CURRENT TRENDS OF SILVER NANOPARTICLE AS A PHARMACEUTICAL TOOL

Abstract

Due to the excellent stability and minimal chemical reactivity in compared to other metals, silver nanoparticles represent a significant advancement in nanotechnology. For their distinctive physicochemical characteristics, silver nanoparticles have attracted a lot of attention in biological applications. Silver nanoparticles may be created using a variety of techniques, including physical and chemical ones. These processes frequently used hazardous compounds as reducing agents to synthesise nanoparticles. To prevent the usage of hazardous compounds, however, various attempts have been made in the last several decades to create green synthesis techniques. The green synthesis of nanoparticles utilising bacteria, fungi, and plants is discussed in this review, along with the function of plant metabolites in the synthesis procedure. Many of the biomolecules included in biological extract, including vitamins, phenolic compounds, alkaloids, flavonoids, and terpenoids, serve as reducing and capping agents throughout the biosynthesis process. Researchers have been interested in the potential use of biosynthesized AgNPs in a variety of domains, including antifungal, antibacterial, antiviral, and agronomic. The morphology and surface area of AgNPs are all significant structural factors to take into account when developing formulations for particular applications. AgNP of different sizes and shapes that are less hazardous have been created using various techniques. This article has covered the formation and processing of AgNPs with their potential - therapeutic applications.

Keywords: Silver nanoparticle, Bio-chemical methods, Physico-chemical characterisation, Stability.

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I. MANUFACTURE OF AGNPS IN SOLUTION

Current researchers are paying attention to silver nanoparticles (AgNPs), which have recently been demonstrated to be a good instrument with a wide variety of industrial applications in several sectors. According to reports, a wide variety of bacteria species are inhibited by the metallic nanoparticles, making them a potential replacement of antibiotics. [1]. AgNPs' potential anti-inflammatory effects and other uses in medicine are also being researched and stated. AgNPs are also reported to be used in the textile sector. [1,2]

1. **Silver Nanoparticles Synthesis:** AgNPs may be produced using the typical bottom-up and top-down approaches for nanoparticle fabrication. Silver metals that have been mechanically ground into nanoparticles are safeguarded in the top-down method by the proper stabilising agents. Metal reduction, electrochemical techniques, and breakdown are all included in the bottom-up strategy. This section discusses several physical, chemical, and biological techniques that have been widely used in the creation of AgNPs [3,4].

2. **Chemical Method:** One of the method for making AgNPs is chemical reduction, which involves turning silver ions (Ag+) in water or organic solvent solutions into metallic silver in the presence of reducing substances and hydroxyl groups. [5]. The three essential ingredients needed for the synthesis of AgNPs are silver precursors, organic or inorganic reducing agents, and stabilising agents. This is an economical method that prevents excessive particle agglomeration and offers excellent output. The rate of reaction, the type of reducing agents, their reactivity to the redox potential of silver, and other factors influence the shape and size of the particles. [6].

3. **Physical Method:** As an alternative to chemical synthesis, researchers have also resorted to the physical method. In addition to these crucial physical processes, laser ablation, evaporation-condensation, and ultraviolet (UV) radiation are also used to create AgNPs. The bulk of physical operations, however, need a lot of energy, which makes them not only time-consuming but also expensive. For the evaporation-condensation process in a tube furnace, a large area, significant energy input, heat discharge to the surroundings, and a protracted duration to create thermal stability are all necessary. As a result, fresh solutions have been developed to deal with these problems. Jung et al. (2006) attempted to produce nanoparticles by nucleating and developing them inside of a small ceramic heater, as an example [7]. By quickly and consistently attaining thermal stability of the surface temperature, this method generates minute particles in high concentration. Another improved method that has been researched is thermal decomposition, which produces monodispersed silver nanocrystallite from the interaction of silver nitrate ($AgNO_3$) with sodium oleate at an elevated temperature of 290 °C [8]. AgNPs' uniformity in size and shape is mostly controlled by the physical synthesis's use of heat, ac power, and arc discharge [2].

