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Silver Nanoparticles: The Good, The Bad and The Future

Mohammed Asadullah Jahangir[1]*, Syed Sarim Imam[1], Abdul Muheem[2], and Yamini K[3]

[1]Department of Pharmaceutics, School of Pharmacy, Glocal University, Saharanpur, India
[2]Department of Pharmaceutics, Faculty of Pharmacy, Jamia Hamdard, New Delhi, India
[3]Department of Pharmaceutical Sciences, JNTU, Hyderabad, India

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***For Correspondence**

Research Scholar, School of Pharmacy, Glocal University, Saharanpur, India
E-Mail: asadullahpharma@gmail.com

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ABSTRACT

Silver nanoparticles are today a standout amongst the most generally utilized nanoparticles both in key therapeutic sciences and clinical practice. These nanoparticles are additionally consolidated into numerous business items and broadly accessible to all inclusive community. Be that as it may, late reports have connected silver nanoparticles to modified cell demise, and expanded cytotoxicity in specific conditions. This review concentrates on the late discoveries in regards to the promising future and atomic collaborations of silver nanoparticles with living cells and tissues. Potential immune-modulatory impacts of silver nanoparticles and in addition late lethality concerns are additionally talked about. This review article discusses the good, the bad and the future impact of silver nanoparticles.

INTRODUCTION

Over the period of last two decade the conventional formulation of medicine has taken a considerable development. Among the different approaches for the development of advanced delivery systems-Nano sized drug delivery [1] has grasped the most contemplation. This new concept of using a nano-approach has opened doors for different treatment possibilities [2]. Numerous approaches are being utilized for the preparation of nanoparticle [3]. The bottom up and the top down technique are the most discussed ones. The synthesis methods includes: Chemical, physical and biogenic method of synthesis of nanoparticles [4]. The field of nanotechnology is emerging day by day, not only having its impact on the pharmaceutical world but also this new science form is being exploited in the field of physics, chemistry, biological applications etc [5]. Nanoparticles or more broadly nano-materials [6] are not only fabricated by single material but also by using organic and inorganic materials [5].

Researchers around the world are now exploiting this tool for developing differently coated nanoparticles which affects the pharmacological properties as well as the pharmacodynamics [7] of the drug. Gold coated nanoparticles [5] and silver coated nanoparticles are the most researched topic in the nanoparticle division. Apart from this iron oxide nanoparticles are also gaining popularity in biomedical and diagnostic purposes [8,9].

The Good

Silver, has been traditionally known for its antibacterial activity [10]. Silver nanoparticles are now widely studied not only due to their application as antimicrobials [11] as well as antivirals, but also for their uses in consumer products like electronics, paint, clothing, food and medical devices [12].

Asadi et al., studied the effect of silver nanoparticle on *Staphylococcus aureus* and *Escherichia coli* colonies, in which the researcher concluded with positive results. The minimum inhibitory concentration of silver nanoparticles for *S. aureus* and *E. coli* were 5 and 10 mg.L^{-1} respectively. Moreover, both bacteria were killed in concentration range 50 mg.L^{-1} of silver nanoparticles [10].

Banach et al., also confirmed in their study that nano-silver at the concentration range of 5-15 ppm was effective as biocidal agent [13]. Nano-silver suspensions are components of paint coatings, thus it may provide the possibility to prevent the growth of micro-organism on walls [14].

Banach et al., [14] reported the antifungal efficacy of building materials enriched with silver nanoparticles. Krishnan et al., determined the Minimum Inhibitory Concentration (MIC) [15] and Minimum Bactericidal Concentration (MBC) of silver nanoparticles and *Enterococcus faecalis* [16]. The result from the study concluded that silver nanoparticles have bactericidal effects against *E. faecalis* at a concentration of 5 mg/ml [17]. Berton et al., evaluated the antimicrobial effectiveness of silver nanoparticles against two *Salmonella enterica* strains (*enteritidis* and *senftenberg*) utilising Transmission Electron Microscopy (TEM) [18]. The researchers reported structural damages in *S. Enteritidis* and *S. senftenberg* following the interactions with silver nanoparticles, proposing the utility of TEM to investigate the effect of nanoparticles on live bacteria [19].

