Nanosilver

Summary

Silver has a rich history of use in medicine and hygiene due to its broad-spectrum toxicity to bacteria, fungi and algae. For a number of years, silver has been used increasingly in its nano-particulate form. This form exhibits an elevated toxic potential compared to traditional silver compounds. Silver is not considered a systemic toxin in humans except at high doses. Products containing nanosilver are one of the most important classes of nanoproducts. Nanosilver coatings on medical devices are used in hospital settings. In addition, items containing nanosilver are sold as various consumer products. Here, the widespread use of nanosilver to fight bacterial growth has raised concerns, as low levels of silver ions could encourage the growth of silver-resistant bacteria. It cannot be excluded that the beneficial healthy microflora of the human skin could be damaged following the use of cosmetic products containing nanosilver ingredients. If discharged with wastewater, silver persists and accumulates to elevated concentrations. Ecological damage to aquatic environments, to the bacteria in waste water treatment plants and to microbial communities of the soil should not be overlooked.

Introduction

Silver is perhaps second only to gold in its use since antiquity as a metal and material for jewelry. Silver has, due to its antibiotic potential, a long history of medical and hygienic uses. During the previous century, the photochemical properties of silver compounds led to an increase of the use of silver and a peak of silver emission into the environment that has since declined considerably, due to the advent of digital photography and the implementation of stricter environmental legislation.

In recent years, the use of silver as a biocide in the form of micro-crystals or nanoparticles has grown substantially, as these preparations are effective against many resistant populations and ‘biofilms’—aggregates of microorganisms in aqueous solution—that grow on the surfaces of bodies of water and inside water pipes. Consumer products utilizing nanosilver to fight bacterial growth constitute the fastest-growing category of nanoproducts. According to an inventory that relies on data supplied by producers (the ‘Project on Emerging Nanotechnologies’), nanosilver is being used in over two hundred consumer products—including clothing, bedding material, cosmetics and beauty soaps. It is being incorporated into plastic storage containers for food, used in kitchen utensils, in paints and in fabric softeners. “Colloidal solutions”—solutions of elementary nanoparticulate silver or silver compounds—are being offered as dietary supplements. Independent scientific data concerning the numerous advertised health claims are lacking.

This dossier presents an overview of the advantages and drawbacks of nanosilver use, possible consequences for human health and the environment, and describes the ongoing debate concerning the regulation of new products containing nanosilver.

Biocidal effects of silver

Silver compounds and particles of elementary silver can release silver ions (Ag+) through oxidation or other processes—that are responsible for the toxicity towards bacteria, fungi and algae. Few studies have investigated the interaction of silver nanoparticles with viruses. Silver ions can attach to the surface of cell membranes and disturb their proper functions. They can penetrate cells and cause damage by interacting with sulphur- or phosphorus-containing compounds (proteins). A study has shown that the bactericidal effect on gram negative bacteria is size-dependent and most pronounced for particles of 1–10 nm in diameter. Silver nanoparticles that have penetrated a cell can continue to release silver ions that exhibit their own antibacterial effect. The smaller particles have a higher antimicrobial activity per equivalent mass unit than their larger particle counterparts as a result of their higher surface to volume ratio.

Recent studies have reported a dose-dependent effect against even bacteria that had acquired resistance to antibiotics. A concentration of nanoparticles between 8 and 70 μg ml⁻¹ was sufficient for the complete inhibition of bacterial growth. Silver particles and silver ions have been demonstrated to be useful and effective in bacterial applications in medical settings. However, the bactericidal mechanism is not completely understood.

