*Nanomed Res J 11(3):221-232, Summer 2026*

REVIEW ARTICLE

# Toxic Effects and Underlying Mechanisms of Silver Nanoparticles on Gut Microbiota: A Systematic Review

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**ARTICLE INFO**

***Article History:***
*Received 2026-05-02*
*Revised 2026-08-01*
*Accepted 2026-08-10*

***Keywords:***
*Silver nanoparticles*
*Microbiota*
*Nanotoxicology*
*Dysbiosis*
*Oxidative stress*
*Mechanisms of toxicity*

**ABSTRACT**

**Objective(s):** silver nanoparticles (AgNPs) are used in many medical, industrial, and consumer products due to their antimicrobial properties. As their use increases, concerns have been raised about potential effects on the gut microbiota and host health. This systematic review aims to evaluate the toxic effects of silver nanoparticles on the gut microbiota and to investigate the mechanisms underlying these changes.

**Methods:** Relevant keywords were identified, and a search protocol was established to retrieve articles from databases. Studies published between 2015 and 2026 were reviewed, and 9 articles were ultimately selected for this review based on the inclusion criteria.

**Results:** The findings showed that exposure to silver nanoparticles can alter microbial diversity and the structure of the intestinal bacterial community. In some studies, dysbiosis, shifts in the Firmicutes/Bacteroidetes ratio, and changes in the abundance of key bacteria, including Akkermansia, Faecalibacterium prausnitzii, Prevotellaceae, and Lachnospiraceae, have been reported. The severity of these changes varied across studies and depended on factors such as nanoparticle size, dose, exposure duration, shape, and surface coating, as well as the rate of silver ion ($Ag^+$) release.

**Conclusions:** In general, the effects of silver nanoparticles on the intestine are not limited to their direct antibacterial activity but result from a complex interaction among the nanoparticles' physicochemical properties, the microbiota, the intestinal epithelial barrier, immune responses, and host metabolism.

**How to cite this article**
*Koohi MK, Hosseini Y, Rasooli R, Sadighara P, Ghanati K, Aghebat Bekheir S. Toxic Effects and Underlying Mechanisms of Silver Nanoparticles on Gut Microbiota: A Systematic Review. Nanomed Res J, 2026; 11(3): 221-232. DOI: 10.22034/nmrj.2026.03.002*

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## INTRODUCTION

Silver (Ag) ions or salts possess significant potential and have been utilized for years across diverse fields like agriculture and medicine. Their low toxicity, high biocompatibility with human cells, and stable ionic form enable a sustained antibacterial effect [1]. Silver nanoparticles (AgNPs) have garnered considerable interest and are extensively researched because of their unique physical and chemical attributes. Throughout history, nanoparticles have played vital roles in areas such as medicine, food, healthcare, consumer products, and industry. Due to their tiny size, AgNPs display different chemical, physical, and biological characteristics compared to larger bulk materials, making them popular for various applications [2]. The significance and properties of AgNPs are depicted in **Figure 1.**

The terms microbiome and microbiota are frequently used as synonyms. The microbiome specifically denotes the genes of microorganisms that coexist symbiotically with humans [3, 4]. Microbiota organisms that live with humans create a complex microecological flora. This symbiotic relationship can impact both the microbial and human systems. For instance, shifts in the abundance and distribution of intestinal microbes may impair the intestinal barrier, boost the release of toxic substances, and decrease beneficial secretions, potentially causing intestinal and other health issues [5]. Age and diet notably influence intestinal microbiology. Many studies on humans and animals indicate that various diets lead to major shifts in microbiota. Additionally, infection and disease can disrupt the host's normal gut flora, causing harmful effects on their health [6-8]. The microbiota significantly influences human health and disease. Specifically, the gastrointestinal (GI) microbiota helps by providing signals vital for health and disease states, supporting immune cell maturation, and enabling the proper development of immune system functions. It does so through absorbing and fermenting undigested carbohydrates [9]. The oral microbiota comprises the interactions between microorganisms (microbiome) within the oral cavity and their hosts [10].Numerous types of microbiotas exist, such as the skin microbiota [11] and the vaginal microbiota [12] Over 70% of the microorganisms in our bodies reside in the large intestine alone [13].