Sing et al. [20] synthesized silver nanoparticles from the stem of *Tinospora cordifolia*, [21] and analysed their antibacterial activity against multidrug-resistant strains of *Pseudomonas aeruginosa*. The researchers concluded that even a small concentration of silver nanoparticles prepared from *T. cordifolia* possess decent antibacterial activity. The silver nanoparticles of stem of *Tinospora cordifolia* showed the zone of inhibition ranges from 10 ± 0.58 to 21 ± 0.25 mm. The MIC of silver nanoparticles from stem extract was found to be 6.25 - 200 μg/ml against *Pseudomonas aeruginosa* strains [20]. Ansari et al., [22] in their study suggested that silver nanoparticles exhibits excellent bacteriostatic and bactericidal activity [23]. The bactericidal effect of silver nanoparticles was found to be prominent towards both sensitive and resistant strains.

Apart from the pharmaceutical application, the antibacterial and antimicrobial activities of silver nanoparticles have been exploited waste water treatment. Shahrokh et al., studied the impact of silver nanoparticles on aerobic nitrate reduction. The results concluded that silver nanoparticle has no significant impact on denitrification [24] process as it is an important part of nitrogen cycle. The silver nanoparticles at certain concentrations showed promising results as biocide for waste water treatment [25].

The aquaculture industry or the global sea food market is expanding [26]. The pacific white shrimp, *L. vannamei* is one of the most prominent marine aquaculture species [27,28]. First introduced in China in the late 1980's, by 2010 it became the world's three major farmed shrimp, accounting 85% of the total shrimp production in China [27]. The world total production of *L. vannamei* is raised from less than 10,000 metric tons in 1970 to more than 3,000,000 metric tons in next four decades [29,30]. However, with the outbreak of *vibriosis*, aquaculture industries faced huge losses. Sivaramasamy et al., in his study demonstrated that administration of biosynthesized silver nanoparticles improved the growth performance as well as immune response with better survival rate against the pathogenic bacterium *V. parahaemolyticus* [31].

The ever increasing demand for milk and milk products has made the Dairy Industry [32] in India to become the world's largest milk producer consuming almost 100% of its own milk production.
Madal et al., [33] showed that Nano composites, hydroxyapatite particle can be effectively used as an absorbent for treatment of dairy wastewater [33].

Green synthesis of Nanoparticles

Green synthesis is gaining popularity for the production of not only nanoparticles but also in other chemical preparations [34].Green chemistry to improve and/or protect our global environment is focal issues in many fields of research [35].

The development of cost efficient and ecologically benign methods of synthesis of nanomaterial's still remains a scientific challenge as metal nanoparticles are of use in various catalytic applications, via electronics, biology and biomedical applications, material science, physics, environmental remediation fields [36,37].
This is a revolutionary step for the environmental friendly synthesis of nanoparticles. The process not only involves the plant extracts [38] as reducing or capping agents but also some microbes in which their internal metabolism is exploited for nanoparticle formation [39].

Sreelakshmy et al., [34] formulated silver nanoparticles from bio-reduction of silver nitrate solution using *Glycyrrhiza glabra* root extract. His study revealed that the green synthesized silver nanoparticles provide a promising approach for gastric ulcer therapy [34]. Yadav et al., [40] in their study biosynthesized silver and iron nanoparticles using the aqueous extract of *Aloe vera* and further tested their antibacterial activity. *Aloe vera* has been shown to have anti-inflammatory [41,42] immune-stimulatory activity [43-45]. The comparative study of biosynthesized silver and iron nanoparticles, suggested that silver nanoparticles of *Aloe vera* are more potent antibacterial than their iron counterpart [40].

Gandhi et al., [46] in their study proposed an economical, eco-friendly [47] and cost effective biosynthetic method in which *Escherichia coli* [48] was used as a source for the synthesis of silver nanoparticles extracellulary [46].

Bindhani and Panigrahi [49] synthesized silver nanoparticles in aqueous medium using leaf extracts of *Ocimum sanctum* L. The researchers concluded that the prepared silver nanoparticles showed significant antibacterial activity against *Enterobacter cloacae, Staphylococcus aureus, Streptococcush aemolytius,* *Pseudomonas aeruginosa, Proteus vulgaris, Proteus mirabilis* [50] whereas less activity against *Pseudomonas aeruginosa* [49].

Prasad et al., [51] formulated silver nanoparticles from the aqueous extract of Papaya peel, which was used as capping and reducing agent. The researcher further concluded that the preparation of silver nanoparticles by their proposed method is eco-friendly and non-toxic compared to conventional physical and chemical methods [51].

