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Advanced sanitation products infused with silver nanoparticles for viral protection and their ecological and environmental consequences



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ABSTRACT

The outbreak of coronavirus ailments (COVID-19) in 2019 resulted in public health crisis leading to global pandemonium. In response to the high prevalence of disease transmission, governments all around the globe implemented emergency measures in various routes (e.g., social distancing, personal hygiene, and disinfection of public/private places) to curb/contain COVID-19 infections. The social media infodemic, released as uncensored publishing and/or views/recommendations, also triggered large-scale behavior changes such as the overuse of advanced sanitation products (ASPs) containing nanomaterials. The majority of these ASPs contain silver nanoparticles (AgNPs) as an active ingredient to enhance their antimicrobial potential. Ecotoxicological concerns such as the transformation and degradation of these AgNP-infused products in terrestrial or aquatic environments are under the jurisdiction of the EPA. However, they are not considered in the FDA approval process. In light of excessive consumption of ASPs, it is time to consider their ecotoxicological screening prior to market approval jointly by the FDA and EPA, along with the implementation of post-market surveillance strategies. At the same time, efforts should be put into running awareness programs to prevent the overuse of ASPs.

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Abbreviations/Acronyms/Symbols

ASPs	Advanced sanitation products
COVID-19	Coronavirus disease
EPA	Environmental protection agency
FDA	Food and drug administration
MIC	Minimum inhibitory concentration
MSPs	Modern sanitation products
NPs	Nanoparticles
VOCs	Volatile organic compounds

1. Introduction

Conventional sanitation products such as soaps, detergents, antiseptics, and disinfectants have been in regular use for several thousands of years (Smith, 2008). These conventional sanitation products are generally subject to biodegradation. In the late 1960s, modern sanitation products (MSPs) such as alcoholic hand sanitizers and sprays were introduced (Berman and Knight, 1969; Judd, 2002). These MSPs were primarily used in the medical and healthcare industries. However, around 1990, these MSPs became popular as luxury products in higher income countries (Gardner, 1972; Huddleston, 2020). At the same time, contemporary research has resulted in a number of modifications to MSPs, primarily involving the infusion of nanomaterials. These nanomaterials are particulates with at least one dimension < 100 nm that possess size-dependent physicochemical properties. MSPs containing permeated nanoparticles are considered advanced sanitation products (ASPs) (Kreyling et al., 2010).

The ASPs include various hygienic supplies such as soap, shampoo, deodorant, sunscreen, hand sanitizer, and disinfectant cleaner. ASPs have great potential for killing causative organisms of infectious diseases, including bacteria, as the nanomaterials with extremely small size and large surface area offer high surface energy and more reactive sites (Gorbunova et al., 2017; Steelandt et al., 2014). In the last two decades, numerous researches have been dedicated to developing diverse functional nanomaterials to meet the various needs (Hobson, 2009; Kostoff et al., 2007). The application of nanomaterials in advanced sanitation techniques has resulted in the development of ASPs containing nanoparticles (NPs) built with silver (Ag) as well as many other metals like zirconium (Zr) or zinc (Zn) (Gottschalk et al., 2013). Some metal oxide, for instance, titanium oxide (TiO₂), is also employed to enhance the biocidal effect of sanitation products (Laxma Reddy et al., 2017).

Among all these, AgNPs are the most common additive for personal care products employed to amplify sanitation/disinfection potential. The available literature suggests great biocidal potential of AgNPs due to their slow release of Ag⁺ so as to interact with thiol groups present in proteins (Jorge de Souza et al., 2019). AgNPs have disinfection potential to stop the growth of bacterial/fungal/viral strains, as silver inhibits DNA replication to induce oxidative stress (Ahn et al., 2014; Li et al., 2013). Moreover, the AgNPs with an extraordinary surface-to-volume ratio and enhanced reactivity can favorably increase their interaction with pathogens as efficient antibacterial materials (Gilbertson et al., 2016). Because of their significant antibacterial and antiviral potential, AgNPs have been employed extensively in ASPs (Chernousova and Epple, 2013).

Until 2019, the production and consumption of these ASPs were relatively limited and environmentally sustainable. However, with the outbreak of COVID-19 in 2019, increases in their production and consumption have been substantial (Berardi et al., 2020; Pradhan et al., 2020a). Such progress was mainly influenced by large-scale behavioral (emotion and sentiments) changes in people due to the fear of COVID-19 infection (Das and Dutta, 2021). This dramatic change in supply and demand developed a market force to accelerate the research toward ASPs (Kusumoputro et al., 2020; Ruiz-Hitzky et al., 2020). Several hundred nanomaterial-infused sanitation products are available on the market such as hand sanitizers which became the most frequently used sanitation product (Table 1). This increase in usage, however, increases the risk of environmental penetration of the nanomaterials (in these ASPs) into aquatic and terrestrial environments (Chakhalian et al., 2020; Mahmood et al., 2020). Among some commercially available products, hand sanitizers are mainly available in four different forms: gels, foams, creams, and wipes (Fig. 1).

