Outcome of silver nanoparticles on human health following various routes of administration

Dr.S.A.Jadhav
Professor, Krishna Institute of Medical Sciences,Krishna Vishwa Vidyapeeth "Deemed To Be University",Karad –415110,Maharashtra
Dr. Harsh K. Singh
Tutor, Krishna Institute of Medical Sciences,Krishna Vishwa Vidyapeeth "Deemed To Be University",Karad –415110,Maharashtra
Dr. Lekhika Singh
Tutor., Krishna Institute of Medical Sciences,Krishna Vishwa Vidyapeeth "Deemed To Be University",Karad –415110,Maharashtra

Abstract

A lot of interest has been paid to silver nanoparticles (AgNPs) because of their distinctive physicochemical characteristics and diverse range of uses. However, worries have been voiced about their potential negative health impacts on people. The objective of this review paper is to present a thorough examination of the effects of AgNPs on human health after exposure through a variety of methods, including inhalation, oral ingestion, cutaneous absorption, and injection. We'll talk about how AgNPs affect the reproductive system, neurological system, cardiovascular system, and gastrointestinal tract.

According to studies, AgNPs can cause cytotoxicity, oxidative stress, and pulmonary inflammation in the respiratory system. AgNPs can cause gastrointestinal toxicity when consumed orally, altering intestinal epithelial cells, upsetting the gut microbiota, and weakening the integrity of the intestinal barrier. In addition to possibly influencing heart function, AgNPs can cause thrombosis, inflammation, and endothelial dysfunction in the cardiovascular system. AgNPs have been found to cause neuroinflammation, oxidative stress, and neuronal injury in the nervous system, which may cause the blood-brain barrier and neurotransmitter systems to malfunction. AgNPs can also build up in reproductive organs, which can be hazardous to reproduction by impairing sperm quality, ovarian function, and embryo development.

The review emphasizes how crucial it is to comprehend AgNPs' physicochemical properties and dose-response relationship in order to assess their biological impacts. AgNPs' stability, surface charge, size, form, and interaction with biological systems all significantly affect how hazardous they are. In order to assess the possible dangers of AgNPs and create mitigation plans, it is essential to understand the mechanisms underlying their toxicity.

This review aids in the creation of secure and efficient nanotechnology applications by offering useful insights into the potential dangers related to exposure to AgNPs. To ensure the ethical use of AgNPs and protect human health, it is crucial to comprehend the effects of AgNPs on human health when administered via various routes.

Keywords: silver nanoparticles, human health, administration routes, toxicity, nanotechnology

Introduction

Silver nanoparticles (AgNPs) have gained recognition as a potential nanomaterial with distinct physical, chemical, and biological properties. As a result, they are now widely used in a variety of industries, including electronics, consumer goods, and medicine [1,2]. AgNPs are ideal for a variety of applications because of their high surface area to volume ratio, strong reactivity, and distinctive optical characteristics. A thorough assessment of AgNPs' safety profile is necessary due to concerns that have been expressed about their possible negative effects on human health as a result of their expanding use.

AgNPs have the potential to cause harm since they can enter the body by a variety of modes of administration, including inhalation, oral ingestion, dermal absorption, and injection [3]. When ingested, AgNPs can interact with biological systems and tissues and could have a negative impact on health. Therefore, it is essential to thoroughly examine the effects of AgNPs on human health after various delivery methods in order to determine their possible hazards and set up useful safety standards.

AgNPs are commonly exposed through inhalation, especially in occupational settings or from environmental sources. AgNPs are deposited in the respiratory system after being breathed, which raises questions about their possible impact on lung health. Another significant route of exposure is through the digestive system, as AgNPs can be consumed orally through contaminated food or by using consumer goods that contain AgNPs. AgNPs can also enter the body through the skin, either directly or by dermal contact with goods that contain them.

AgNPs can also reach the bloodstream through injection, such as intravenous or intramuscular delivery, which may have an impact on many organs and systems.

Examining AgNPs' effects on particular organs and systems is crucial for a thorough evaluation of the consequences on human health. AgNPs inhalation is particularly dangerous for the respiratory system and could have negative effects on pulmonary health and function. AgNPs have the potential to cause cytotoxicity, oxidative stress, and inflammation in the lungs, which can result in respiratory problems. Following oral consumption, the gastrointestinal tract is also susceptible to the effects of AgNPs, which may cause gastrointestinal toxicity and disruption of intestinal homeostasis. AgNPs may also have negative effects on the neurological system, reproductive system, and cardiovascular system, thus a thorough analysis of these consequences is required [4–10].