AgNPs, ranging from 1 to 100 nm in size, have a large surface area, which influences their biological properties. The varying diameters affect how particles interact biologically, with surface charge playing a key role in toxicity [14, 15]. Critical factors impacting nanosilver toxicity include the route of entry into the human body, concentration, duration of exposure, bioavailability, accumulation, size, tissue distribution, penetration, and cellular uptake [16]. Nanosilver applications are rapidly evolving, raising concerns about potential negative health effects [17]. Its increasing use in consumer products is driven by its unique properties, leading to higher human exposure

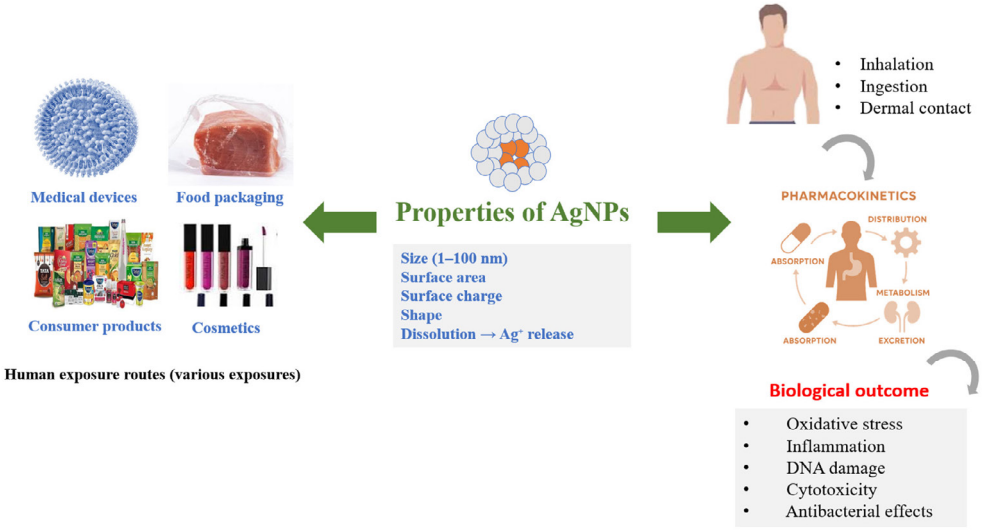



Fig. 1. The significance and properties of AgNPs



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through diverse channels [18]. However, research on nanosilver toxicity is limited and often yields conflicting results [19]. Promising developments like green synthesis, using natural materials, aim to improve safety [20]. Nanometallic solutions including silver, gold, and copper are popular in online communities, where nanosilver products are sold under various names such as colloidal silver. Growing interest in AgNPs has spurred extensive research across scientific disciplines [21]. Despite its benefits in microbiology, health, and consumer sectors, nanosilver is not yet classified under the European Chemicals Regulation (REACH) [22].

Despite the widespread use of AgNPs in medicine, pharmaceuticals, food, cosmetics, and industrial applications, concerns are rising about their biological impact and potential toxicity on microbial communities. Research indicates that exposure to AgNPs can alter microbiota composition and diversity, disrupt microbial balance, and cause dysbiosis, all of which could significantly affect host health and ecosystems. However, current evidence remains limited, and most reviews have focused either on general nanoparticle toxicity or on effects on specific microbes. A comprehensive evaluation of how AgNPs affect different microbiotas, along with the mechanisms involved, is lacking. This study aims to fill that gap by providing an integrated analysis of the toxic effects of AgNPs and their underlying mechanisms, considering factors like particle size, dose, exposure time, and physicochemical properties. The goal is to systematically review existing research, identify knowledge gaps from in vitro and animal studies, and offer future insights for safer nanoparticle use.

## MATERIAL AND METHODS

In accordance with the inclusion and exclusion criteria, two authors carried out all steps outlined in the PRISMA checklist to minimize bias.