The fate, transport, and degradation of these additives are mostly overlooked when these products are approved and registered at the Food and Drug Administration (FDA) in USA or associated government agencies in the rest of the world. According to the Environmental Protection Agency (EPA) of the USA, hand wash/sanitizers, antiseptic liquids, and soaps(antibacterial) are approved/registered by the FDA. However, the surface disinfectants (in either liquid or wipe forms) for dermal/oral use of humans are essentially not regulated by Environmental Protection Agency (EPA) (EPA, 2020b). Products with antiseptic properties and that can be used for disinfection should receive approval from both the FDA

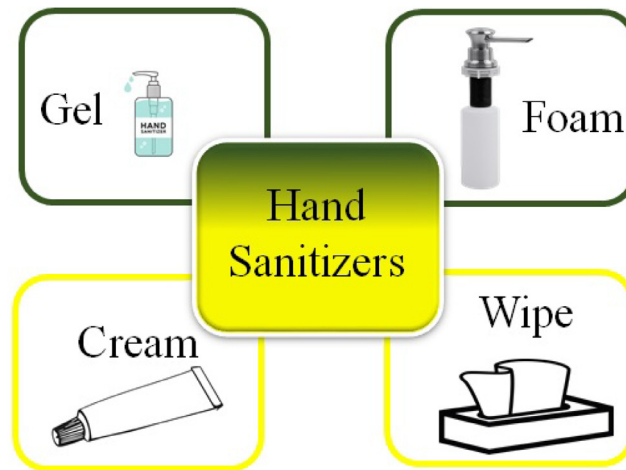


Fig. 1. Types of hand sanitizers commonly available commercially.

Table 1

List of commercially available advanced sanitation products.

Order	Name of product	Type	Base solvent	Nanomaterial	Name of manufacturer	Country	Website
1	Organic sanitizer	Gel	Ethanol	Ag	Nanoshel LLC	USA	https://www.nanoshel.com/Silver-nanoparticle-based-organic-sanitizer
2	Hand sanitizer+	Gel	Ethanol	Ag	Nanolife	India	https://nanolife.in/hand-sanitizer.php
3	Evolut hand sanitizer	Gel/Spray	Water	Ag	EVOLUT	USA	http://evolutsilver.com/shop-silver-nanoparticles/
4	ALLOUT Ultra	Spray	Isopropyl Alcohol	Ag	ALLOUTnano	USA	https://www.alloutnano.com/product-page/ultra-alloutnano-hand-sanitizer-spray
5	Colloidal silver hand sanitizer	Spray	glycerin	Ag	Mimi's Apothecary	Canada	https://mimisapothecary.com/hand-sanitizer-spray/
6	Silver hand sanitizer	Spray	Water	Ag	Centaur Packaging	Australia	https://www.centaurpackaging.com.au/colloid-silver-hand-sanitiser-100-ml.html#demoTab1
7	Nano silver hand sanitizer	Gel	Ethanol	Ag	Nanogist Co., Ltd.	ROK	http://www.nanogist.com/English/products/spray.htm
8	SilvoSept hand sanitizer	Foam	Water	Ag	ChitoTech	Iran	https://chitotech.com/page/692/silvosept-for-hand
9	Nkill hand sanitizer	Spray	Ethanol	Ag	JK Nanosolutions	India	https://www.jknanosolutions.com/index.php
10	DR OH hand wash	Gel	Ethanol	Ag	SHTPLabs	Vietnam	http://shtplabs.org/en/listPage/path/laboratory/laboratory_nano
11	Disposable hand sanitizer	Gel	Ethanol	Ag	Yurui Chemical Co., Ltd	China	http://www.riyngroup.com/portable-nano-silver-hand-sanitizer-gel-1588898951965875.html
12	Nano hand sanitizer	Gel	Ethanol	Ag	Nanopac Innovation	Australia	http://www.nanopacinnovation.com/index.php/about-us
13	Nolla hand sanitizer	Foam	Water	Ag	Nolla Antimicrobial	Finland	https://www.nollaantimicrobial.com/en/

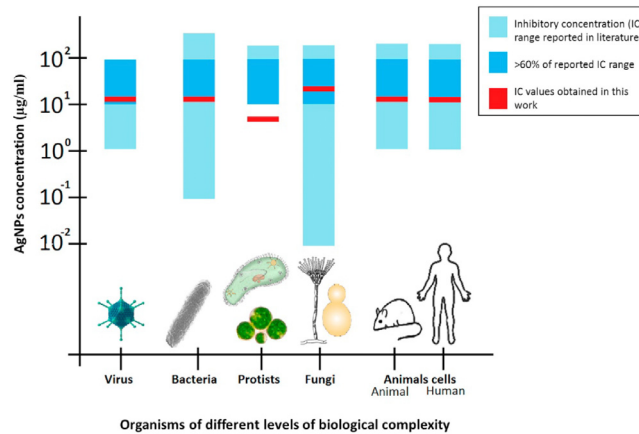


Fig. 2. Inhibitory effects of AgNPs on various taxonomic groups (Vazquez-Muñoz et al., 2017).

