Silver and Gold Nanoparticles

Subjects: Biology

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Silver and gold nanoparticles can be found in a range of household products related to almost every area of life, including patches, bandages, paints, sportswear, personal care products, food storage equipment, cosmetics, disinfectants, etc. Their confirmed ability to enter the organism through respiratory and digestive systems, skin, and crossing the blood–brain barrier raises questions of their potential effect on cell function. Therefore, this manuscript aimed to summarize recent reports concerning the influence of variables such as size, shape, concentration, type of coating, or incubation time, on effects of gold and silver nanoparticles on cultured cell lines. Due to the increasingly common use of AgNP and AuNP in multiple branches of the industry, further studies on the effects of nanoparticles on different types of cells and the general natural environment are needed to enable their long-term use. However, some environmentally friendly solutions to chemically synthesized nanoparticles are also investigated, such as plant-based synthesis methods.

Keywords: silver nanoparticles ; gold nanoparticles ; nanotoxicology ; nanoparticle interactions ; nanoparticle applications

1. Introduction

Nanoparticles are defined as structures with at least one of the dimensions in the 1 to 100 nm range [1]. These particles enter cells mostly through endocytosis, particularly endocytotic vesicles formation and the release of ions into the cytoplasm [2][3][4].

From the clinical standpoint, the use of nanoparticles (NPs) is mainly motivated by their relatively large surface-to-volume area during interaction with cells. Further advantages include their specific physicochemical characteristics, such as catalytic properties and relatively low melting point (compared to the macroscopic properties of the metal they are derived from). Moreover, to ensure the safety of their use and appropriate dosage, correlations between these characteristics and the potential toxicity of nanoparticles can be determined using nanotoxicology techniques [5][6][7].

NPs can be characterized according to their shapes. These include simple spherical, triangular, rod, triangle, and round, and more complex octagonal or polyhedral [4][8][9]. Gold nanoparticles can come in a variety of shapes including nanorod, nanostar, nanosphere, nanocube, nanoshell, nanocluster, suboctahedral, icosahedral tetrahedral, decahedral, and oroctahedral [10]. Silver nanoparticles also exhibit different shapes including spherical, nanorod, nanowire, nanobar, nanoplatele, triangles, five or six diagonal, cubic, and pyramid [11]. The shape and size of nanoparticles affect their use in various industries, as these properties reflect their optical, electronic, magnetic, and catalytic characteristics [11][12].

It has been proven that silver nanoparticles (AgNP) have the ability to penetrate the cellular walls of bacteria, altering their cell membranes and even potentially causing cell death. Moreover, through the release of silver ions, it is possible to increase cell membrane permeability, produce reactive oxygen species, and disturb DNA replication [13][14][15][16].

Gold nanoparticles (AuNP) exhibit significant biocompatibility, promote corrosion, and possess optical and electronic properties depending on their shape and size [16][17][18]. AgNP also exhibit optical and electronic properties dependent on size, shape, surface coverage, and agglomeration [19][20][21]. Due to the optical properties of silver nanoparticles, they strongly interact with specific wavelengths of light, to which they have found wide use in biomedical applications, e.g., in vitro cellular imaging systems [21]. Due to their optical properties, noble metal nanoparticles can be used, for example, as an active ingredient in SPR (surface plasmon resonance) biosensors [22][23][24][25].

2. Nanoparticle Applications

The rapid development of nanotechnology is constantly affecting the methods of diagnosis, prevention, and treatment of various diseases, enabling novel therapeutic approaches. NPs currently have a range of applications, including, e.g., antibacterial agents, and components of drug delivery systems and diagnostic tools. It is worth noting that they are also commonly used as components of skincare products and cosmetics [26][27].

AgNPs are among the most commonly used substances in consumer products, such as laundry machines, dusting cloths, and personal hygiene products. Hence, NPs contained in everyday household items are often discarded directly in sewage and can potentially be transported into waterways. They are mainly described to exhibit antibacterial properties [28][29][30][31]. Typical AgNP applications include coatings of cloth and other textiles, food storage appliances, and cosmetics. They are also present in various applications used in the public health sector, and in medical products, such as disinfectants, wound dressings, central venous caterers, and surgical nettings. Furthermore, study results indicate that AgNPs may also exhibit cytotoxic properties, as they induce a typical cellular reaction of reactive oxygen species (ROS) formation [12][16][32][33][34]. AgNPs have also shown antibacterial (against *Staphylococcus aureus, Pseudomonas aeruginosa*, *Xanthomonas axonopodis pv. Citri*), fungicidal (against *Candida albicans, Candida parapsilosis*), and antiviral properties, also affecting the SARS-CoV-2 virus [35][36][37]. In addition, the AgNPs toxic effect, in the range of 50% of lethal concentration (LC 50) on certain young and adult fish species (zebrafish), daphnia, and at least two algae species, has been described [38][39]. Silver in ionic form (Ag^+) is also known to be toxic to aquatic organisms even at g/L concentrations by inhibiting the effects of ATPase Na^+/K^+ and causing ionic imbalance. These effects of AgNPs were similar in different marine animals, such as fish, daphnia, and crayfish [40][41].