Clinical studies have reported the existence of silver-resistant variants of bacteria. Experts have recommended abstaining from regular and widespread use of bactericidal agents in low doses as this could encourage the emergence of resistant strains. Silver ions should be used only in high doses for well defined medical purposes.
Medical use

Silver – in the form of silver nitrate (AgNO₃) – has been used since the 18th century for the disinfection of wounds. Until recently, a weak solution of silver nitrate was applied to the eyes to prevent or cure infections. The discovery of penicillin and sulphonamide drugs have, after the end of the Second World War, replaced silver as an antibiotic in most areas. An antibacterial combination product containing silver (Silver sulfadiazine) is still being used as a topical burn cream on second- and third-degree burns and for wound dressings after skin transplants. The efficacy of silver in the management of chronic wounds has not been confirmed. Due to its antimicrobial activity, silver may have a positive effect on the wound bed, but it seems to be less useful in the treatment of infected wounds. Some adverse effects of silver products, such as damage to human cells and delayed wound healing, have also been described.

For a number of years, coatings of silver oxide or silver alloy have been used on medical devices – such as catheters, implants and heart valves. Reports of postoperative complications following the use of silver coated prosthetic heart valves led to a recall in the year 2000. Contradictory findings concerning the risks of these types of heart valves have been reported; the contribution of the antimicrobial silver coating to the reported risks is being investigated.

Other uses of nanosilver

The “Project on Emerging Nanotechnologies” at the Woodrow Wilson Center (USA) collects data of nanotechnology-based consumer products that are currently on the market. This inventory is using information supplied by the producer (“manufactured-identified”). Among the more than 800 entries are over 200 products containing nanosilver. The information given by the producers about the character and the amount of silver particles is incomplete and not always trustworthy; in some cases ‘nano’ may have been used solely as an advertising claim.

Dietary supplements

Water-based solutions of silver nano particles – under the name of “colloidal silver” – are claimed to have effects against germs, pathogens and diseases if used internally (a ‘colloid’ consists of the dispersion medium and the small dispersed particles with a diameter between approximately a few nm and 10 μm). Some of these preparations of “colloidal silver” contain silver salts in the place of elementary silver. According to the manufacturers, only products containing metallic silver particles bring beneficial health effects. Substantial scientific evidence supporting the use of these products for disease treatment does not exist, and their safety is not generally recognized.

Cosmetics and personal care products

According to the claims of the producers, some brands of cosmetics contain bactericidal nano- or micro-particles of silver in order to protect the skin of people suffering from neurodermitic skin and itching. The German firm ‘Bio-Gate AG’ has developed a patented process that allows the use of antimicrobial silver in cosmetics. Advertisements for creams, body lotions, toothpaste, toothbrushes and combs mention the advantages of using silver nanoparticles in those products.

Water treatment

Silver is – similarly to copper – a substance that can control microorganisms in water treatment works. Silver has been used for a number of years as biocidal agent in filter systems and as algicide to control algae in swimming pools. The US Environmental Protection Agency (EPA) approved the use of silver for this purpose in 1993. However, due to the toxicity of silver to fish and the aquatic environment, the discharge of effluents containing silver is subject to restrictions. Products containing silver have been applied in water pipes to eliminate the dangerous biofilms of bacteria that can cause Legionnaires’ disease (Legionella pneumophila). In Japan, silver zeolite has been used as a bactericidal agent since 1983. Products containing silver salts are available to campers and hikers wishing to treat potable water and to remove bacteria. Ceramic or charcoal water filters are being offered with nanosilver incorporated in their outer layers, thus inhibiting bacterial growth on the filter.

Kitchens, utensils and household appliances

The biocidal effect of nanosilver is already being used in numerous appliances (according to the claims of the manufacturers), such as on the inner surfaces of refrigerators, in air purifiers, vacuum cleaners, hair cutters and trimmers. Silver nanoparticles have been incorporated into the plastic of food containers. Since 2005, a washing machine equipped with a ‘Silver Nano Health System’ has been available, containing a mechanism that produces bactericidal silver ions that are added during the wash. After objections concerning the increased burden of silver into the environment were raised by the Swedish environmental agency and the association of water treatment works, this product was removed temporarily from the Swedish market.