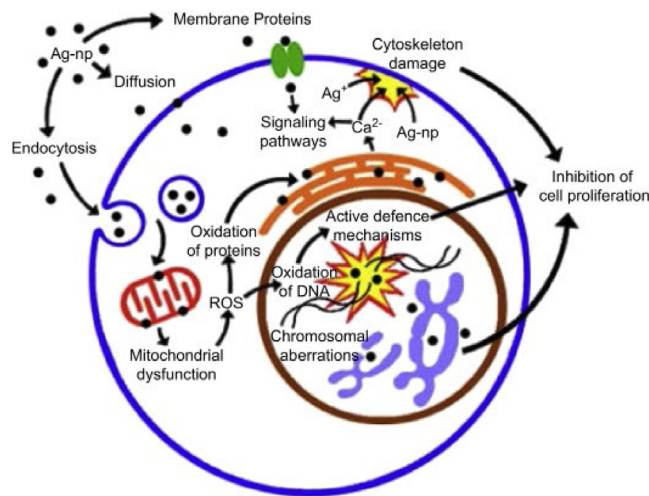


Fig. 3. Interaction of the AgNPs with animal cells and potential cytotoxic mechanisms (McShan et al., 2014).

and EPA (EPA, 2020b). Despite the fact that ASPs contain infused nanoparticles with the potential for disinfection, their categorization as antiseptics means that the FDA only approves them. Their fate, transport, and degradation in aquatic and terrestrial environments are largely unknown (Liu et al., 2014).

This article aims to present a critical overview of MSPs and ASPs concerning their possible cytotoxicological and ecotoxicological adverse effects on terrestrial and aquatic ecosystems. The challenges of AgNP-based ASPs have been explored to further evaluate the induced risk of their overuse during COVID-19. To begin with, a brief introduction is provided for the development of MSPs and ASPs, followed by a discussion on the rising demand for ASPs due to COVID-19 distress. Further, we explored the environmental hazards and consequences of overused ASPs in Section 3. In addition, the discussion is extended to describe the fate of ASPs in the environment. Finally, conclusions are drawn to highlight the need of more stringent regulatory measures and the efforts needed to explore the environmentally benign ASP alternatives. To the best of our knowledge, this is the first attempt to consider the ecotoxicology of ASPs and offer guidelines for future research efforts in this field.

2. Environmental hazards

The increased use of AgNP-containing ASPs may result in emissions of AgNPs into the air as particulate matter and/or suspended nanoparticles in wastewater streams (Colman et al., 2014; Pradhan et al., 2020b; Quadros and Marr, 2010). AgNPs may also act as nuclei for other primary emissions such as SO₂, NO_x, VOC, NH₃, and OH⁻ to form secondary pollutants like particulate matter (PM) (Behera and Sharma, 2010), which can cause cardiovascular problems (EPA, 2021c). Exposure of various cell lines and Sprague–Dawley rats to AgNPs has been shown to elicit cytotoxic responses such as reactive oxygen species generation, oxidative stress, apoptosis, and necrosis (Foldbjerg et al., 2009; Ji et al., 2007).

Table 2
In vitro cytotoxicity assessment of AgNPs in different cell lines and types.

Order	Size	Model	Method	Dose	Exposure time	Toxicity assessment	Ref.
1	15 nm	Mouse spermatogonial stem cells (C18-4)	In vitro	5–10 $\mu\text{g ml}^{-1}$	24 h	Reduction in mitochondrial function, increased LDH leakage leading to apoptosis	Braydich-Stolle et al. (2005)
2	25 and 100 nm	BRL 3A rat liver cells	In vitro	5–50 $\mu\text{g ml}^{-1}$	24 h	Reduction in mitochondrial function and GSH level, increased level of ROS	Hussain et al. (2005)
3	15 nm	Rat neuroendocrine cells (PC-12)	In vitro	50 $\mu\text{g ml}^{-1}$	24 h	Reduction in mitochondrial function and dopamine level	Hussain et al. (2006)
4	15, 30 and 55 nm	Rat alveolar macrophages	In vitro	10–75 $\mu\text{g ml}^{-1}$	24 h	ROS generation and oxidative stress leading to size-dependent toxicity	Carlson et al. (2008)
5	1–100 nm	Mouse fibroblasts (NIH3T3)	In vitro	5–50 $\mu\text{g ml}^{-1}$	24 h	ROS and JNK-induced apoptosis via the mitochondrial pathway	Hsin et al. (2008)
6	25 nm	Mouse embryonic stem cells and fibroblasts	In vitro	50 $\mu\text{g ml}^{-1}$	4–72 h	Induction of DNA damage and apoptosis	Ahamed et al. (2008)
7	7–20 nm	Human skin carcinoma (A431) and human fibrosarcoma (HT-1080)	In vitro	6.25–50 $\mu\text{g ml}^{-1}$	24 h	Reduction in cell viability, oxidative stress, DNA fragmentation, and higher caspase-3 activity	Arora et al. (2008)
8	7–20 nm	Mouse fibroblasts and liver cells	In vitro	10–200 $\mu\text{g ml}^{-1}$	24 h	Reduction in cell viability, oxidative stress, and apoptosis	Arora et al. (2009)
9	100 nm	Human mesenchymal stem cells (hMSCs)	In vitro	2.5–5.0 $\mu\text{g ml}^{-1}$	24 h	Cell proliferation, reduced chemotaxis, increased IL-8 release	Greulich et al. (2009)
10	5–10 nm	Human hepatoma HepG2 cells	In vitro	0.5–10 $\mu\text{g ml}^{-1}$	28 h	Cytotoxicity and oxidative stress	Park et al. (2010)
11	7–10 nm	Human hepatoma HepG2 cells	In vitro	0.1–3.0 $\mu\text{g ml}^{-1}$	24 h	Accelerated DNA damage and micronuclei induction	Kawata et al. (2009)
12	25 nm	Human abdominal full thickness skin obtained from surgical waste	In vitro	0.46 ng cm^{-2} to 2.32 ng cm^{-2}	24 h	Permeation of damaged skin in an <i>in vitro</i> diffusion cell system	Larese et al. (2009)