AgNPs are easily assimilated by cells. Therefore, they are mainly applied in the biomedical industry due to their unique surface, electronic, and optical properties. They are also used as innovative tools in diagnostic research, e.g., the detection of heart disease or cancer biomarkers, and in drug delivery systems [16][42][43][44][45][46][47]. Numerous reports have been published regarding the toxicity of gold nanoparticles depending on their size, shape, or structure of the coating and the spectrum of experimentally measured parameters. Toxicity depending on the size of gold nanoparticles in relation to different cell types has been described, demonstrating that smaller nanoparticles are generally more toxic [48][49].

In contrast, other teams of scientists have found no cytotoxic effects in cancerous cell lines treated with gold nanoparticles [25][50][51]. Subsequent works noted adverse effects on cytoskeleton components and a decrease in the growth of human cells exposed to AgNPs under culture conditions. Furthermore, increased levels of ROS were reported in aquatic organisms exposed to gold nanoparticles [52][53][54][55][56].

3. Absorption of Silver Nanoparticles

Silver nanoparticles can be absorbed through the respiratory and digestive systems, and through the skin [33][57].

In Sprague–Dawley rats subject to inhalation exposure, silver nanoparticles were detected in the blood and lungs. In smaller amounts, they were also seen in other internal organs such as the liver, kidneys, spleen, heart, and brain. These experiments did not describe changes in body weight gain, internal organ weight, or biochemical parameters. However, there were some differences in respiratory parameters in rats, e.g., decreased respiratory volume and minute ventilation, and histopathological changes in the lungs at 90-day exposure to 20 nm silver nanoparticles at 49, 133, and 515 $\mu g/m^3$ doses [55]. In Sprague–Dawley rats subjected to 28-day exposure to AgNP aerosol, the appearance of multinucleated macrophages was observed in the lungs, which indicates inflammation and active absorption of nanoparticles at the dose of 30.5 $\mu g/m^3$ [58].

Spherical AgNP (20 nm) at doses of 50, 150, 300 mg/kg can be ingested orally, absorbed through the intestines into the bloodstream, and then accumulate in other organs such as the duodenum, liver, kidneys, and spleen. While this has been confirmed in mice, the authors of the study did not report any associated pathological changes [59]. Moreover, mice subjected to 14-day oral AgNP administration (dose: 1 mg/kg, size: 22, 42, 71, and 323 nm) also showed no histopathological changes in the liver, kidneys, testicles, or lungs. After 28 days and only in a dose of 1 mg/kg (size: 42 nm), only a small cellular infiltration was observed in the renal cortex. However, based on an increase in pro-inflammatory cytokines, induction of inflammation by AgNP incubation was confirmed. Furthermore, there was also an increase in liver enzymes [60].

In addition, Guinea pigs were found to accumulate free aggregate AgNP in the epidermis layers after 24 h of exposure at the highest dose used (100,000 ppm). However, microscopic evaluation did not reveal any abnormalities in the epidermis and skin layers in exposed areas of groups treated with colloidal AgNPs (spherical or polygonal shape, size: 10–20 nm) compared to controls [61]. The permeability of silver nanoparticles from textiles was also investigated. In the study by Bianco et al. (2016), volunteers wore an AgNP-containing sleeve on their forearm (average concentration 3.6 *w/w*), 8 h at night for five consecutive days. While the study confirmed the presence of AgNP aggregates in the skin, deeper layers there were less affected than those closer to the surface [62].

Previously, George et al. (2014) demonstrated the presence of clusters of silver in the stratum corneum and deeper layers of the epidermis after five days of skin exposure of healthy individuals to nanocrystal silver dressing (amount of silver released by dressing: 70 ppm of silver ions, size of particles: 10–40 nm). Thus, they confirmed the possibility of AgNP penetration through intact skin. However, despite the deposition of silver in the dermis, silver nanoparticles did not reach systemic circulation and should therefore not have systemic consequences [63].