Bhakya et al., [52] reported biosynthesis of silver nanopartilces using the different parts of Vishanika or Indian screw tree, which is an ayurvedic medicinal tree [53]. They further concluded that silver nanoparticles synthesized from different extract of *H. isora* had better reduction properties [52].

Ahmed and Ikram [54] reported the biosynthesis of silver nanoparticles using *Terminalia arjuna* leaf extracts. The researcher further reported that the prepared silver nanoparticles showed significant antimicrobial activity [54]. Ghozali et al., [55] reported the biosynthesis [56] of silver nanoparticles from the extract of *C. roseus* leaf extracellular by rapid reduction of silver ions.

Pandian et al., [57] reported the synthesis of silver nanoparticles by bacteria *Pseudomonas aeruginosa* AMB AS7 and the role of bio-surfactant in enhancing the stability of silver nanoparticles.
The researcher analysed both chemical and biological method and concluded that silver nanoparticles synthesized from biological method showed significant stability. The bio-surfactants [58] showed superior property than their chemical counterparts [57].

Balashanmugam et al., [59] reported fungus mediated synthesis of silver nanoparticles using Microporus xanthopus. The biosynthesized silver nanoparticles showed potent activity against *Bacillus subtilis, Staphylococcus aureus* [60] *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae* and *shigella sp.* Agrawal et al., [61] reported the synthesis of silver nanoparticles using *Azadirachta indica* [62] extract and incorporated it into dental fillings material to confer its antibacterial activity. The researcher further confirmed antibacterial activity of developed silver nanoparticles by agar diffusion test against *E. coli* and *S. mutans* [61].

Hungund et al., [63] synthesized nanoparticles using extract of various fruit juices like sweet lime, lime and orange as reducing and capping agent for silver nitrate. Furthermore, the researcher concluded that the prepared silver nanoparticle showed antibacterial property against *E. coli, Salminella typhi, Klebsiella pneumonia* [64] and *Staphylococcus aureus* which was supported by the results of agar well diffusion method.

Mani et al, [65] reported the synthesis of silver nanoparticles using the aqueous extract of the in ripe fruits of *Piper nigrum.* The prepared silver nanoparticles were further evaluated for its *in vitro* anti-inflammatory activity. The result of their study confirmed the enhanced anti-inflammatory activity of the prepared formulation due to the synergistic effect of alkaloids of *Piper nigrum* [66] extract and silver ions. Omaparkash and Sharada [67] reported the green synthesis of silver nanoparticles using *Elettaria cardamom* seed extract as reducing agent. The prepared silver nanoparticles showed antibacterial activity against *Bacillus subtilis* [68].

El-Deeb et al., [69] demonstrated the synthesis of silver nanoparticles using honey bee [70] extract. The researchers further investigated the anti-colon cancer activity of biogenic silver nanoparticles. Their result concluded that both silver nanoparticles and its capping biomolecules have anti-proliferative effect.

Singh et al., [71] evaluated the antimicrobial efficacy of silver nanoparticles biosynthesized from aqueous extracts of *Phyllanthus amarus* and *Tinospora cordifolia.* The researchers concluded that the antimicrobial activity of biosynthesized nanoparticles was higher than that of the standard drug streptomycin and ketoconazole [72].

Durairaj et al., [73] synthesized silver nanoparticles using *Penicillium notatum* [74] and further quantified the potential of fungi based silver nanoparticles against *Culix quinquefasciatus* larvae. The study concluded that the prepared formulation was induced constituent mortality against 2nd and 3rd stage of *C. quinquefasciatus* larvae. The study suggested that silver nanoparticles can be used to control vector and vector borne diseases.

Banu and Rathod [75] reported the biosynthesis of mono-dispersed silver nanoparticles and further evaluated its antibacterial activity against *Mycobacterium tuberculosis* [76]. The researchers reported the synthesis of silver nanoparticles using a cell free filtrate of *R. stolonifer*. The study concluded the synergistic antibacterial effect of biosynthesized silver nanoparticles with antibiotics against clinically isolated ESBL-strains.

Singh et al., [77] biosynthesized silver nanoparticles from *Tinospora cordifolia* and further evaluated it against multi drug resistant (MDR) strains of *Pseudomonas aeruginosa* [78] isolated from burn patients. The study concluded excellent potential of biosynthesized silver nanoparticles as an antibacterial agent against MDR strains of *P. aeruginosa.*

Shahaby et al., biosynthesized silver nanoparticles from *Rumex dentatus* and further evaluated it for its antimicrobial activity against pathogenic bacterial and fungal strains [79]. Borase et al., [80] reported the larvicidal [81] and insecticidal properties of biosynthesized nanoparticles from the leaf extracts of *J. gossypifolia, E. tirucalli, P. tithymaloides* and *A. macrophylla*.