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Table 2 (continued).

Order	Size	Model	Method	Dose	Exposure time	Toxicity assessment	Ref.
13	69 nm	Human acute monocytic leukemia cell line (THP-1)	In vitro	0–7.5 $\mu\text{g ml}^{-1}$	24 h	ROS generation and apoptosis	Foldbjerg et al. (2009)
14	45 nm	Rat coronary endothelial cells (CECs)	In vitro	0.1–100 $\mu\text{g ml}^{-1}$	24 h	Low concentrations - anti-proliferative/ vasoconstrictive factors that impaired NO production, high concentrations stimulated NO-mediated proliferation/ vasorelaxation	Rosas-Hernández et al. (2009)
15	2–5 nm	HeLa S3 cells	In vitro	92 $\mu\text{g ml}^{-1}$	3, 4 and 24 h	Cytotoxicity, apoptosis, and induction of oxidative stress	Lubick (2008)
16	50 nm	Bovine retinal endothelial cells	In vitro	100–500 nM	24 h	Induction of caspase-3 activity and DNA ladder formation	Kalishwaralal et al. (2009)
17	20–80 nm	Human epidermal keratinocytes (HEKs)	In vitro	0.34 $\mu\text{g ml}^{-1}$ –1.7 $\mu\text{g ml}^{-1}$	24 h	Dose-dependent decreased cell viability. Carbon-coated Ag NPs were non-toxic	Samberg et al. (2010)
18	18 nm	Baby hamster kidney (BHK21) and human colon adenocarcinoma (HT29) cells	In vitro	11 $\mu\text{g ml}^{-1}$	0, 12, and 24 h	p53-mediated apoptosis	Gopinath et al. (2010)

The results of numerous *ex vivo* and *in vivo* toxicity assessment of AgNPs using different cell lines and animal models suggest that AgNPs have cytotoxic potential (Tables 2–3). The inhibitory effects of AgNPs on various taxonomic groups spanning the kingdoms of life are shown in Fig. 2. In mammals, repeated exposure to Ag has been suggested as the causes of various diseases such as cardiac enlargement, anemia, restriction related to development, and degenerative transformation in the liver (Butler et al., 2015). Toxicity studies have indicated variation in toxicokinetics of AgNPs on the basis of size, time of exposure, dose, and method of exposure. Moreover, the biological interactions of AgNPs are influenced by factors such as inhalation, dermal absorption, and ingestion (Sajid et al., 2015). Additionally, the absorption, distribution, metabolism, and excretion (ADME) of AgNPs are important to consider when evaluating their possible health consequences. The size, size distribution, surface charge, and surface coating of AgNPs influence their toxicity by determining the rate of release of ionic silver (Ag^+) under different environmental conditions. AgNPs might directly cause disintegration of cell membranes, interruption in ATP production/transportation, replication of DNA, modification in gene expression, generation of toxic Ag^+ ions, and engendering reactive oxygen species (ROS) to oxidize intracellular constituents of cells (Fig. 3).

O_2 and organic and inorganic molecules in air and waste streams can oxidize AgNPs and liberate toxic Ag^+ ions. Consequently, the toxicity stemming from AgNPs is meticulously linked to the discharge of Ag^+ ions (De Matteis et al., 2015). Typically, cellular exposure to Ag^+ results in the generation of reactive oxygen species that can damage DNA, stimulate antioxidant enzymes, reduce antioxidant molecules (such as glutathione), cause conformational changes in proteins, and impair cell membrane function (He et al., 2011; Stoccoro et al., 2013).

An *in vivo* toxicokinetic study of AgNPs in zebrafish suggested size-dependent effects on gills and intestines via localized Ag deposition on basolateral membranes (Osborne et al., 2015). AgNP exposure has also been shown to exert toxic effects on cells, including DNA damage and apoptosis (Ahamed et al., 2010). The outcomes of a dose-based *in vivo* toxicity study of AgNPs on Wistar rats suggested that a dose $<10 \text{ mg kg}^{-1}$ did not result in any side effects while a dose $>20 \text{ mg kg}^{-1}$ resulted in the deposition of nanoparticles in organ tissues. This may cause damage to DNA strands, chromosome aberrations, and conformational changes to protein (Tiwari et al., 2011).

