SYNTHESIS AND BIOFUNCTIONALISATION OF SILVER NANOPARTICLES

Aleksandar Chanachev

University of Mining and Geology “St. Ivan Rilski”, 1700 Sofia; E-mail: a.chanachev@mgu.bg

ABSTRACT. Nanoparticles are widely used in various studies in chemistry, biology, pharmacy, and medicine. Their specific chemical and physical properties make them excellent carriers of biomolecules and proteins, which creates a very good environment for the development of drugs for targeted delivery, biosensors, systems for monitoring various enzyme reactions, as well as for the development and improvement of a number of diagnostic methods. Silver nanoparticles are of special scientific interest both because of their bactericidal properties and because of their ability to be biofunctionalised with various proteins. This allows this type of nanostructures to be used in the cosmetics and pharmaceutical industries as carriers of various proteins and leads to significant interest both in optimisation and research of synthesis methods and in the study of their surface biofunctionalisation and stabilisation of molecules.

Key words: silver nanoparticles, biofunctionalisation, nanomaterials

СИНТЕЗ И БИОФУНКЦИОНАЛИЗИРАНЕ НА СРЕБЪРНИ НАНОЧАСТИЦИ

Александър Чаначев

Минно-геоложки университет „Св. Иван Рилски“, 1700 София

РЕЗЮМЕ. Наночастиците намират широко практическо приложение в различни изследвания от областта на химията, биологията, фармацията и медицината. Техните специфични химични и физични свойства ги правят отличен носител на различни биомолекули, което създава много добра среда за създаването на лекарствени носители за целева доставка, биосензори, системи за проследяване на различни ензимно-каталитични химични реакции, както и за развиването и усъвършенстването на редица диагностични методи. Сребърните наночастици са обект на особен научен интерес както заради техните бактерицидни свойства, така и поради възможността да бъдат биофункционализирани с различни протеини. Това дава възможност този тип наноструктури да бъдат използвани в козметичната и фармацевтична индустрия като носители на различни протеини и води до съществен интерес както към оптимизиране и изследване на методите за синтез, така и към изследване на тяхната повърхностна биофункционализация и стабилизация на молекулите.

Ключови думи: сребърни наночастици, биофункционализиране, наноматериали.

Introduction

Silver nanoparticles (AgNPs) have been the subject of numerous studies due to their specific properties which make them suitable for various purposes in chemistry, biology, medicine, pharmacy, and agriculture. Their surface allows them to make varied complex compounds by coordinating a large number of ligands around them. This allows them to be used both as drug delivery systems and in the diagnosis of various types of cancer. Studies show that they have antibacterial and antiviral properties and improve the activity of many antibiotics. Due to the constant growth of multi-drug resistant bacterial and viral strains, scientists are looking for new drug systems that show better results in fighting such infections. The successful use of AgNPs in such systems, due to their antibacterial properties and their ability to inhibit the growth of many infectious bacteria, has generated a huge amount of research in this area (Silver, 1996; Jones et al., 2004; Siddiqi et al., 2018).

Due to these specific properties and applications, the synthesis of AgNPs, and especially the green synthesis of AgNPs, has been the subject of extensive research in recent years. The green synthesis of nanomaterials is based on their production by various micro-organisms and plants and occupies an important place in the methods of synthesis of AgNPs due to its efficiency and environmental friendliness (Kanimozhi et al., 2022).

Silver nanoparticles can be functionalised with bacitracin, peptides, and other molecules as their size can be optimised and they can be used for external wound healing because of their substantially low silver content with reduced toxicity and good antibacterial and antibiofilm activity (Singh and Mishra, 2022).

The synthesis and functionalisation of silver nanoparticles are fields of continuous scientific research due to their unique chemical properties that allow them to be excellent systems for targeted drug delivery, and interest in them is growing continuously.

Synthesis of silver nanoparticles

Due to the fact that silver nanoparticles are obtained through chemical, physical and biological processes, the methods for their synthesis can be divided into chemical, physical, and biologica (Vishwanath and Negi, 2021).

They differ both in their basic principles and in their impact on the environment. Chemical methods are the most common, but correspond to the least extent to the concept of green synthesis. Physical methods are closer to this concept. However, biological methods apply the ideas of green synthesis to the greatest extent (Ijaz et al., 2020; Aisidaet al., 2021a b; Vishwanath and Negi, 2021).

Physical methods

The most common physical methods for the synthesis of silver nanoparticles are evaporation-condensation and laser ablation. The former is based on obtaining particles by tube furnace under atmospheric pressure. Its disadvantages are the huge amount of energy the process consumes and the slow time it takes for the synthesis to take place. With the laser ablation method, nanoparticles are synthesised by nucleation and growth of vaporised species through laser in attendance of gas. Due to the possibility to control the size of the particles, the purity of the obtained silver nanoparticles and the lack of use of chemical reagents, this type of synthesis is ecological and very efficient. The laser ablation method, however, has a few disadvantages. Its use requires very high temperatures, which requires the consumption of a lot of energy, and due to its low productivity, it cannot be imposed in industry (Vishwanath and Negi, 2021).