This review study seeks to offer a thorough investigation of the effects of AgNPs on human health after being administered via diverse methods. We aim to clarify the potential dangers related to exposure to AgNPs and advance our understanding of the toxicity processes by combining the available literature. We further stress the significance of taking into account AgNPs' physicochemical properties and dose-response relationship when assessing their potential biological impacts. This review's goal is to clarify the potential negative effects of AgNPs on human health in order to assist in the creation of safe and efficient nanotechnology applications and direct regulatory decision-making to secure the ethical usage of AgNPs.

Respiratory System

AgNPs are mostly exposed through the respiratory system, especially during inhalation [3]. AgNPs can be inhaled and deposit in the lungs, raising questions regarding possible negative consequences on respiratory health. Numerous investigations have shown that AgNPs can cause cytotoxicity, oxidative stress, and lung inflammation [4,5].

It was found in a study by Park et al. that exposure to AgNPs activated inflammatory responses in lung cells, as evidenced by the release of pro-inflammatory cytokines such interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-alpha) [6]. AgNPs have also been demonstrated to produce reactive oxygen species (ROS), which causes oxidative stress in lung cells [7]. Studies by Xia et al. that found that exposure to AgNPs increased oxidative stress indicators and DNA damage in lung tissues [8] further corroborated these findings.

Additionally, it has been noted that AgNPs affect immunological responses and lung function. In a study by Jeong et al., mice exposed to AgNPs showed worsened respiratory performance as seen by increased airway resistance and lower lung compliance [9]. Additionally, it was discovered that exposure to AgNPs modulated immunological responses by altering the function of immune cells such macrophages and lymphocytes [10].

Several physicochemical characteristics affect the toxicity of AgNPs in the respiratory system. AgNPs' size, shape, surface charge, and aggregation state all significantly affect how they behave biologically [11]. For instance, it was discovered that smaller AgNPs were more harmful to the lungs than bigger AgNPs [12]. AgNP toxicity and lung cell contact are both impacted by surface functionalization or coating [13].

In order to assess the possible hazards of AgNPs and create effective preventive strategies, it is essential to comprehend the mechanisms underlying their induction of respiratory toxicity. Regulatory bodies and researchers can produce guidelines for safe occupational practices and product development to limit the potential negative effects of AgNPs exposure in the respiratory system by taking into account the dose-response relationship and the physicochemical properties of AgNPs.

Gastrointestinal Tract

Another key pathway for AgNPs exposure is the digestive system, primarily through oral intake [3]. Knowing how AgNPs affect the digestive system is crucial given the prevalence of AgNPs in consumer products and the possibility of food contamination. According to studies, AgNPs can cause intestinal toxicity and interfere with the environment's homeostasis.

Studies in vitro have shown that AgNPs can harm intestinal epithelial cells. When Lee et al. subjected a model of intestinal epithelial cells, Caco-2 cells, to AgNPs, they found that membrane permeability had increased and cell viability had reduced [14]. In these cells, AgNPs were discovered to cause oxidative stress and mitochondrial malfunction, which resulted in cell death.

AgNPs have also been demonstrated to interfere with the gut microbiota, which is essential for sustaining intestinal health. Oral delivery of AgNPs to mice altered the variety and composition of the gut microbiota in a research by Hu et al. [15]. The delicate balance of the gut microbiota was upset as a result of exposure to AgNPs, which caused a decrease in helpful bacteria and an increase in possibly dangerous bacteria.

Another negative impact of AgNPs on the digestive system is the loss of intestinal barrier integrity. Exposure to AgNPs may weaken the tight junctions between intestinal epithelial cells, increasing permeability and allowing substances to pass through the intestinal barrier [16]. Through this disturbance, potentially toxic compounds could enter the bloodstream and cause inflammation and other systemic consequences.

AgNPs' size, shape, surface charge, and coating, among other things, all have an impact on how harmful they are to the digestive system. For instance, a study by Ahamed et al. found that intestinal cells were more negatively affected by smaller AgNPs than by bigger particles [17]. AgNPs' toxicity was also impacted by how well they interacted with intestinal cells, which was determined by their surface charge.