*Search strategy*

The search for this systematic review was conducted in June 2026 in three databases: PubMed, Web of Science, and Scopus, without applying any publication date restrictions. The keywords were defined before the search in consultation with the study team as follows: ("nano-silver" OR "Nano silver" OR "silver nanoparticles") AND (toxicity) AND (microbiota)

*Inclusion and exclusion criteria*

This study's inclusion criteria covered experimental in vivo (animal) and/or in vitro studies, along with clinical trials if available, and original research articles examining the effects and toxicities of silver nanoparticles on microbiota. Eligible studies needed to investigate alterations induced by nanosilver exposure in microbiota, particularly focusing on gut microbial flora and probiotic bacteria. Studies evaluating changes in microbiota composition and nanosilver-induced toxic effects on intestinal bacterial communities and probiotics were included.

Studies addressing bacterial resistance, environmental effects of nanosilver and its impact on plant populations, microbiota-mediated reduction of nanosilver toxicity, antimicrobial effects of nanosilver, transformation of nanosilver in the environment, and the effects of nanosilver on organs other than microbiota, including the reproductive system and skin epidermis, were excluded. Studies focusing on soil microflora or investigating the effects of nanoplastics on microbiota were also excluded. Additionally, review articles and book chapters were excluded from the analysis.

## RESULTS AND DISCUSSION

*Characteristics of included studies*

The studies included range from 2015 to 2026, indicating increasing research interest in the biological impacts of AgNPs during the last ten years. As shown in **Table 1**, Most studies have used in vivo rodent models, especially C57BL/6 mice and Sprague-Dawley or Wistar rats. In addition to these animal studies, one study used an in vitro model based on human intestinal microbial fermentation. Therefore, the available evidence is mainly derived from rodent models, and the contribution of laboratory studies simulating the human intestine is more limited. The main aim of the reviewed studies was to evaluate the intestinal microbiota's response to exposure to AgNPs. In most cases, fecal samples or cecal and colonic contents were used to investigate the composition of microbial communities. 16S rRNA gene sequencing has been the primary method for identifying and analyzing bacterial composition, although more advanced methods such as NGS, metagenomics, PICRUSt, and plasma metabolomics have also been used in more recent studies. Alpha and beta diversity indices, along with the examination of the relative


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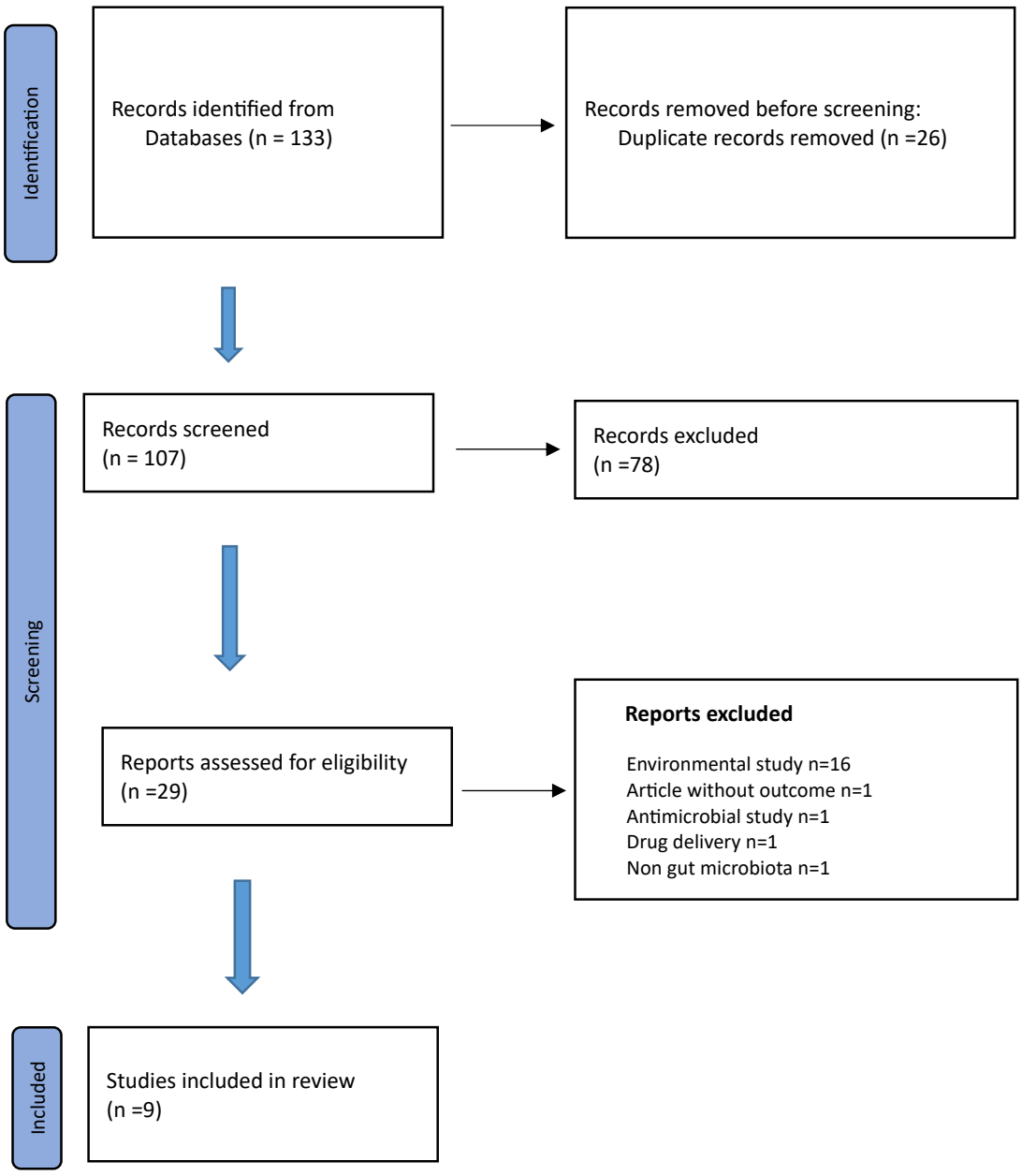