Chemical methods

There are many chemical methods for obtaining silver nanoparticles. They are based on similar principles and what they have in common is that the reaction always needs a metal precursor, reducing, and stabilising agents. These three reactant components are required for the chemical syntheses of silver nanoparticles (*ibid.*).

One of the interesting syntheses of silver nanoparticles was proposed by Fang, Zhang and Mu (2005) and it is based on the use of silver nitrate to which solution of trisodium citrate is added and after heating, the solution is allowed to cool with vigorous stirring. They have an absorption maximum at 420 nm because of their surface plasmon resonance peak and scanning electron micrographs show an average particle size of 21.22 ± 5.17 nm.

The majority of simple methods for the synthesis of silver nanoparticles use the reduction of silver nitrate in aqueous solution under the action of reducing and stabilising agents. A number of substances can be used as reducing agents, like citrate, ascorbate, borohydride, etc, while surfactants, ligands, or polymers with specific functional groups are used as stabilising agents. An example of such a specific group is polyvinylpyrrolidone. The sizes of the obtained nanoparticles depend to a great extent on the concentration and ratio of these three components - silver nitrate, stabilising, and reducing agent (Gudikandula and Maringanti, 2016; Vishwanath and Negi, 2021).

The main principles of the syntheses of silver nanoparticles are schematically presented in Fig.1.

An interesting approach to obtain silver nanoparticles is the polyol process. In this method, silver nitrate is reduced in the presence of ethylene glycol. In this method, silver nitrate is reduced in the presence of ethylene glycol, with the compound acting as both a stabilising agent and a solvent. The size and shape of the nanoparticles can be regulated by the reducing agents, as well as by other chemical reagents involved in the synthesis.

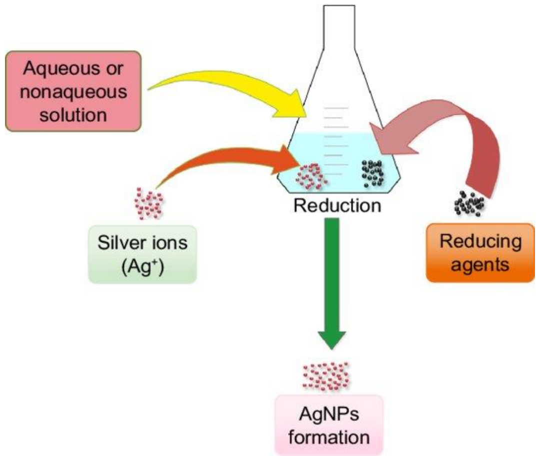

Fig. 1. Schematic representation of silver nanoparticle synthesis methods (Ullah Khan et al., 2018)

Examples of the influence of such reducing agents are sodium citrate and sodium borohydride. Due to the weaker reducing action of the former, the obtained nanoparticles have a larger size than those obtained under the action of sodium borohydride, which has a stronger reducing effect (Vishwanath and Negi, 2021).

Methods for the synthesis of silver nanoparticles lead to the production of particles of a certain size and shape. These characteristics of the particles, as well as the monodispersity of the solution, have an extremely important role for their application as drug delivery systems, as well as for any of their applications in pharmacy or diagnostics.

Chemical methods for the synthesis of silver nanoparticles have both their advantages and disadvantages. The advantages of chemical methods are low cost and a wide variety of syntheses, as well as the possibility of adjusting the size, shape, and monodispersity of the system (*ibid.*).

Significant problems and shortcomings in the chemical methods for the synthesis of silver nanoparticles are the dangers that the reagents used create for both the environment and human health. In this respect, the chemical methods for obtaining silver nanoparticles have a low rating in the sense of "greenness". Due to the use of many toxic reagents in the syntheses, the preparation of silver nanoparticles by chemical methods contains many risks when using them as a drug delivery system. Examples of toxic chemicals that are used in these reactions are ethylene glycol, liquid paraffin, oleyl amine, etc., as oleyl amine has a harmful effect on marine flora and fauna (*ibid.*).

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Biological methods

Biological methods for the synthesis of silver nanoparticles show the best results in terms of environmental and health impact. Due to the fact that they do not use toxic chemicals and large amounts of energy, they are an excellent alternative to other syntheses.

Biological synthesis methods use living organisms to produce silver nanoparticles. This process is presented in Fig.2. Such organisms are plants, algae, microbes, fungi and even animals.