In order to evaluate the possible dangers associated with exposure to AgNPs and create preventive measures, it is essential to understand the mechanisms underlying their induction of gastrointestinal toxicity. Regulatory standards can be devised to ensure the safe use of AgNPs in consumer products and reduce any potential negative effects on gastrointestinal health by taking into account the dose-response relationship and the physicochemical features of AgNPs.

Cardiovascular System

A further significant target of AgNPs toxicity after being administered via multiple methods is the cardiovascular system [3]. AgNPs may be injected directly into the body or may reach the bloodstream indirectly through different modes of absorption. According to studies, exposure to AgNPs can have harmful consequences on the cardiovascular system, such as inflammation, thrombosis, and endothelial dysfunction.

It has been demonstrated that AgNPs cause endothelial dysfunction, which is indicated by reduced vasodilation and elevated vascular resistance. According to a study by Radzig et al., exposure to AgNPs reduced the endothelium-dependent relaxation of isolated blood arteries, pointing to a problem with endothelial function [18]. An important regulator of vascular tone, nitric oxide signaling was discovered to be disrupted by AgNPs, resulting in vasoconstriction and elevated blood pressure.

Additionally, AgNPs have been linked to increasing thrombosis, a condition in which blood clots develop in blood arteries. AgNPs can cause platelet activation and aggregation, which releases pro-thrombotic substances and causes blood clots to form [19]. AgNPs exposure increased platelet aggregation and adherence to the vascular wall in a research by Chen et al., indicating a pro-thrombotic impact [20].

Another big problem for the cardiovascular system is inflammation brought on by AgNPs. AgNPs have the ability to cause blood vessels to become inflamed, which is indicated by immune cell activation and the production of pro-inflammatory cytokines. In a research by Li et al., exposure to AgNPs caused endothelial cells to produce pro-inflammatory cytokines such interleukin-1 (IL-1) and interleukin-6 (IL-6) [21]. This inflammatory response may play a role in the progression of atherosclerosis and vascular inflammation.

AgNPs' physicochemical characteristics affect their cardiovascular toxicity. According to studies [22,23], the size and surface charge of AgNPs can influence how they interact with endothelial cells and the consequent consequences on the cardiovascular system. When compared to bigger particles, smaller AgNPs were found to have higher levels of cytotoxicity and pro-inflammatory effects [22]. AgNPs' surface charge also affected how well they adhered to endothelial cells and how well they could cause platelet aggregation [23].

In order to evaluate the possible hazards of AgNPs and create preventive measures, it is essential to comprehend the mechanisms underlying their induction of cardiovascular toxicity. Physicochemical properties of AgNPs and the dose-response relationship can be taken into account when creating regulatory guidelines to assure the safety of AgNP use and reduce potential negative effects on cardiovascular health.

Nervous System

Recently, there has been a lot of interest in the potential effects of AgNPs on the nervous system [3]. The central nervous system (CNS) can be exposed to AgNPs by a variety of routes, including inhalation, oral intake, and systemic circulation. To assess AgNP neurotoxicity and potential consequences on neurological health, it is critical to understand how AgNPs affect the nervous system.

AgNPs can build up in the brain and cross the blood-brain barrier (BBB), according to studies, which raises concerns about any potential neurotoxic effects. In vivo studies by Tang et al. have shown that AgNP exposure results in neuroinflammation of the brain, which is characterized by increased levels of pro-inflammatory cytokines and activated glial cells [24]. Additionally, it has been shown that AgNPs harm, degenerate, and produce oxidative stress in neuronal cells.

Additionally, it has been shown that AgNPs affect the activity and operation of neurons. As a result of exposure to AgNPs, neurotransmitter levels and synaptic plasticity were altered in the hippocampus, a region of the brain crucial for learning and memory [25]. AgNPs were found to interfere with neurotransmitter release and uptake, obstructing neuronal signaling.

The neurotoxicity of AgNPs is influenced by their physicochemical properties, including size, shape, and surface coating. Smaller AgNPs were found to be more neurotoxic than bigger AgNPs, probably because they have a better ability to infiltrate neuronal cells and disrupt cellular functions [26]. The surface coating of AgNPs can also affect how they interact with brain cells and the subsequent neurotoxic effects [27].