Fig. 2. The diagram of study

abundance of taxa, have been the most important tools in these studies to describe microbial changes and dysbiosis caused by nanoparticles. Overall, the review of the extracted data shows that the physicochemical properties of AgNPs, especially size, shape, surface coverage, dose, and duration of exposure, play a decisive role in the intensity and type of intestinal microbiota response.

*Effect of size, dose, and duration of exposure*

Nanoparticle sizes in Table **1** studies range from 10 nm to 150 nm, including nanowires. Size affects surface area, silver ion ($Ag^+$) release, stability, and microbiota interactions. However, results on the effects of size and dose have not been entirely consistent. In some studies, exposure to AgNPs of 20 and 110 nm at a dose of 10 mg/kg


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Table1. Data extraction

| Author /Year/Country | Study Design/ type of Model | AgNP Size/Dose/ Duration | Microbiota Type | Analysis Method | Microbiota Changes | Toxicity Mechanism | Key Findings |
|---|---|---|---|---|---|---|---|
| **Laura A. Wilding et al./ / 2015 / USA [23]** | In vivo / Murine model | 20 nm, 110nm / 10 mg/kg/day – 28 days | Murine gut microbiome | Culture-independent 16 s rRNA gene fragment sequencing | No significant alteration in microbiome membership, structure, or diversity | Not identified; no detectable gut microbiome toxicity under tested oral exposure conditions | Oral AgNPs exposure (10 mg/kg/day, 28 days) did not significantly disturb the indigenous murine gut microbiome, regardless of particle size or coating |
| **Van den Brule et al. / 2016 / Belgium [24]** | In vivo / 3-month-old C57BL/6 female mice | - 0, 46, 460, 4600 ppb/ 28 days | Fecal gut microbiota/ | Next generation sequencies | Disturbed bacterial evenness (α-diversity); increased Firmicutes and decreased Bacteroidetes; changes in Lachnospiraceae and S24-7 family; similar effects after fresh vs aged pellets | Antibacterial activity; disturbance of gut microbiota; possible effect of Ag ion release / sulfidation aging | Dietary AgNPs disturbed gut microbiota without overall toxicity; AgNP aging in food reduced effects by limiting release of toxic Ag ions |
| **Javurek et al. / 2017 / USA [25]** | In vivo experimental/Male Sprague-Dawley rats | AgNS: 50 nm; AgNC: 45 nm/3.6 mg/kg/day (oral)/14 days | Fecal gut microbiota/ | 16S rRNA sequencing, LEfSe, PICRUSt | ↓ *Clostridium*, *B. uniformis*, Christensenellaceae, *Coprococcus* (AgNC); ↓ *Oscillospira*, *Dehalobacterium*, Peptococcaceae, *Corynebacterium* (AgNS) | Selective antimicrobial activity; possible gut–brain axis disruption | AgNPs induced gut dysbiosis and behavioral alterations without obvious histopathological damage |