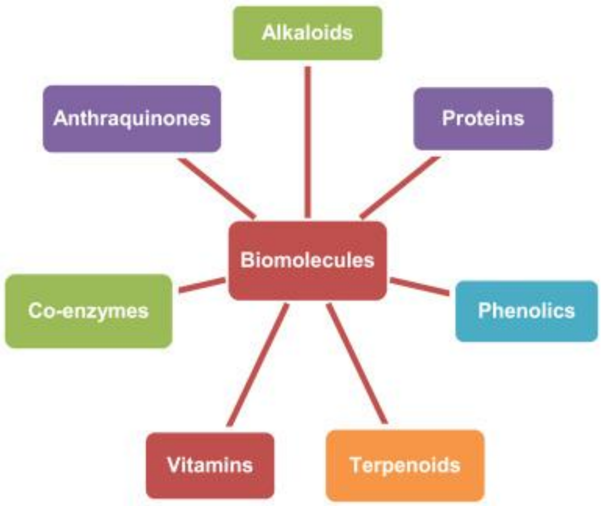

Fig. 2. Chemical compounds that are produced by living organisms and used in the synthesis of silver nanoparticles (Vishwanath and Negi, 2021)

Nanoparticles obtained by such methods can achieve a large degree of monodispersity and can also be obtained with certain sizes and shapes. They have the lowest residual synthesis toxicity and are therefore particularly suitable for drug delivery systems. They correspond to the greatest extent to the basic principles of green chemistry (Vishwanath and Negi, 2021).

The process of obtaining nanoparticles from plants is called phytosynthesis and is a preferred technique among other biological methods because of its qualities in industrial use. Apart from it, other synthesis methods used are from microbes, agrowaste, and metabolites of animals. An example of the use of animal metabolites is spider webs. They are rich in a variety of amino acids including alanine, glycine, and pyrollidine and although the method is not widespread it is efficient and very ecological (*ibid.*).

Biofunctionalisation of silver nanoparticles

Appropriate methods for the biofunctionalisation of silver nanoparticles are the first step towards their use as drug carriers or as sensors, as well as in most of the fields in which they find application. This also defines different strategies by which they can be linked to different biomolecules and these approaches can be divided into four main groups: binding of the molecule to the surface of the inorganic particle core through ligand; electrostatic interactions between positively charged biomolecules to negatively charged nanoparticles; covalent binding and a noncovalent affinity-based receptor-ligand system (Ravindran et al., 2013).

Different biofunctionalising molecules are used to make the interaction between the surface of the nanoparticle and the molecule. They can be as small molecules - lipids, vitamins, peptides, sugars, or larger ones, such as natural polymers including proteins, enzymes, DNA, and RNA (*ibid.*).

Different chemical functional groups create the connection between the surface of the silver nanoparticles and the molecule that functionalizes it. One such group is the thiol group as can be seen in Fig.3.

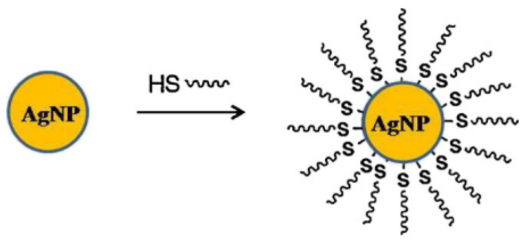

Fig. 3. Schematic representation of the chemical binding of thiol groups to silver nanoparticles (Ravindran et al., 2013)

The reason is that the thiol group has a strong affinity to the surface of both silver and gold nanoparticles, which makes it possible to bind molecules to the surface of the particle through it (*ibid.*).

After the biofunctionalisation of silver nanoparticles, due to their interaction, an aggregation or deaggregation process can occur. For example, the interaction of silver nanoparticles with cysteine leads to a rapid aggregation of the particles (*ibid.*).

Silver nanoparticles can be biofunctionalised with protein, antibodies, and peptides. Also, DNA-based nanoparticle systems can be built with their help. The systems thus obtained are used in various fields of science. Biofunctionalised silver nanoparticles can be used as bioanalysers. These are colorimetrically based nanosensors. Because of their simplicity, rapidity, high sensitivity, and ease of measurement, they have attracted strong attention from the scientific community and research on their capabilities has become a growing field in nanoparticle research (*ibid.*).

Biomedical applications of functionalised silver nanoparticles are undoubtedly the most actively investigated possibilities of silver nanoparticles due to the promising results they have shown in recent decades both in the pharmaceutical industry and in the development of more complex drug delivery systems. An example of such a system is glutathione stabilised water soluble silver nanoparticles bind covalently with a model protein BSA (Qingzhi et al., 2008; Ravindran et al., 2013).

Silver nanocrystals show excellent capabilities as antibiotic and antiviral agents in biological systems. Their antibacterial properties remain their trademark and are widely used in the pharmaceutical industry (Ravindran et al., 2013).

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