Textiles

The bactericidal properties of silver particles can be used to fight bacterial growth that causes unpleasant smells – and therefore many textiles incorporating nanosilver ingredients are available for purchase. Until recently, the production of textiles containing silver required considerable amounts of this metal, but the availability of nanosilver allows for a significant reduction. Products include Nano-Silver socks, undergarments, sportswear, bedding material and shoe liners. A study presented in 2008 on different brands of socks containing nanosilver found different levels of silver, ranging from 0.02 mg up to 30 mg per sock. Some of these socks released almost 100 % of the silver particles after only four consecutive washings. Both silver particles and silver ions could be detected in the wash water.

Kitchen utensils and household appliances

The biocidal effect of nanosilver is already being used in numerous appliances (according to the claims of the manufacturers), such as on the inner surfaces of refrigerators, in air purifiers, vacuum cleaners, hair cutters and trimmers. Silver nanoparticles have been incorporated into the plastic of food containers. Since 2005, a washing machine equipped with a ‘Silver Nano Health System’ has been available, containing a mechanism that produces bactericidal silver ions that are added during the wash. After objections concerning the increased burden of silver into the environment were raised by the Swedish environmental agency and the association of water treatment works, this product was removed temporarily from the Swedish market.

Paints, lacquers and sprays for surfaces

Hospital acquired (nosocomial) infections caused by multi-resistant organisms have increased significantly. In the United States alone, more than 1.7 Million patients are affected each year, leading to about 100,000 deaths. Antimicrobial paint containing nanosilver particles could replace currently used organic biocides. In hospitals as well as in schools, offices, and in public transportation these new antimicrobial paints are already being used.

Other uses

According to the manufacturers, nanosilver is a component of a multitude of products, such as fabric softener, drinking bottles, baby pacifiers, comforters, computer keyboards, condoms, female hygiene products, and fortifying agents for plants.
Health effects

The World Health Organization (WHO) considers silver to be a toxic substance, although it only exhibits toxicity in humans and other mammals at very high doses. The US Environmental Protection Agency (EPA) declared silver to be a pesticide in 1954 and recommends the observation of limits for silver exposure: a maximal concentration of 0.10 mg in one liter of drinking water and of 0.01 mg per m³ of air at the working place should not be exceeded. A ‘reference dose’ of not more than 0.005 mg silver per kilogram of body weight per day was recommended. The US Agency for Toxic Substances and Disease Registry (ATSDR) presented a general toxic profile for silver in 1990, where results of silver exposure on brain activity and lung function gained from animal studies are described. While these limits are valid for silver, they do not, however, consider the specific properties of silver nanoparticles.

An observed detrimental effect of considerable doses of silver in humans is the permanent bluish-grey discoloration of skin and nails (argyria) and of the eyes, mucous membranes and internal organs (argyrosis). Silver is thereby deposited in tissues of the basal membranes of the skin, is no longer bioavailable, and does not damage the cells. It is not known whether silver nanoparticles are taken up by human tissue in the same manner. Argyria and argyrosis are cosmetic changes, and no resulting long-term health effects are known. It has been reported that workers who were exposed to silver and silver compounds in their workplaces for long periods of time showed changes of their blood cells and degenerative processes in the liver and kidneys. An in vitro study of rat liver cell cultures found changes in form and size of cells as well as the induction of oxidative stress resulting from concentrations between 5 and 50 μg/ml of silver nanoparticles. Another study reported that silver nanoparticles are capable of penetrating – in vitro – human cells. This experiment was performed using a diffusion cell in which a membrane consisting of intact human skin separated two chambers. The silver nanoparticles in one chamber could permeate this membrane. The location of silver nanoparticles was verified by TEM (transmission electron microscopy). Some particles could be detected in deeper skin layers.

The effects of continuous exposure to nanosilver – through nanosilver-treated fabrics (underwear, socks, bedding, etc.) on the beneficial layer of skin bacteria on healthy human skin have not been investigated. An ongoing clinical study compares the effects of a type of silver nanoparticle hand gel versus a common antibacterial hand gel.