| **Cristina Catto, et al. /2018/ Italy [26]** | In vitro gut model / No live animal – Batch fermentation model inoculated with human fecal matter | - 1 microgram /ml 24 h | - | NGS, FISH, metagenomic inference | Core fecal microbiota unchanged; rare taxa significantly altered; Firmicutes/Bacteroidetes ratio increased after 24 h; co-exposure with Bacillus subtilis resulted in the lowest F/B ratio | AgNPs acted as gut microbiota disruptors at non-lethal concentration; induced functional changes in specific microbial pathways; toxicity further assessed via SCFA profiling, cytotoxicity, and genotoxicity assays on Caco-2 cells | AgNPs caused subtle but measurable disturbances in gut microbiota composition and function, primarily affecting rare species and community ratios rather than the core microbiota; probiotic Bacillus subtilis showed a chemopreventive effect |

Continued Table1. Data extraction

| Author /Year/Country | Study Design/ type of Model | AgNP Size/Dose/ Duration | Microbiota Type | Analysis Method | Microbiota Changes | Toxicity Mechanism | Key Findings |
|---|---|---|---|---|---|---|---|
| **Wang S., et. al / 2022 / China [27]** | In vivo / Mouse | - - 10 days | Gut microbiota | 16S rRNA sequencies | Significant alteration in gut microbiota composition; reduced diversity; increased potential pathobionts; increased Akkermansia muciniphila; increased colonic mucus | Dysbiosis of gut microbiota with altered host gene expression; enrichment of apoptotic cell death pathways and RNA metabolism in colon tissue | Oral nAg exposure altered gut microbiota composition and colonic transcriptome in colitic mice, indicating microbiome-associated intestinal immunotoxicity under inflammatory conditions |
| **Landsiedel, et al. /2022/ Germany [28]** | In vivo / wistar Rat | 50 nm 100mg/kg bw/day 28 days | Fecal gut microbiota | 16srRNA sequencin g | Bacteroidota increased (23.5% → 30.4%); Firmicutes nearly unchanged (60.8% vs 57.5%); Firmicutes/Bacteroidetes ratio decreased; Akkermansia depleted to hardly detectable levels; Prevotellaceae increased | Alteration of the microbiota-metabolome axis; depletion of indole-3-acetic acid (IAA) in plasma (AHR ligand) | AgNPs induced significant gut dysbiosis and metabolic shifts (IAA) as sensitive indicators before obvious histopathological damage. |
| **Quanzhong Ren, et al. / 2023 / USA [29]** | In vivo 6-week-old male C57BL/6N mice | 18.03nm 5mg/kg bw/day 4 weeks | Gut microbiota | 16SrRNA sequencing | AgNPs altered/disturbed intestinal microbiota | Reduced mucosal layer thickness, increased DC phagocytosis, ROS generation, uncontrolled apoptosis, reduced CD103+ CD11b+ DCs, Th17 activation, Treg inhibition | Oral AgNPs caused intestinal injury and disrupted the intestinal immune microenvironment through microbiota and dendritic-cell mediated mechanisms |
| **Xiaoyu Wang, et.al / 2023 / china [30]** | In vivo 7-week-old male C57BL/6JMice | AgNPs :60-150 nm Ag NWs: 1-2mm length, hydrodynamic diameters: 110 nm (NPs), 233nm (NWs) 0/5 mg/kg and 2/5 mg/kg 14 and 28 days | Gut microbiota | 16S rRNA gene sequencies + metabolomics | 14-day exposure altered microbiota structure, inhibited Gram-negative bacteria, and decreased diversity; 28-day exposure showed partial recovery of the microbial community | Altered gut microbiota and metabolic profile, linked to changes in serotonin (5-HT) secretion; 1H-indole-3-carboxylic acid implicated | Silver nanomaterials disturbed gut homeostasis; microbiota changes were stronger at 14 days, while 28 days showed community recovery but persistent metabolic/5-HT effects |