The presence of metal nanoparticles in the soil can inhibit plant growth as a result of the accumulation of metal ions that can reduce photosynthesis and alter protein expression of antioxidant enzymes (Fig. 4) (Mustafa and Komatsu,

Table 3
In vivo cytotoxicity assessment of AgNPs in different models.

Order	Size	Model	Method	Dose	Exposure time	Toxicity assessment	Ref.
1	18 nm	Sprague–Dawley rats	Inhalation	$1.73 \times 10^4 \text{ cm}^{-3}$, $1.27 \times 10^5 \text{ cm}^{-3}$, $1.32 \times 10^6 \text{ cm}^{-3}$	6 h/day, 5 days/week, for 90 days	Decreased tidal volume and alveolar inflammation, increased bile duct hyperplasia and liver inflammation	Sung et al. (2008)
2	18 nm	Sprague–Dawley rats	Ingestion	30 mg kg ⁻¹ , 300 mg kg ⁻¹ and 1000 mg kg ⁻¹	Ag NPs mixed with diet for 28 days	Dose-dependent significant changes in alkaline phosphatase activity, cholesterol level, and slight liver damage	Kim et al. (2008)
3	29 nm	Male C57BL/6 N mice	Intraperitoneal injection	100 mg kg ⁻¹ , 500 mg kg ⁻¹ , and 1000 mg kg ⁻¹	24 h	Alteration in gene expression associated with oxidative stress in the caudate, frontal cortex, and hippocampus regions of the brain	Rahman et al. (2009)
4	13–15 nm	Sprague–Dawley rats	Inhalation	$1.73 \times 10^4 \text{ cm}^{-1}$, $0.5 \mu\text{g m}^{-3}$, $1.27 \times 10^5 \text{ cm}^{-3}$, $3.5 \mu\text{g m}^{-3}$, and $1.32 \times 10^6 \text{ particles cm}^{-3}$, $61 \mu\text{g m}^{-3}$	6 h/day, 5 times/week, 28 days	Increase in size and number of goblet cells containing neutral mucins in the lungs	Hyun et al. (2008)
5	22 nm	C57BL/6 mice	Inhalation	$1.91 \times 10^7 \text{ particles cm}^{-3}$	6 h/day, 5 days/week, 14 days	Expression of several genes in the brain associated with motor neuron disorders, neurodegenerative disease, and immune cell function	Lee et al. (2010)
6	18 nm	Sprague–Dawley rats	Inhalation	$0.7 \times 10^6 \text{ particles cm}^{-3}$ (low dose), $1.4 \times 10^6 \text{ particles cm}^{-3}$ (medium dose), and $2.9 \times 10^6 \text{ particles cm}^{-3}$ (high dose)	6 h/day, 5 days/week, for 90 days, sacrificed 1 day post last exposure	Compromised lung function	Sung et al. (2008)

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2016). A proteomic study of soybean found that exposure of soybean plants to Ag nanoparticles resulted in superoxide accumulation in the leaves (Hossain et al., 2016). These studies suggest that biomagnification/bioaccumulation of AgNPs in primary producers may lead to adverse effects in herbivores (Luo et al., 2016; Yoo-iam et al., 2014).

3. Social media infodemic and consumer awareness

To date, the use of social media platforms such as Facebook, Twitter, Instagram, YouTube, and Reddit has become an indispensable part of social life (Zafarani et al., 2014). In the past 2 years, these social media platforms have been excessively used due to restrictions on social gatherings and fear of COVID-19 infection (Ahmad and Murad, 2020; Siddiqui et al., 2020). Despite such upsurge, the content created and shared by their users including COVID-19 is largely unregulated

Table 3 (continued).