4. **Bio-Synthetic Method:** However, materials like sodium borohydride are used in the chemical synthesis of AgNPs, which may adhere to the surface of the particles and contribute to any unfavourable effects the final product may have [9]. Because heat treatment is also required, the conventional technique of making AgNPs is costly and consumes a lot of energy [10]. In light of the current "going green" movement, researchers are trying to find more affordable and ecologically friendly techniques to make nanoparticles.

Several biological resources, including plants and microorganisms (yeast, fungus, and bacteria), are used in the sustainable production of silver nanoparticles. The reduction process is aided by the presence of biomolecules in the extracts from various sources, such as secondary metabolites, amino acids, proteins, vitamins, enzymes, and polysaccharides [11,12]. For instance, Sahoo et al. used the cyanobacterium Chroococcus minutus as a biological reductant to create AgNPs as novel antibacterial agents against upper respiratory tract infection [13].

Green algae (Botryococcus braunii) generated silver nanoparticles with cubical, spherical, and truncated triangular forms with an average size of 88.87 nm in another experimental study [14]. Using the rare medicinal plant Withania coagulans, spherical-shaped AgNPs with an average size of 14 nm were produced. Results showed that the studied microorganisms may be subject to an antibacterial and antioxidant action by these particles [15].

II. PHYSICOCHEMICAL PROPERTIES OF AgNPs

Since a particle's physicochemical qualities may have a substantial influence on its biological properties, accurate particle characterisation is required after production. To address safety concerns and fully use the potential of any nanomaterial for human welfare, in nanomedicines, or in the healthcare industry, etc., it is essential to define the created nanoparticles before usage [16,17]. Before determining if a nanomaterial is toxic or biocompatible, it is necessary to assess its essential properties, including size, shape, size distribution, surface area, form, solubility, aggregation, surface charge, redox potential, surface functionalization, and composition [18].

III. STABILITY OF AgNPs

To reduce agglomeration and regulate the size of the nanomaterials, capping agents and stabilisers such as chitosan, celluloses, and other polymers such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), and polymethacrylic acid (PMAA), as well as other surfactants, can be used. Stabilising AgNPs in suspensions can be accomplished by using electrostatic or steric repulsion between the NPs. Electrostatic fields are often stabilised using anionic species, which coat AgNPs and leave a negative charge on their surface. Examples of these species include citrate, halides, carboxylates, and polyoxanions. For instance, the surface can be coated with a positive charge using polyethyleneimine (PEI). These charging-coatings in AgNPs may be tracked by monitoring the zeta potential. For steric stability, AgNPs can interact with big molecular groups like organic polymers and alkylammonium cations. The synthesis, shape, size, and properties of the NPs may be controlled using a green method by varying the pH, temperature, reaction time, pressure, and the biological reducing agent [19,20].

IV. CHARACTERIZATION OF AgNPs

The synthesised nanomaterials have been characterised using a variety of analytical methods, including scanning electron microscopy (SEM), transmission electron microscopy (TEM), dynamic light scattering (DLS), atomic force microscopy (AFM), X-ray photoelectron spectroscopy (XPS), X-ray diffractometry (XRD), Fourier transform infrared spectroscopy (FTIR), and others. [21,22].

Due to their nanoscale size, AgNPs are undetectable to standard optical microscopy. Electron microscopy (EM) techniques are frequently used for the imaging and characterization of NMs due to their much higher resolution and use of an electron beam. The two most crucial techniques are scanning electron microscopy (SEM) and transmission electron microscopy (TEM). In addition to displaying the size and form of the particles, TEM images also display the morphology and state of the particle aggregation. With a high-resolution TEM, even the layers of atoms in crystalline materials may be observed clearly.

However, as TEM specimens must be dry and no thicker than hundreds of nm, the initial goal is to develop an appropriate sample. In solutions, solvent evaporation may cause surface modifications and undesirable particle coagulation. For biological tissues and other complex samples, chemical fixing and a straining operation are commonly needed to maintain their pristine form and improve contrast. In addition, the samples must be cut into tiny slices and implanted in resin in order for the electron beam to pass through them [23].