Continued Table1. Data extraction

| Author /Year/Country | Study Design/ type of Model | AgNP Size/Dose/ Duration | Microbiota Type | Analysis Method | Microbiota Changes | Toxicity Mechanism | Key Findings |
|---|---|---|---|---|---|---|---|
| **Zhang, et al. / 2024 / China [31]** | In vivo / Mouse | - - 90 days | Gut microbiota | Microbial characterization exact sequencing | Gut microbial alterations; changes in microbial functional abundances; microbiota responses sensitive to microplastic dose | Co-exposure with PS plastics aggravated AgNP toxicity; altered energy and choline metabolism; microplastics promoted fatty acid peroxidation and inflammatory responses; nanoplastics may cross the blood-brain barrier and enhance neuronal/vascular damage | Co-exposure to AgNP and PS plastics in mice worsened toxicity compared with AgNP alone, with associated gut microbial and microbial functional alterations; toxicity was influenced by plastic type/size and microplastic dose |

**Abbreviations:** silver nanoparticles (AgNPs), silver Nanospheres (AgNS) , silver Nanocubes (AgNC) , Ribosomal Ribonucleic Acid (rRNA) , Linear Discriminant Analysis Effect Size ( LEfSe), Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt) , Parts Per Billion (ppb) Fluorescence In Situ Hybridizatio(FISH), Short-Chain Fatty Acids (SCFA) , Indole-3-acetic acids (IAAs) , Dendritic Cell(DC), Reactive Oxygen Species(ROS),T helper 17 cells (Th17),Regulatory T cells(Treg), 5-Hydroxytryptamine (5-HT) , Polystyrene (PS)

did not cause significant changes in the structure of the microbiome, whereas in more recent studies, nanoparticles of about 60 nm were able to disrupt intestinal homeostasis even at lower doses of about 2.5 mg/kg . These differences indicate that the effect of AgNPs is not dependent on a single factor but rather on a combination of several factors, including size, dose, surface coating, physical shape, and exposure conditions. The duration of exposure is also an important factor in determining the severity of the biological effects of AgNPs. In the included studies, the duration of exposure has varied from short-term periods of 10 to 14 days to chronic exposures of 90 to 120 days. The available evidence suggests that in long-term exposures, even low doses of AgNPs can increase the likelihood of developing persistent dysbiosis due to the gradual accumulation and continuous release of $Ag^+$. In addition, the physical shape of the nanoparticles, such as the difference between spherical nanoparticles and nanowires, has been proposed as one of the factors affecting their toxicity and persistence in the gastrointestinal environment.

*Microbiota changes and dysbiosis*

Several studies have shown that oral exposure to AgNPs can affect the composition and diversity of the gut microbiota, although the magnitude and direction of these changes vary across studies. Some studies have reported limited or non-significant changes in microbial diversity and bacterial community structure [23, 32], whereas others have described dysbiosis, altered abundance of bacterial families and genera, and shifts in major microbial groups [33-35]. One frequently reported indicator is a change in the Firmicutes/Bacteroidetes ratio [24, 26]. An increased ratio has been proposed as a sign of altered microbial balance and a possible shift toward dysbiosis. Changes in families such as Lachnospiraceae, S24-7, and Prevotellaceae, together with reductions in bacteria such as Akkermansia and Faecalibacterium prausnitzii, have also been reported [27, 28]. Because some of these microbial groups contribute to mucosal layer maintenance, inflammation regulation, and epithelial barrier support, such changes may be functionally important [24]. The inconsistency across studies is likely related to differences in experimental design, animal model, baseline microbiota, dose, exposure duration, and nanoparticle size, shape, and surface coating [36-38]. Therefore, AgNP-induced dysbiosis should not be reduced to a fixed general pattern but considered a response dependent on exposure conditions and host characteristics [38, 39].