Order	Size	Model	Method	Dose	Exposure time	Toxicity assessment	Ref.
7	18 nm	Sprague–Dawley rats	Inhalation	0.6×10^6 particle cm^{-3} , $49 \mu\text{g m}^{-3}$ (low dose), 1.4×10^6 particle cm^{-3} , $133 \mu\text{g m}^{-3}$ (medium dose), and 3.0×10^6 particle cm^{-3} , $515 \mu\text{g m}^{-3}$ (high dose)	6 h/day, 5 days/week, for 90 days, sacrificed 1 day post last exposure	Gender-dependent accumulation of silver in the kidney, and dose-dependent increase of bile duct hyperplasia in the liver	Sung et al. (2009)
8	15 nm; 410 nm	Male Fischer rats	Inhalation	$179 \mu\text{g m}^{-3}$ and $167 \mu\text{g m}^{-3}$ or 7.9×10^6 particles mm^{-3} and 118 particles mm^{-3} for 15 and 410, respectively	Inhalation 6 h/day, 4 consecutive days, sacrifice at 1 and 7 days post-exposure	Size-dependent pulmonary toxicity on inhalation	Braakhuis et al. (2014)
9	20 nm; 110 nm (PVP- and CT-coated)	Male Sprague–Dawley rats	Pulmonary	0.5, 1 mg kg^{-1}	Single i.t. instillation, sacrifice at 1, 7, and 21 days post-exposure	Sacrifice at 1, 7 and 21 days post exposure	Anderson et al. (2015)
10	20 nm (CT-capped)	Male Sprague–Dawley rats	Pulmonary	1 mg kg^{-1}	Single i.t. instillation, sacrifice at 1 and 7 days post-exposure	Exacerbation of cardiac ischemic-reperfusion injury	Holland et al. (2015)
11	50 nm; 200 nm (PVP-coated)	Female Wistar rats	Pulmonary	0.1875, 0.375, 0.75, 1.5, 3 mg kg^{-1}	Single i.t. instillation, sacrifice at 3 and 21 days post-exposure	Focal accumulation of Ag in peripheral organs along with transient inflammation in the lung	Wiemann et al. (2017)
12	50 nm; 200 nm (PVP- and CT-coated)	Female BALB/C mice	Pulmonary	0.05, 0.5, 2.5 mg kg^{-1}	Single i.t. instillation, sacrifice 1 day post-instillation	Size-, dose-, and coating-dependent pro-inflammatory effects in healthy and sensitized lungs	Alessandrini et al. (2017)
13	10 nm		Pulmonary	0.05, 0.5, 5 mg kg^{-1}	Single i.t. instillation, sacrifice at 1 and 7 days post-exposure	Oxidative stress, DNA damage, apoptosis in heart muscle, induced prothrombotic events, and altered coagulation markers	Ferdous et al. (2019)
14	56 nm	F344 rats	Oral	30, 125, 500 mg kg^{-1}	Daily exposure for 90 days, sacrifice 24 h post last exposure	Gender-biased accumulation of silver in kidneys, 2-fold increase in female kidneys, Liver damage	Kim et al. (2010)

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or uncensored ([Samy et al., 2020](#)). Consequently, knowledge generated in a vacuum based on flawed hypotheses or intuitive ideas kept on proliferating with parallelized infodemic ([Bridgman et al., 2020](#); [Cinelli et al., 2020](#)). Such infodemic contributed to large-scale behavioral change against COVID-19 infection ([Lin et al., 2020](#)). These sentiments led to panic buying of protective gear, essential medicines, and sanitation products to protect themselves from COVID-19 ([Naem, 2021](#)).

Table 3 (continued).

Order	Size	Model	Method	Dose	Exposure time	Toxicity assessment	Ref.
15	15 nm; 20 nm	Male Sprague–Dawley rats	Oral	90 mg kg ⁻¹	Daily exposure 28 days, sacrifice 24 h, 1 week, 8 weeks post last exposure	Liver and spleen showed Ag accumulation. All organs free from Ag after 8 weeks post-dosing except the brain and testes	van der Zande et al. (2012)
16	20 nm	Male Sprague–Dawley rats	Oral	820 mg kg ⁻¹	Daily exposure for 81 days, sacrifice 24 h post last exposure	Liver and cardiac oxidative stress and a mild inflammatory response in the liver	Ebabe Elle et al. (2013)
17	20, nm; 110 nm (PVP- and CT-coated)	Male C57BL/6NCrl mice	Oral	0.1, 1, 10 mg kg ⁻¹	3 days exposure, sacrifice at 1 and 7 days post-exposure	Acute dose well-tolerated in rodents, high dose was associated with predominantly fecal accumulation	Bergin et al. (2016)
18	15–40 nm	Male Wistar rats	Intravenous injection	4, 10, 20, 40 mg kg ⁻¹	32 days i.v., sacrifice 24 h post last i.v. administration	Doses <10 mg kg ⁻¹ were safe, while doses >20 mg kg ⁻¹ were toxic	Tiwari et al. (2011)
19	21.8 nm	ICR mice	Intravenous injection	7.5, 30, 120 mg kg ⁻¹	Single i.v., parameters measured at 1, 7, 14 days post-injection	Inflammatory response in lung and liver cells to high dose, gender bias in distribution ADME, elimination time for females longer than for males	Xue et al. (2012)
20	20 nm; 200 nm	Male Wistar rats	Intravenous injection	5 mg kg ⁻¹	Single i.v., sacrifice at 1, 7, 28 days post i.v. administration	Greater accumulation for 20 nm group than 200 nm group	Dziendzikowska et al. (2012)

The general consumers have little knowledge on the environmental significance of nanomaterial-based consumer products ([Kim et al., 2014](#)). Despite the great potential of nanotechnology, the lack of the awareness on the risks involved in their production and consumption is yet significant ([Joubert et al., 2020](#)). To fulfill the expectations and concerns of customers, a communication channel needed to be established among the various shareholders engaged in nanoindustry. Furthermore, a safety evaluation method must be established and implemented by a group of experts both before and after commercialization. Moreover, socio-political influence of corporate houses in the quick commercialization of nanomaterial-based products is also very critical issue ([Kahan et al., 2008](#)). Most of this quick rollout of nanomaterial-based products are an outcome opportunistic capitalism that may end up with wealth polarization ([Hornyak et al., 2018](#)). In this regard, coalitions of stakeholders such as civil society, government bodies, and industrialists is needed to learn about alternatives. These partnerships between one and all should be able to adjust risks by evaluating potential environmental concerns of ASPs to make them generally acceptable with less environmental hazards ([Daniell et al., 2014](#)).

