromising beneficial bioactivity. reproduced with permission**



from Skalickova et al., 2017

THE PHYSICAL WAYS OF PRODUCING NANO-SIZED ELEMENTAL SELENIUM

The physical techniques for the preparation of SeNPs, synthesis by pulsed laser ablation (PLA) or deposition was described in a study (Quintana et al., 2002). Generally, physical methods have distinct advantages over chemical ones, since these often require a final calcination step, which makes them unsuitable for certain applications. Furthermore, with sputtering and laser ablation, the stoichiometry of the material is maintained. In PLA, the size of the nanoclusters can be controlled by laser parameters, such as fluence, wavelength, and pulse duration, as well as by ambient gas conditions, such as pressure and flow parameters (Marine et al., 2000).

Zeng et al., synthesized nanoparticles using this method wherein Se was dissolved in ethylenediamine and incubated in an autoclave maintaining the temperature at 160ºC for 2 hours and then cooled to room temperature to form a brown homogeneous solution followed by storage in acetone at -18ºC to make amorphous SeNPs and further transforming it into trigonal Se of hexagonal rod-shaped structures (Zeng et al., 2012).

A study conducted by An and Wang (2007) reported the synthesis of trigonal Se nanowires of 10–60 nm in size using sodium selenite and thiosulfate salts as starting materials using steam under pressure with a set temperature of 180ºC (An and Wang, 2007). In addition, SeNPs can be synthesized using microwave. For example, In 2011 Ju-Ying et al. reported the use of selenious acid as a source of Se, which was further reduced to spherical senp using protein (silk fibroin) prepared from the cocoon under microwave radiations for 10 mins (HOU et al., 2011). The size obtained was around 50 nm as measured by TEM.

A recent study reported by Yu et al. (2016) proposed a microwave-assisted approach to synthesize different se nanostructures including nanoball, nanotube, and multi-armed nanorods, by reducing H_2SeO_3 with L-asparagine in polyethylene glycol solution (Yu et al., 2016).

THE BIOLOGICAL WAYS OF PRODUCING NANO-SIZED ELEMENTAL SELENIUM

Biosynthesis of nanomaterials using plant extracts has more advantages than other biological methods because it is inexpensive and does not require any special conditions (Ramamurthy et al., 2013). NPs synthesis using bacteria is more effective than chemical synthesis, thanks to the following advantages:

- high purity of selenium spheres (which are relatively regular and uniform, and their size depends on the bacterium)
- cheaper and faster production process
- better possibility to control the parameters (Eszenyi et al., 2011)

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Microorganisms are capable of synthesizing metal NPs (Shoeibi and Mashreghi, 2017). The biogenic SeNPs have exhibited promising application perspectives in the field of medicine, biosensors, and environmental remediation (Tan et al., 2016). Interestingly, two halotolerant *Bacillus megaterium* strains (BSB6 and BSB12), isolated from saline mangrove habitat without selenium contamination, were found to be capable of reducing Se^{+IV} to elemental selenium, even in the presence of high salt concentrations (Mishra et al., 2011).

The synthesis of SeNPs by macro- or microorganisms, due to the diversity of reducing enzymes in organisms, involves morphological and shape changes of the particles. By changing the redox state, the reducing enzymes of microorganisms convert metal ions (Se^{-II}) to SeNPs without charge (Se^0). The biological activity of senps includes their protective role against DNA oxidation (Shoeibi and Mashreghi, 2017). It was found that certain anaerobic bacteria respire toxic selenium oxyanions and as a result cause extracellular accumulation of elemental selenium (Se^0). The spectral properties differ considerably from those of amorphous Se^0 formed by chemical oxidation of hydrogen selenide (H_2Se) and of black, vitreous Se^0 formed chemically by reduction of selenite with ascorbate.

The microbial synthesis of Se^0 nanospheres results in unique, complex, with compact nanostructural arrangement of Se atoms. This probably reflects a wide diversity of enzymes involved in the dissimulator reduction that are slightly different in various bacteria. Remarkably, these conditions cannot be achieved by current methods of chemical synthesis (Oremland et al., 2004). Different types of bacteria have been used for the biosynthesis of SeNPs, such as the species of phylum proteobacteria (*Escherichia coli* ATCC 35218, *Ralstonia eutropha, Enterobacteri Cloacae* Z0206, *Pantoea agglomerans, Zooglea ramigera, Stenotrophomonas maltophilia*), firmicutes (*Lactobacillus casei, Lactobacillus acidophilus* [LA-5], *Lactobacillus helveticus* [LH-B02], *Enterococcus faecalis, Streptococcus thermophilus, Staphylococcus carnosus, Bacillus sp*. MSh-1, *Bacillus subtilis, Bacillus mycoides* SelTE01, *Bacillus licheniformis* JS290), Actinobacteria (Streptomyces sp. ES2-5, Bifidobacterium BB-1272), and Cyanobacteria (Arthrospira [Spirulina] platensis).

In 2008, Prokisch et al., developed and patented a technology to produce nano-sized (100-500nm) elemental selenium by using probiotic yogurt bacteria in a fermentation procedure. This technique is the first to use lactic acid bacteria and other probiotic bacteria (*Species of Lactobacillus and Bifidobacteria, Streptococcus thermophilus*) to form the product, Se nanospheres. The invention enables the production of red and grey elemental Se nanospheres in high purity by using microorganisms applied in the food industry. These bacteria are commonly used, non-toxic and harmless. The main advantage of the process makes it possible to produce uniform nanospheres in a specific size of 50-500 nanometers (with 5-20% standard deviation) in diameter depending on the species used for the fermentation. Compared to the conventional used chemical synthesis it is better regulated technology (Prokisch et al., 2011).

CONCLUSION

The biological properties of nano-sized selenium have a beneficial role in nanomedicine and biomedicine applications. SeNPs have a high bioavailability, low toxicity, affordability and are most appropriate for supplementation, especially in ruminants, in which traditionally used selenium compounds exhibit very low absorption in the digestive tract. However, there are still some concerns about the use of SeNPs for therapeutic purposes. Therefore, it is compulsory to carry out further preclinical studies in the living system and animal models.

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