In a scanning electron microscope (SEM), secondary electrons, backscattering electrons, and unique X-rays are observed when an electron beam interacts with a specimen surface. By using focused ion-beam SEM, a 3D image may be obtained. Although SEM samples are not need to be as thin as TEM samples, conductive material may occasionally be needed to cover the sample in order to minimise the development of static electric charge on the sample during electron irradiation. However, there's a danger that some of the superficial information may be lost [24].

This problem could be resolved by using environmental SEM (ESEM), which allows for the imaging of materials while they are under vacuum. A drawback of the reduced resolution is [23]. EM techniques may directly see the shape and size of NMs, but because there are so few samples analysed, it is laborious and time-consuming to count thousands of particles to provide a representative result. Energy-dispersive X-ray spectroscopy (EDS), an analytical method for detecting elements, must also be used. It is frequently used with TEM or SEM to produce an element distribution of the AgNPs. In addition, it is a particularly valuable method for detecting AgNPs in challenging materials. [25,26].

AgNPs may be characterised using UV-Vis because their optical properties differ from those of bulk metal. The full width at half maximum (FWHM) of a UV-Vis spectrum can give information regarding particle dispersion, whereas the maximum absorption wavelength in a UV-Vis spectrum is frequently correlated with the average particle size, as shown by Leopold and his collaborator using TEM and UV-Vis to characterise freshly synthesised AgNPs [27]. Due to its cheap cost and ease of handling, it is also preferred as an alternative method to ascribe quality [28,29] and to detect the presence of AgNPs [26].

REFRENCES

[1] Pirtarighat, S., Ghannadnia, M., Baghshahi, S., 2019. Green synthesis of silver nanoparticles using the plant extract of Salvia spinosa grown in vitro and their antibacterial activity assessment. Journal of Nanostructure in Chemistry 9 (1), 1–9.
[2] Haider, A., Kang, I.-K., 2015. Preparation of Silver Nanoparticles and Their Industrial and Biomedical Applications: A Comprehensive Review. Advances in Materials Science and Engineering 2015, 1–16.
[3] S. Prabhu, E.K. Poulose, Silver nanoparticles: mechanism of antimicrobial action, synthesis, medical applications, and toxicity effects, Int. Nano Lett. 2 (2012) 32.