4. Potential concerns on the overuse of ASPs

AgNPs and silver ions are both hazardous to living organisms and ecosystems ([Tortella et al., 2020](#)). The Agency for Toxic Substances and Disease Registry (ATSDR) designated AgNPs and silver ions in the water system as hazardous materials ([ATSDR, 1990](#)). A widespread use of AgNPs leads to their release into ecosystems through many processes such as washing, transport, and discharge ([Du et al., 2018](#)). The subsequent discharge and presence of AgNPs in sewage sludge

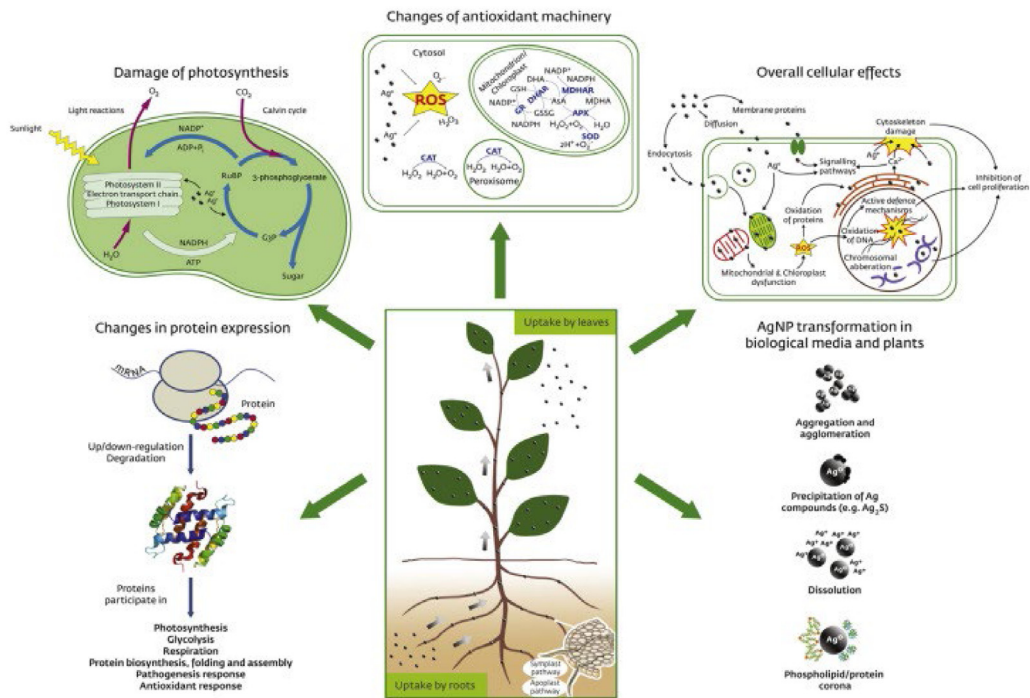


Fig. 4. Interactions of AgNPs with terrestrial plants and possible mechanisms of phytotoxicity (Tkalec et al., 2019).

and wastewater effluent have often been reported (Kraas et al., 2017; Mitrano et al., 2012; Moreno-Martín et al., 2022). The presence of AgNPs in sewage can exert an inhibitory effect on the wastewater treatment process (Ma et al., 2013). Additionally, its interaction with complexing ligands may alter the bioaccumulation and amplification of AgNPs in the water (Ramzan et al., 2022). Moreover, it can also affect bioavailability, toxicity, and transfer of AgNPs in food chain organisms to enhance the chances of their human exposure via many different pathways (Du et al., 2018).

The concentration of AgNPs in ASPs and other commercial products such as cosmetics, textiles, food packaging, and biomedical products ranges from 17 to 30 mg L⁻¹ (Khaksar et al., 2019). A large fraction of the global world population has started to use or is expected to use ASPs to prevent the spread of COVID-19. Hence, as per our estimates, if 7.8 billion peoples start using as little as 10 mL of ASPs per day in their daily life, 2.8 billion liters of ASPs will be discharged or released every year into waste streams and the environment. This discharge may contain at least 483 metric tons of AgNPs. Mammals are less sensitive (threshold: 100 µg L⁻¹) to AgNPs (Deshmukh et al., 2019) than aquatic species (threshold: 1–5 µg L⁻¹) (Nowack et al., 2011). Based on the non-biodegradability of ASPs and our above estimation, ASPs pose health risks to living creatures and are of ecotoxicological concern. ASPs therefore need extensive cytotoxicological and ecotoxicological evaluation.