4. Absorption of Gold Nanoparticles

Studies in rats show that gold nanoparticles can be absorbed through the respiratory and digestive systems [33][64].

In Sprague–Dawley rats subjected to spheroid AuNP (diameter under 6 nm) inhalation for 90 days, a decrease in respiratory parameters, i.e., lung function, respiratory volume, and minute volume, was observed compared to the control. Furthermore, histopathological examination demonstrated minimal alveoli, inflammatory infiltration of mixed cell type (lymphocytes/neutrophils/macrophages), and increased macrophage counts in rats receiving high doses of AuNP (20 $\mu g/m^3$) [64].

Moreover, studies by Kreyling et al. (2018) also confirmed the absorption of “potato-shaped” gold nanoparticles (size: 20 nm, density: 19.5 g/cm^3) by inhalation in rats. About 30% of AuNP accumulated in the epithelium of the respiratory tract, causing rapid mucociliary removal and swallowing into the gastrointestinal system. Long-term removal (after 28 days) of AuNP was dominated by macrophage-mediated transport through interstitial tissue to the larynx and gastrointestinal tract. Furthermore, AuNP retention has also been observed in the liver, spleen, kidneys, uterus, and brain [65].

In Wistar rats, ten days after intravenous administration of 25 nm colloidal AuNPs (0.3619 mg of particles/mL, per 1 kg), more than 50% of AuNP accumulated in the liver with smaller amounts in the lungs and spleen. This occurrence was associated with the collection of AuNPs from the circulation by the mononuclear phagocyte system. The total AuNP content of all organs represented 60% of the initial dose. In contrast, oral administration showed almost 50 times lower AuNP levels at the same amount (1.4% of the initial dose). Most AuNP was excreted in feces within four days after exposure. In turn, alterations in biochemical parameters were observed 72 h after intravenous AuNP administration. An increase in AST (aspartate aminotransferase) was observed, with a decrease in ALT (alanine aminotransferase), which affects the physiology of the liver. Furthermore, an increase in blood glucose has also been noted; thus, the effect of AuNP on pancreatic functions cannot be excluded [66].

The penetration of gold nanoparticles through the skin of the hind paw and the anterior abdominal wall of Sprague–Dawley rats was also confirmed by Raju et al. (2018), with smaller AuNPs (22 nm) showing higher penetration compared to larger nanoparticles (105 and 186 nm). The effect of 3-hour AuNP incubation on a fibroblast cell line (L929 mouse fibroblast cells) was also investigated, with no observed effect of AuNP on cell viability at any of the concentrations used (0.1, 1, and 10% *v/v*) [67].

In mice, the kidneys were the primary site of AuNP accumulation after oral administration for 8 days at 25, 22, 20, 18, and 15 µg gold/kg bodyweight concentrations, and subsequent intestinal absorption. AuNP can induce anti-inflammatory effects in macrophage RAW264.7 cells pretreated with 1/1000 OD of the AuNP for 5 h before stimulation with lipopolysaccharides (LPS) and incubation for another 20 h. AuNP reduce by reducing the lipopolysaccharide receptor expression on the cell surface, as well as catalytic detoxification of nitrite peroxide and hydrogen peroxide. The highest accumulation of gold nanoparticles was shown by those that were 5 nm in size and coated with PVP, compared to 5 nm AuNPs coated with citrate or tannic acid (TA) [68].

In other studies conducted in men subjected to nanoparticle inhalation for 2 h during intermittent exercise, AuNP was also confirmed to enter the lungs. Gold was detected in the urine after exposure to 4 nm AuNPs, but not in the urine of volunteers exposed to larger particles (34 nm). In mice, gold nanoparticles were also detected in urine only after exposure to particles ≤5 nm. AuNP found in human blood was usually at low levels after inhalation of AuNP, although the concentration of smaller particles was notably higher. This effect was also confirmed in mice, in which the incidence of detected gold and blood gold levels were significantly higher after exposure to smaller particles [69].

The possibility of absorption through human skin has been studied using surgically resected dermal fragments incubated for 24 h with AuNP. The permeability of spherical nanoparticles (15 and 100 nm) was confirmed by using a TEM (transmission electron microscope), with nanoparticles observed in the deeper stratum corneum, epidermis, and dermis [70].

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