*$Ag^+$-dependent mechanisms*

One of the main mechanisms proposed for the effects of AgNPs on the intestinal microbiota is their antibacterial activity, driven by the release of $Ag^+$ [40]. $Ag^+$ can interact with bacterial cell surfaces and exert selective pressure on the microbial ecosystem by damaging cell membranes, disrupting metabolic functions, and reducing the survival of certain bacterial populations [41]. This selective pressure can lead to changes in α- and β-diversity indices, shifts in bacterial relative abundance, and ultimately dysbiosis. The importance of this mechanism is underscored by studies reporting reduced AgNP effects after aging or sulfidation. This finding indicates that the severity of microbiota disruption largely depends on the rate of $Ag^+$ release and its bioavailability. Therefore, the antibacterial effects of AgNPs are not only related to the physical presence of the nanoparticle, but also to the rate of $Ag^+$ release and the chemical conditions of the digestive environment, which play an important role in determining the intensity of the microbial response [24, 42-44]. On the other hand, the physical shape of the nanoparticles can also be a model of their effect. The reported differences among spherical, cubic, and nanowire nanoparticles suggest that the surface area, stability, and behavior of nanoparticles in the intestinal environment may differ depending on their physical form. Therefore, the $Ag^+$-dependent mechanism must be interpreted in conjunction with other physicochemical properties of the nanoparticles [25, 45, 46].

*Effect on the epithelial barrier and the immune system*

In addition to microbial changes, there is evidence that AgNPs can directly or indirectly affect the epithelial barrier and the intestinal immune system [47]. In some studies, exposure to AgNPs has been associated with damage to the intestinal epithelium, thinning of the mucosal layer, and increased contact between nanoparticles and mucosal immune cells [30, 48]. These changes can create conditions in which local immune responses become dysregulated. One proposed pathway in this context is the barrier injury–DC dysfunction–


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Th17/Treg imbalance axis [29, 49]. According to this model, AgNPs first damage the epithelial barrier and reduce the integrity of the mucosal layer [50]. Subsequently, further contact of nanoparticles with dendritic cells can increase the production of reactive oxygen species (ROS) and cause abnormal activation or apoptosis of these cells. Disruption of the $CD103^{+}CD11b^{+}$ DC population can also disrupt the balance between Th17 and Treg cells, ultimately leading to inflammation and mucosal immune dysfunction[28, 51].

*Microbiota–metabolome–host axis*

In addition to structural changes in the microbiota, some studies show that the effects of AgNPs extend to changes in microbiota-derived metabolites and host signaling pathways [28]. These findings suggest that the consequences of exposure to AgNPs cannot be explained solely by changes in bacterial abundance; functional and metabolic changes in the intestinal ecosystem should also be considered [52, 53]. In some studies, changes in bacteria such as Prevotellaceae and Akkermansia have been associated with changes in inflammatory status and intestinal barrier function. An increase in Prevotellaceae can be associated with inflammatory states, while a decrease in Akkermansia may lead to a weakening of the mucosal layer and a decrease in the stability of the epithelial barrier [27, 54, 55]. On the other hand, decreases in metabolites such as indole-3-acetic acid (IAA) further underscore these changes, since IAA is a microbiota-derived metabolite and a ligand of the AhR pathway. The AhR pathway plays a role in immune regulation, maintenance of epithelial homeostasis, and metabolism of xenobiotics [30, 56, 57].Therefore, decreased IAA may attenuate AhR signaling, resulting in impaired intestinal barrier function and immune regulation. Accordingly, the microbiota–metabolome–host signaling axis may be an important framework for explaining the complex effects of AgNPs on the intestine [28, 58, 59].