5. The fate of ASPs in the environment

The transformation and degradation of AgNPs discharged into wastewater and therefore the aquatic environments are governed by interactions with the surrounding environment. These interactions are mainly controlled by AgNP characteristics such as shape, size, and charge (El Badawy et al., 2011). Moreover, some environmental factors such as light, oxygen, ions, organic compounds, inorganic compounds, and ambient temperature can also affect the process of transformation into new products or intermediates (Fig. 1S). AgNPs are not stable in the environment and usually oxidize or react with organic or inorganic components (Sharma et al., 2014). The anticipated reaction pathways (chemical Eqs. (1) and (3)) suggest the triggered release of reactive oxygen species (ROS) in the presence of dissolved organic matter (DOM) in the environment:



Generally, the transformation of AgNPs takes place through various routes (such as oxidation, sulfidation, chlorination, dissolution, and aggregation) once transported into ambient environment (Fig. 2S). The transformation of AgNPs in terrestrial as well as aquatic environments is further influenced by dissolution, aggregation, redox reactions, sulfidation, flocculation, and sorption of organic materials (Zhu et al., 2016). Redox behavior depends on the availability of oxygen and sulfides, which also alter dissolution and sulfidation rates, respectively (Abbas et al., 2020). Moreover, other physical and biological interactions may mediate transformations of AgNPs (Azimzada et al., 2017). For example, photo-transformation of organic compounds may yield oxygenated or hydroxylated species. These hydrophobic species affect the stability of AgNPs (Akter et al., 2018). Molecular interactions of AgNPs in different environments are shown in Fig. 3S.

6. A call for affirmative action

The FDA and EPA in the USA are in charge of safeguarding human wellbeing and the environment, respectively. FDA is mainly responsible for protecting public health by ensuring the quality and safety of food and drugs that may utilize nanotechnology (FDA, 2020d). In contrast, the EPA is responsible for mitigation/regulation to address potential environmental issues (EPA, 2021a). Both agencies work globally, often leading the international cooperation of their counterparts around the world to promote sustainable development, protect public health, promote commerce, and harmonize legislation (EPA, 2021b; FDA, 2019). In August 2006, the FDA commissioned a Nanotechnology Task Force to regulate products based on nanotechnology or nanomaterials (FDA, 2020c). In Aug 2012, the EPA released their final report based on a case study relating to nanoscale silver as a disinfectant spray without drawing any final conclusions about the potential risks of nanomaterials (EPA, 2020a). The report identified research required to support future assessments of nanomaterials (EPA, 2020a). According to the EPA, products that fall under the category of surface disinfectants need to be registered in *List N* - a document newly launched by the EPA to make it easier to find the most suitable disinfectant. However, hand wash/sanitizers, antiseptic liquids, and soaps (antibacterial) are exempted because they are generally registered by the FDA (EPA, 2020c). The FDA evaluates active ingredients and determines the safety and effectiveness of antiseptic/antibacterial products for their intended use (FDA, 2020a). The FDA also hosts a database that the public can access to find approved and occupationally safe sanitation products (FDA, 2020b). However, ecotoxicity concerns about the active ingredients of sanitation products (such as AgNPs) appear to fall between these two regulatory regimes.

The COVID-19 pandemic has greatly increased the use of ASPs, and this sudden and large increase in their use may be adding significant surplus nanomaterials to the environment and wastewater streams, where these materials can pose hazards to terrestrial and aquatic life. Hence, we recommend that the FDA and EPA collaborate to prepare regulatory guidelines that consider the cytotoxicity and ecotoxicity of nanomaterials. This will also serve to stimulate other equivalent national bodies to do the same. Additionally, the FDA and EPA should consider premarket approval and postmarket surveillance of such ASPs. In addition, the government should also consider promoting the public awareness campaign to educate people about risks associated with the overuse of ASPs. Moreover, the influence of wealth in commercialization of nanomaterial-based products without toxicity clearance must not be overlooked. This may help the sustainable commercialization and eco-safe application of ASPs.

7. Conclusions

In many published reviews on COVID-19 scenarios, the direct and indirect potential concerns on COVID-19 have been described with respect to health hazards, economic disruption, and environmental pollution stemming from the pandemic. Nevertheless, relatively little efforts have been put to describe the cytotoxicity and ecotoxicity of AgNPs used in ASPs along with their environmental fate upon consumption and subsequent disposal. Further, there is a growing demand to properly establish and implement legislative control on the use of nanomaterials in sanitation products in view of the rise in COVID-19 infection.

Numerous studies have shown that nanomaterials can be toxic to both terrestrial and aquatic ecosystems and that AgNPs are cytotoxic to mammalian cell lines and animal models. However, whether they have genotoxic effects in mammals and whether they are cytotoxic to plant cells requires further investigation. Thus, rigorous studies of the toxicological impacts of nanomaterials are needed before their extensive application and commercialization. There is a need for strict regulatory measures such as new approval/regulatory schemes for ASPs. The enforcement of such regulations may help protect biodiversity and the environment from irreversible ecological damage. The above-mentioned strategies may be helpful to offer better insights into the essential requirements for the regulated production and commercialization of ASPs to accommodate consumer demand with the least environmental side effects. To summarize, this review addressed the challenges associated with the applications of AgNPs in ASPs and possible health and environmental hazard on overuse. As the specific toxicological evaluation of ASPs is necessary, the techniques for their recovery from waste streams need to be explored in various respects.

CRedit authorship contribution statement

Bhaskar Anand: Formal analysis, Investigation, Methodology, Writing – review & editing. **Ki-Hyun Kim:** Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. **Christian Sonne:** Formal analysis, Writing – review & editing. **Neha Bhardwaj:** Formal analysis, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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