[4] M.J. Firdhouse, P. Lalitha, Biosynthesis of silver nanoparticles and its applications, J. Nanotechnol. 10 (2015) 18.
[5] Siegel, J., Kvitek, O., Ulbrich, P., Kolska, Z., Slepika, P., Svorcik, V., 2012. Progressive approach for metal nanoparticle synthesis. Material Letters 89, 47–50.
[6] Suriati, G., Mariatti, M., Azizan, A., 2014. Synthesis of silver nanoparticles by chemical reduction method: effect of reducing agent and surfactant concentration. International Journal of Automotive and Mechanical Engineering 10, 1920–1927.
[7] Jung, J.H., Hyun, C.O., Hyung, S.N., Ji, J.H., Sang, S.K., 2006. Metal nanoparticle generation using a small ceramic heater with a local heating area. Journal of Aerosol Science 37 (12), 1662–1670.
[8] Lee, D.K., Kang, Y.S., 2004. Synthesis of silver nanocrystallites by a new thermal decomposition method and their characterization. Electronics and Telecommunications Research Institute (ETRI) Journal 26 (3), 252–256.
[9] Rauwel, P., Kuunal, S., Ferdov, S., Rauwel, E., 2015. A Review on the Green Synthesis of Silver Nanoparticles and Their Morphologies Studied via TEM. Advances in Materials Science and Engineering 2015, 1–9.
[10] Ahmed, S., Saifullah, A., M., Swami, B. L., Ikram, S., 2016. Green synthesis of silver nanoparticles using Azadirachta indica aqueous leaf extract. Journal of Radiation Research and Applied Science 9 (1), 1–7.
[11] Keat, C.L., Aziz, A., Eid, A.M., Elmarzugi, N.A., 2015. Biosynthesis of nanoparticles and silver nanoparticles. Bioresources and Bioprocessing 2 (1), 47.
[12] Siddiqi, K.S., Husen, A., Rao, R.A.K., 2018. A review on biosynthesis of silver nanoparticles and their biocidal properties. Journal of Nanobiotechnology 16 (1), 1–28.
[13] Sahoo, C.R., Maharana, S., Mandhata, C.P., Bishoyi, A.K., Paidesetty, S.K., Padhy, R.N., 2020. Biogenic silver nanoparticle synthesis with cyanobacterium Chroococcus minutus isolated from Baliharachandi sea-mouth, Odisha, and in vitro antibacterial activity. Saudi Journal of Biological Science 27 (6), 1580–1586.
[14] Arya, A., Mishra, V., Chundawat, T.S., 2019. Green synthesis of silver nanoparticles from green algae (Botryococcus braunii) and its catalytic behavior for the synthesis of benzimidazoles. Chemical Data Collections 20, 100190.
[15] Tripathi, D., Modi, A., Narayan, G., Rai, S.P., 2019. Green and cost-effective synthesis of silver nanoparticles from endangered medicinal plant Withania coagulans and their potential biomedical properties. Materials Science and Engineering C 100, 152–164.
[16] Lin, P.C.; Lin, S.; Wang, P.C.; Sridhar, R. Techniques for physicochemical characterization of nanomaterials. Biotechnol. Adv. 2014, 32, 711–726.
[17] Pleus, R. Nanotechnologies-Guidance on Physicochemical Characterization of Engineered Nanoscale Materials for Toxicologic Assessment; ISO: Geneva, Switzerland, 2012.
[18] Murdock, R.C.; Braydich-Stolle, L.; Schrand, A.M.; Schlager, J.J.; Hussain, S.M. Characterization of nanomaterial dispersion in solution prior to in vitro exposure using dynamic light scattering technique. Toxicol. Sci. 2008, 101, 239–253.
[19] Ivanova, N.; Gugleva, V.; Dobreva, M.; Pehlivanov, I.; Stefanov, S.; Andonova, V. Silver Nanoparticles as Multi-Functional Drug Delivery Systems. Nanomedicines 2018.
[20] Lee, S.H.; Jun, B.-H. Silver Nanoparticles: Synthesis and Application for Nanomedicine. Int. J. Mol. Sci. 2019, 20, 865.
[21] Gurunathan, S.; Han, J.W.; Kim, E.S.; Park, J.H.; Kim, J.H. Reduction of graphene oxide by resveratrol: A novel and simple biological method for the synthesis of an effective anticancer nanotherapeutic molecule. Int. J. Nanomed. 2015, 10, 2951–2969.
[22] Sapsford, K.E.; Tyner, K.M.; Dair, B.J.; Deschamps, J.R.; Medintz, I.L. Analyzing nanomaterial bioconjugates: A review of current and emerging purification and characterization techniques. Anal. Chem. 2011, 83, 4453–4488.
[23] A. Dudkiewicz, K. Tiede, K. Loeschner, L.H.S. Jensen, E. Jensen, R. Wierzbicki, A.B.A. Boxall, K. Molhave, Trends Anal. Chem. 30 (2011) 28.
[24] K. Tiede, A.B.A. Boxall, S.P. Tear, J. Lewis, H. David, M. Hassellov, Food Addit. Contam. 25 (2008) 795.
[25] T.M. Benn, P. Westerhoff, Environ. Sci. Technol. 42 (2008) 4133.
[26] J.F. Liu, J.B. Chao, R. Liu, Z.Q. Tan, Y.G. Yin, Y. Wu, G.B. Jiang, Anal. Chem. 81 (2009) 6496.
[27] N. Leopold, B. Lendl, J. Phys. Chem. B 107 (2003) 5723.
[28] K.J. Lee, P.D. Nallathamby, L.M. Browning, C.J. Osgood, X.H.N. Xu, ACS Nano 1 (2007) 133.
[29] P.V. AshaRani, G.L.K. Mun, M.P. Hande, S. Valiyaveettil, ACS Nano 3 (2009) 279.