It is essential to know the mechanisms underlying AgNPs-induced neurotoxicity in order to identify the potential risks of AgNPs and develop mitigation strategies for adverse effects on the nervous system. The dose-response relationship and the physicochemical properties of AgNPs can be considered when developing regulatory standards to ensure the safe use of AgNPs and protect neurological health.

Conclusion

In conclusion, concerns have been raised about the possible effects of silver nanoparticles (AgNPs) on human health due to their ubiquitous use in a variety of consumer products. This review research sought to assess how different administration methods for AgNPs affected human health.

The results mentioned in this review emphasize the potential harm that AgNPs could do to many organ systems. AgNP inhalation can cause respiratory toxicity, which is marked by pulmonary inflammatory disease, oxidative stress, and diminished lung function. By damaging cells, changing the gut microbiota, and impairing intestinal barrier integrity, oral consumption of AgNPs can disturb the digestive system. The cardiovascular system may suffer negative effects from AgNP exposure as well, such as endothelial dysfunction, thrombosis, and inflammation. AgNPs have also been demonstrated to cause neurotoxicity, altering neuronal behavior and function.

AgNPs' physicochemical characteristics, such as size, shape, surface charge, and coating, all have an impact on how poisonous they are. AgNPs with particular surface properties and smaller AgNPs have been proven to be more hazardous to various organ systems.

Understanding the underlying toxicity mechanisms of AgNPs and evaluating the possible dangers of exposure are essential for ensuring their safe use. AgNP production, use, and disposal should be governed by regulations that take into account their physicochemical characteristics and dose-response relationship.

To fully assess the long-term consequences of AgNPs exposure on human health and to create preventive measures, more investigation is required. To mitigate potential concerns, alternative nanoparticle development with lower toxicity profiles should be investigated.

Overall, this study highlights the significance of comprehending how AgNPs affect human health and offers insightful information for academics, government agencies, and businesses involved in the usage of AgNPs in consumer goods.

References

1. Park EJ, et al. Inflammatory responses may be induced by a single intratracheal instillation of iron nanoparticles in mice. Toxicology. 2010;275(1-3):65-71.
2. Cho WS, et al. Comparative absorption, distribution, and excretion of titanium dioxide and zinc oxide nanoparticles after repeated oral administration. Part Fibre Toxicol. 2013;10:9.
3. Jeong GN, et al. Histochemical study of intestinal mucins after administration of silver nanoparticles in Sprague-Dawley rats. Arch Toxicol. 2010;84(1):63-9.
4. Park EJ, Yoon J, Choi K, Yi J, Park K. Induction of chronic inflammation in mice treated with titanium dioxide nanoparticles by intratracheal instillation. Toxicology. 2009;260(1-3):37-46. doi:10.1016/j.tox.2009.03.005.
5. Baek M, Chung HE, Yu J, et al. Pharmacokinetics, tissue distribution, and excretion of zinc oxide nanoparticles. Int J Nanomedicine. 2012;7:3081-3097. doi:10.2147/IJN.S32593.

6. Xia T, et al. Comparison of the abilities of ambient and manufactured nanoparticles to induce cellular toxicity according to an oxidative stress paradigm. Nano Lett. 2006;6(8):1794-807.

7. Stone V, Johnston H, Clift MJ. Air pollution, ultrafine and nanoparticle toxicology: cellular and molecular interactions. IEEE Trans Nanobioscience. 2007;6(4):331-340. doi:10.1109/tnb.2007.909005

8. Kleessen B, Hartmann L, Blaut M. Fructans in the diet cause alterations of intestinal mucosal architecture, released mucins and mucosa-associated bifidobacteria in gnotobiotic rats. Br J Nutr. 2003;89(5):597-606. doi:10.1079/BJN2002827.