The Bad

The present comprehension about silver nanoparticles inclination of tissue statement and related unfriendly impacts is constrained [82,83] be that as it may, the oral harmfulness of silver nanoparticles is of specific worry to guarantee open and buyer wellbeing. Kidney could be an objective in view of its part in disposal of xenobiotics [84]. Heydrnejas et al., [85] studied the sex differential influence of silver nanoparticles on the kidney of mice *Mus musculus* [86]. The researchers concluded that the silver nanoparticles had a more maintained lethal impact on the capacity of female as opposed to male mice kidney.

Abdolsamad et al., [87] reported the effect of silver nanoparticles on chlorophyll A and carotene content in the microalgae *Chlorella vulgaris* [88] The researcher reported that the exposed silver nanoparticles can all the more effectively discharge their valance layer electrons, so in the high focus valance layer electrons comes in fast response with other accessible electrons in the media, it cause a great deal undesirable and undesirable response, which cause the cell to experience stresses and in some cases dead.

Bruneau et al., [89] reported the immune-toxic effects of silver nanoparticles on Rainbow Trout in natural water. The researcher concluded that brown water expands the Ag+ openness in media, advancing their accessibility for fish tissues, and immune-stimulation without oxidative anxiety. In green water, silver was just bio-accumulated [90] in gills when presented to $AgNO_3$. $AgNO_3$ triggers leucocytes incitement and hepatic professional provocative reaction (COX). The bioavailability of colloidal $AgNO_3$ in faucet water instigated high aggregation in the liver without hepatic damage. Resistant bothers were seen as immunosuppression and oxidative anxiety in pronephros [89].

If there should be an occurrence of silver nanoparticles discharge in nature, water like cocoa water could build the scattering of silver nanoparticles in monomeric structure or little totals, advancing their long haul bioavailability and their assimilation as NP. Further research on nano-toxicity [91] ought to consider presentation conditions and silver nanoparticles destiny in water media for danger appraisals [89].

Morris and Behzad [92] examined the impacts of gold (Au) and silver (Ag) nanoparticles on an ordinarily utilized enzymatic response between horseradish peroxidase (HRP) and the substrate, 3,3',5,5'-tetramethylbenzidine (TMB). Two unique systems were utilized as a part of their study. The first was the expansion of little amounts of nanoparticles, specifically onto an answer of streptavidin peroxidase (streptavidin bound to HRP), before its response with TMB. The second was the expansion of nanoparticles to immobilized streptavidin peroxidase, covalently limited to wells of a microtiter plate. In both cases, responses with TMB were measured by noticeable absorbance spectroscopy, utilizing a microtiter plate reader. The outcomes demonstrate that both gold and silver nanoparticles have a noteworthy effect; with gold smothering the response and silver improving it. Enzymatic responses are impacted by nanoparticles. The instrument of these nanoparticle-protein communications are as of now under scrutiny. This is a critical territory of exploration, since the capacity to direct enzymatic action could conceivably prompt new procedures for chemical control and alteration, with conceivable use in new medication advancements and modern applications. It additionally connotes likely lethality of nanoparticles as they turn out to be all the more generally present in ordinary life by means of off-the-counter accessible beautifying agents and family unit products [92].

Coccini et al., [93] reported as per an extensive number of writing information, bolster the confirmation of the capacity of silver nanoparticles to bring about natural and dangerous impacts that are impossible to miss of their nano-scale [94] properties, and may add to give data expected to figure out whether the as of now settled ACGIH gauges (for word related introduction to silver mixes) are additionally sufficient to shield laborers and buyers from any potential unsafe exposures to silver nanoparticles [93].

