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Review article

Exposure, tissue biodistribution, and biotransformation of nanosilver

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ABSTRACT

With the wide application of nanosilver or silver nanoparticles (AgNPs) in a diverse spectrum of fields, the environmental exposure of this kind of nanomaterial has become inevitable. Lots of attention was paid to its potential adverse effects based on multiple experimental models; nevertheless, the translocation, distribution, and possible biotransformation of nanosilver in organisms are the essential prerequisites for its biological effects. This work focused on this point and provided a comprehensive review of the behavior of nanosilver in multiple mammals, in view of its administration routes, biouptake, translocation, biodistribution, bioaccumulation, biotransformation, elimination, and retention. The regulatory factors for the bioavailability of nanosilver included the characteristics of the nanoparticle per se and the ambient condition. This review brings insights on the biological processes of nanosilver and may help explain its potential effects on mammals, including human beings.

Contents

1. Introduction

The usage of silver based on its antibacterial activity can be dated back to centuries ago. The nanosized formulation endures it with promising new applications in diverse fields. Nanosilver or silver nanoparticles (AgNPs) have now been used worldwide in food packaging

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materials, food supplements, textiles, electronics, household appliances, cosmetics, medical devices, water disinfectants, and room sprays due to their excellent antibacterial activities and surface plasmon resonance properties (Anker et al., 2008; Wu et al., 2016; Kim et al., 2007; Guidelli et al., 2016; Rycenga et al., 2011; Goesmann and Feldmann, 2010; Pulit-Prociak et al., 2015; Mallevre et al., 2016). Nanosilver has been reported to rank first in annual production among all nanomaterials (WilsonCenter, 2015). However, the manufacture, transportation, and use of AgNPs can cause their intentional release or unintentional leak, resulting in consequential environment exposure and human contact. Many concerns currently have been raised regarding the unexpected toxicities of nanosilver. The risks and benefits are being hotly debated and weighed (Seltenrich, 2013). More and more studies are being performed to investigate the potential adverse effects of this kind of nanomaterial. Due to their small size, ion release, and high ability to bind with various functional proteins, AgNPs have been found to cause diverse toxicities, thus becoming potential hazards (Bagheri-Abassi et al., 2015; Sung et al., 2008; Silva et al., 2015; Braakhuis et al., 2014).

In human-involved scenarios, mainly including medical applications (Murphy et al., 2015), health care, and consumer products (Lem et al., 2012), the usage of nanosilver can have attractive advantages. Wound dressings containing AgNPs or silver colloids are widely used for medical purposes for their contributions against bacterial infection, resulting in better cell attachment and proliferation (Kim et al., 2015). Catheters coated with AgNPs also show significant efficiency on preventing contamination and colonies of bacteria (Thomas et al., 2015). Clothing employing AgNPs as an antimicrobial agent is another potential source of nanosilver release directly to humans by wearing, using, and washing such items (Benn and Westerhoff, 2008). Other consumer products, including respirators, household water filters, antibacterial sprays, and toys may contain certain amounts of nanosilver for antimicrobial purposes as well (Marambio-Jones and Hoek, 2010). Fig. 1 shows the extensive use of nanosilver in consumer products that may introduce multiple kinds of potential exposure of this kind of nanomaterial to humans, such as oral administration, inhalation, and dermal contact. Humans are also accessible to nanosilver potentially through some other routes, including nanosilver-coated medical catheters, cardiovascular implants, dental instruments, coated contact lenses, biodiagnosis and treatment, bone cement and other implants, intranasal instillation, and eye drops specifically in clinical treatments (Shin and Ye, 2012; Ge et al., 2014).

Given the increasing demands for nanosilver applications in many aspects, their potential adverse effects on human beings are worthy of concerns. Previous research demonstrated that long-term administration of silver-based medications may cause obvious clinical symptoms in human bodies. The most representative case is argyria, which is associated with irreversible silver deposition in the skin caused by chronic ingestion of silver-based products in patients. For example, it was reported that argyria occurred in a patient who ingested a colloidal silver product as a natural alternative to antibiotics in an attempt to treat Lyme disease (Newman and Kolecki, 2001). Because the symptom of argyria is exaggerated in sun-exposed areas of the body, some tissues, including nail bed, sclera, and oral mucous membranes, can all become a slate blue-gray to gray to gray-black color due to the prolonged systemic contact with silver in humans. In vitro experiments showed that silver nanoclusters could cause significant cytotoxic effects on human peripheral blood mononuclear cells (PBMC) even at relatively low concentrations (<1 μg/mL) (Orta-Garcia et al., 2015), showing the possible hazardous risks of human exposure. In vivo studies of AgNPs using animal models can provide crucial indications of their potential effects on humans. Nanosilver was found to cause hematological effects, pulmonary problems, hepatic risks, neurotoxicities, physiological impacts, and genetic issues, according to the studies on some mammal animal models (Park et al., 2010; AshaRani et al., 2009; Arora et al., 2009; Tang and Xi, 2008; Braydich-Stolle et al., 2005; Ahamed et al., 2008; Carlson et al., 2008; Hsin et al., 2008). These findings have revealed some clues that imply adverse effects of silver-based applications on human health, despite several comments emphasize its benefits, especially for the newly developed nanosized silver products.

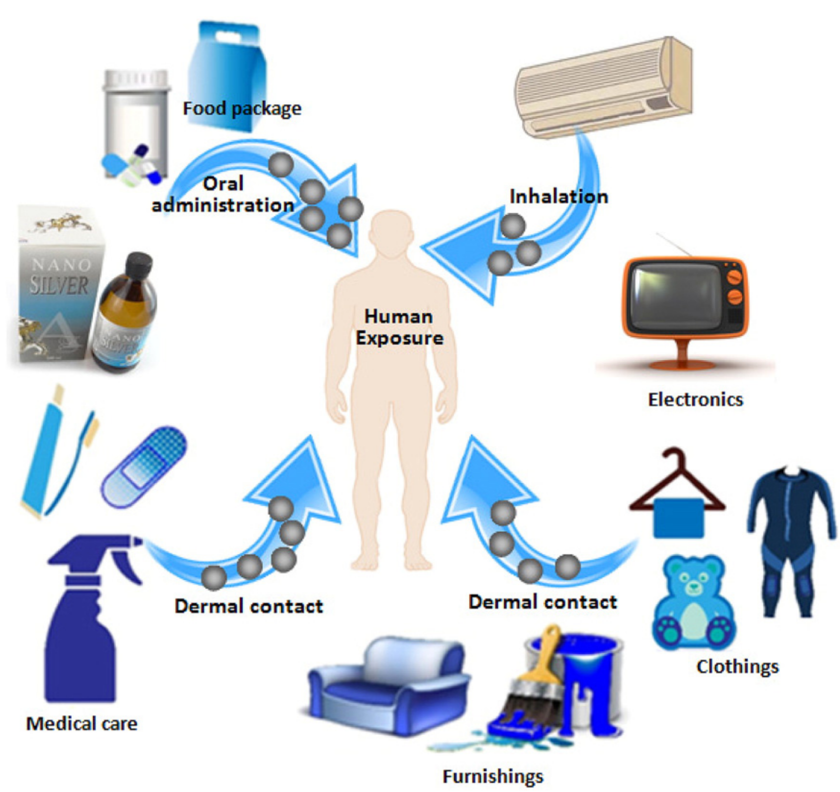

Fig. 1. The extensive use of nanosilver in consumer products introduces multiple ways for human exposure.