*Gut-Liver and Gut-Brain Axes*

AgNPs metabolic effects extend beyond the gut, impacting systemic metabolism via the gut-liver axis. Long-term exposure alters gut microbiota and liver metabolites, with changes in genera like Turicibacter, Ruminococcus_1[28], and others linked to energy, carbohydrate, and lipid metabolism Pathways such as energy, amino acid, and lipid metabolism are affected, supporting the idea that gut microbiota modulates AgNPs systemic effects through the gut-liver axis [27, 60-62].

Additionally, the gut–brain axis may play a role [63]. Microbial changes from AgNPs have been linked to behavioral shifts without tissue damage, indicating that microbiota functional changes can influence host physiology [64]. Altered tryptophan metabolites, like increased 1H-indole-3-carboxylic acid and serotonin levels, suggest AgNPs impact the gut-brain axis by disrupting tryptophan-related metabolic pathways [65, 66].

*Co-exposure to other pollutants and the role of modulating interventions*

Evidence suggests that the effects of AgNPs may be exacerbated in the presence of other pollutants [28, 31]. In some studies, co-exposure to AgNPs and polystyrene micro/nanoplastics has been shown to increase toxicity and alter metabolic pathways, including energy and choline metabolism [67]. Microplastics have also been reported to cause cellular damage by increasing fatty acid peroxidation and inducing inflammatory responses [68]. Nanoplastics have been suggested to cross the blood-brain barrier. In an in vitro model of human fecal fermentation, AgNPs at non-lethal concentrations may not cause major changes in the overall microbiota structure, but they can affect rare species and specific functional pathways. The reduction of bacteria such as Faecalibacterium prausnitzii is important in this context, as this bacterium is considered a beneficial component of the gut microbiota. The presence of the probiotic Bacillus subtilis has also been reported to partially modulate the effects of AgNPs. These findings suggest that probiotic interventions may partially reduce the negative effects of nanoparticles on the gut microbial ecosystem [26, 69, 70]. Overall, the available evidence suggests that the effects of AgNPs on the gut result from a complex interaction among the nanoparticles' physicochemical properties, the gut microbiota, the epithelial barrier, immune responses, and host metabolic pathways. Therefore, the intestinal toxicity of AgNPs cannot be interpreted simply as a direct antibacterial effect but should be considered the result of a multilevel interaction among the nanoparticle, the microbiota, and the host.

## CONCLUSION, LIMITATIONS, AND FUTURE STUDY

The current findings suggest that AgNPs can


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have beneficial applications under certain conditions due to their antimicrobial properties, but continuous or uncontrolled oral exposure is more likely to be associated with adverse consequences for the gut. These effects include microbial dysbiosis, changes in microbiota-derived metabolites, disruption of the epithelial barrier, and alterations in mucosal immune responses. Therefore, the effect of AgNPs cannot be considered a simple antibacterial effect but rather a result of the interaction among the nanoparticle, microbiota, and the host. However, the response of the gut microbiota to AgNPs has not been uniform across studies. In some cases, limited or reversible changes have been reported, while in others, more pronounced disturbances in microbial composition, metabolism, and immunity have been observed. These differences are likely related to factors such as dose, exposure duration, size, shape, surface coverage, $Ag^+$ release rate, and the initial state of the host microbiota. One limitation of the existing studies is that many were conducted in animal or laboratory models, and sufficient human evidence is still lacking. In addition, the large differences in study designs and nanoparticle characteristics make it difficult to directly compare the results. Future studies should be conducted using doses closer to real human exposure, examining chronic low-dose exposures, and using more advanced intestinal models to better elucidate the causal relationship between AgNPs, microbiota, metabolites, and host immune responses. Also, examining the role of modulating factors such as diet, age, gender, initial microbiota status, and probiotic consumption can be effective in more accurately assessing the risks and safer applications of AgNPs.

## AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the work reported in this manuscript. This includes the conception and design of the study, the acquisition, analysis, and interpretation of data, as well as drafting the article and revising it critically for important intellectual content. **MKK, YH and RR** were involved in the conception and design of the study, the collection of data, or the analysis and interpretation of data**. MKK, YH and PS** contributed to the drafting of the article and revising it critically. **KGH and SAB** participated in the edition and approval of the manuscript.

## DATA AVAILABILITY

Data will be made available on request.

## FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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