The utilization of silver nanoparticles in restorative and buyer items, for example, wound dressings, garments and corrective has expanded essentially as of late. Still, the impact of these particles on our wellbeing and particularly on our mind has not been inspected sufficiently up to now [95]. The study considered the impact of AgEO-(Ethylene Oxide) and AgCitrate-Nanoparticles (NPs) on the defensive obstructions of the cerebrum, to be specific the blood brain barrier (BBB) [96] and the blood-cerebrospinal liquid (blood-CSF) boundary in vitro. The NPs lethality was assessed by analyzing changes in layer uprightness, cell morphology, boundary properties, oxidative anxiety and incendiary responses. Silver nanoparticles diminished cell feasibility, aggravated obstruction uprightness and tight intersections and activated oxidative anxiety and DNA strand breaks. Be that as it may, all said impacts were, at any rate somewhat, smothered by a Citrate-covering and were most maintained in the phones of the BBB when contrasted with the epithelial cells speaking to the blood-CSF boundary. AgEO-however not AgCitrate-NPs additionally set off a provocative response in porcine mind hair like endothelial cells (PBCEC), which speak to the BBB. Our information demonstrates that silver nanoparticles may bring about unfriendly impacts inside the blood brain barrier, yet their poisonous quality can be decreased by picking a proper covering material. The outcomes were the first proof for the poisonous quality of silver nanoparticles towards cell of brain origin [95].

Lee et al., [97] reported that silver nanoparticles prompt hepatotoxicity [98] by means of oxidative anxiety. The oxidative anxiety prompted mitochondrial harms are known not directed by mitochondrial unfurled protein reaction (mtUPR) and autophagy/mitophagy frameworks. The result of the study demonstrated that initiation of autophagy/mitophagy markers coincided with up-regulation of Ub-proteins and lessening of ATP substance without changing mtUPR in rodent liver after silver nanoparticles organization. These discoveries demonstrate that defensive impacts of autophagy/mitophagy markers were overpowered by inconvenient activities of Ub-proteins on the control of mitochondrial capacity, and the offset of the two frameworks in the end bringing about weakened mitochondrial capacity, i.e., diminishment of ATP substance [97].

The Future

Silver nanoparticles are viewed as imperative expansion in the range of nano-materials due to the differing qualities it gives as far as application in different stroll of science. Because of their mitigating and antimicrobial movement silver nanoparticles have occupied fascination of the masses towards themselves to be utilized as embedded material as a part of counterfeit organs. Silver nanoparticles have demonstrated it worth in repressing the microbial multiplication and microbial disease. Moreover silver nanoparticles have included another measurement in the field of prescription concerning wound dressing and simulated implantation and in anticipating postsurgical sullying brought about by organisms. Aside from that silver nanoparticles assume a crucial part and are considered as vital fixings in the planning of monetarily utilized items as a part of commercial ventures [99]. New bits of knowledge about the pharmacological applications, for example, anticancer, larvicidal, therapeutic materials, and gadgets are gathered with these extraordinary silver nanoparticles. Consequently, these biogenetically incorporated silver nanoparticles will bring about a noteworthy result for the field of bio-nano-medicine [100].

Much accentuation has been committed to the antimicrobial and anticancer capability of silver nanoparticles demonstrating their promising qualities for treatment, prophylaxis and control of contaminations, and additionally for conclusion and treatment of various tumor sorts [101].

For an effective interpretation of nanoparticles to the facilities, a few elements should be considered. As a matter of first importance, the properties and attributes of nanoparticle therapeutics should be entirely and thoroughly characterized. All through the writing, it is obvious that the bio-distribution and pharmacokinetics is to a great extent subject to the nanomaterial. Consequently important measures should be done to inspect conceivable poisonous impacts of each nanoparticle created. Despite the fact that there are a few reports expressing "stripped" gold nanoparticles are organically idle (apparent since its restorative use in olden times), the topping specialists may change the poisonous profile of the molecule. Essentially, the hydrodynamic distance across and surface charge may likewise influence the adequacy of the nanoparticle [102].

CONCLUSION

Silver nanoparticles are picking up prevalence in pharmaceuticals as well as in other partnered and non-unified ventures. Numerous specialists have exhibited the antibacterial, antimicrobial and anti-parasitic action of silver nanoparticles. With the developing awareness for creating natural well-disposed or eco-accommodating procedure in the compound and pharmaceutical ventures, green chemistry is being exploited for developing silver nanoparticles. Several studies have been directed to create silver nanoparticles utilizing plant extracts as reducing or capping agents. Despite giving numerous chances to advancement silver nanoparticles additionally have some potential peril. Numerous studies have been led to bring the light the harmful effects of silver nanoparticles.

Collection of data

The data was collected from different free online sources like-Google scholar, Jamia Hamdard University database and other free online sources.

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Conflict of interest

The authors declare no conflict of interest.

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