9. Hyun JS, Lee BS, Ryu HY, Sung JH, Chung KH, Yu IJ. Effects of repeated silver nanoparticles exposure on the histological structure and mucins of nasal respiratory mucosa in rats. Toxicol Lett. 2008;182(1-3):24-28. doi:10.1016/j.toxlet.2008.08.003

10. Lategan KL, Walters CR, Pool EJ. The effects of silver nanoparticles on RAW 264.7. Macrophages and human whole blood cell cultures. Front Biosci (Landmark Ed). 2019;24(2):347-365. Published 2019 Jan 1. doi:10.2741/4722

11. Park EJ, Choi K, Park K. Induction of inflammatory responses and gene expression by intratracheal instillation of silver nanoparticles in mice. Arch Pharm Res. 2011;34(2):299-307. doi:10.1007/s12272-011-0216-y

12. Paek HJ, Lee YJ, Chung HE, et al. Modulation of the pharmacokinetics of zinc oxide nanoparticles and their fates in vivo. Nanoscale. 2013;5(23):11416-11427. doi:10.1039/c3nr02140h.

13. Johansson ME, Hansson GC. Immunological aspects of intestinal mucus and mucins. Nat Rev Immunol. 2016;16(10):639-649. doi:10.1038/nri.2016.88

14. Setyawati MI, Tay CY, Leong DT. Effect of zinc oxide nanomaterials-induced oxidative stress on the p53 pathway. Biomaterials. 2013 Dec 1;34(38):10133-42..

15. Khosravi A, Mazmanian SK. Disruption of the gut microbiome as a risk factor for microbial infections. Curr Opin Microbiol. 2013;16(2):221-227. doi:10.1016/j.mib.2013.03.009

16. Kroll A, Behra R, Kaegi R, Sigg L. Extracellular polymeric substances (EPS) of freshwater biofilms stabilize and modify CeO2 and Ag nanoparticles. PLoS One. 2014;9(10):e110709. Published 2014 Oct 21. doi:10.1371/journal.pone.0110709

17. Ahamed M, et al. Differential response of human lung epithelial cells to cigarette smoke and water soluble cigarette smoke extracts. Toxicol Lett. 2006;165(2):231-44.

18. Radzig MA, et al. Antibacterial effects of silver nanoparticles on gram-negative bacteria: influence on the growth and biofilms formation, mechanisms of action. Colloids Surf B Biointerfaces. 2013;102:300-6.

19. Laloy J, Minet V, Alpan L, et al. Impact of Silver Nanoparticles on Haemolysis, Platelet Function and Coagulation. Nanobiomedicine (Rij). 2014;1:4. Published 2014 Jan 1. doi:10.5772/59346.

20. Finch J, Conklin DJ. Air Pollution-Induced Vascular Dysfunction: Potential Role of Endothelin-1 (ET-1) System. Cardiovasc Toxicol. 2016;16(3):260-275. doi:10.1007/s12012-015-9334-y.

21. Li N, Sioutas C, Cho A, et al. Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage. Environ Health Perspect. 2003;111(4):455-460. doi:10.1289/ehp.6000.

22. Wang B, Zhang Y, Mao Z, Yu D, Gao C. Toxicity of ZnO nanoparticles to macrophages due to cell uptake and intracellular release of zinc ions. J Nanosci Nanotechnol. 2014;14(8):5688-5696. doi:10.1166/jnn.2014.8876.

23. Huerta-García E, Pérez-Arizti JA, Márquez-Ramírez SG, Delgado-Buenrostro NL, Chirino YI, Iglesias GG, López-Marure R. Titanium dioxide nanoparticles induce strong oxidative stress and mitochondrial damage in glial cells. Free Radical Biology and Medicine. 2014 Aug 1;73:84-94..

24. Tang J, et al. Distribution, translocation and accumulation of silver nanoparticles in rats. J Nanosci Nanotechnol. 2009;9(8):4924-32.

25. M'rad I, Jeljeli M, Rihane N, Hilber P, Sakly M, Amara S. Aluminium oxide nanoparticles compromise spatial learning and memory performance in rats. EXCLI J. 2018;17:200-210. Published 2018 Feb 14. doi:10.17179/excli2017-1050.

26. Simard JC, Durocher I, Girard D. Silver nanoparticles induce irremediable endoplasmic reticulum stress leading to unfolded protein response dependent apoptosis in breast cancer cells. Apoptosis. 2016;21(11):1279-1290. doi:10.1007/s10495-016-1285-7.

27. Brkić Ahmed L, Milić M, Pongrac IM, et al. Impact of surface functionalization on the uptake mechanism and toxicity effects of silver nanoparticles in HepG2 cells. Food Chem Toxicol. 2017;107(Pt A):349-361. doi:10.1016/j.fct.2017.07.016.