Effects of silver and nanosilver on the environment

Around the middle of the previous century, the concentration of silver in rivers was about 300 mg/l. These emissions into the environment resulted from mining activities and from enterprises using silver as a photochemical agent. With the passage and implementation of environmental legislation such as the Clean Water Act in the USA in 1972, and the declining use of silver in photography, the concentration of silver in aquatic systems has declined in the developed world. Environmental studies during these years have demonstrated that many aquatic organisms were only able to survive in natural waters after the silver concentration decreased.

When silver ions (Ag⁺) are present, silver is second only to mercury (Hg) as the most toxic metal for all aquatic organisms. The UN International Program on Chemical Safety points out that silver ions exhibit considerable toxicity for microorganisms (1–5 μg/l) and delay the development of young trout in concentrations as low as 0.17 μg/l. A recent study summarized the available data on the eco-toxic effects of silver. Crabs and fish suffer at low concentrations (IEC₉₀ > 1 μg/l). In algae, shellfish and oysters, the silver concentration in water can be enhanced – by bio-accumulation – by more than 10⁴.

A study on the impact of silver nanoparticles found increases in mortality and hatching delay for zebrafish embryos. The later embryonic growth stages were found to be more resistant to treatment by silver nanoparticles. Among the effects observed were oedema and degeneration of body parts. TEM (transmission electron microscopy) images showed the presence of silver nanoparticles in the cells and brain of the embryos. Comparable effects were not observed following exposure to Ag⁺ ions released from a silver nitrate (AgNO₃) solution.

Silver may exert greater toxicity to aquatic organisms (such as zooplankton) if accumulated following dietary uptake. The reproductive success of small copepods diminished considerably (by 50%) when their food – algae – had been exposed to silver in a concentration of 50–100 ng/l silver in the water. Dissolved silver accumulated in the algae, resulting in 20–40 mg/g dry weight. The reason for the importance of the exposure pathways for the toxicity of aquatic contaminants and the higher toxicity of silver nanoparticles following ingestion is not completely understood.

The effects of low levels of nanosilver particles have been researched through the observation of the photosynthesis of green algae (Chlamydomonas reinhardii). It was found that the toxicity of nanosilver particles is dependent upon their concentration and is more pronounced than that of silver salts. The authors assume that the interaction of silver nanoparticles with the algae results in a more pronounced response of the Ag⁺ ion.

The environmental risks from silver can be lessened by the tendency of silver to form tightly bound complexes that are often of very low bioavailability and toxicity. In particular, complexes with sulfides reduce bioavailability under certain circumstances. It is not yet clear whether the toxicity of nanosilver is affected in the same way. It should be noted that some forms of silver nanoparticles are engineered to remain dispersed in water, and the bio-persistence of these particles in aquatic systems is not known. Despite several studies, the relation between dose and effect remains unknown. In order to be able to determine the level of contamination that will result in toxicity, the development of realistic tests remains an urgent task.

Nanosilver and silver in waste streams

A study presented by Swiss researchers estimates that in 2010 about 15% of the total burden of silver in the river Rhine could originate from nanosilver products. The researchers stressed that the majority of the nanosilver – more than 90% – contained in the waste water would be retained in the waste treatment plants, as the silver ions would form complexes with chloride and sulphide. The nanosilver particles contained in the sludge could reach agricultural soils if the sewage sludge was used as fertilizer. Silver nanoparticles may affect the microorganisms that are employed for organic and nutrient removal in the wastewater treatment. A study showed that a concentration of 0.5–1.0 mg/l of silver nanoparticles (Ø 14 nm) prevented the growth of bacteria (Escherichia coli) in order to safeguard the performance.
10.  The origin of the silver contained in the municipal wastewater of Vienna has been the subject of a study presented in the year 2000. Almost half of the total contamination was due to photographic laboratories, mainly from the processing of x-ray film. Additional sources are galvanic factories and the photo shops of printers. However, for more than a third of the silver dispersed a source could not be identified, and it was found that the permitted levels for the discharge of effluents had not been monitored. In Vienna, the amount of silver contained in the sewage sludge is more than 900 kg per year (in 2000). After incineration, the remaining ash contains about 50 mg silver/kg ash, the maximum level that is permitted.

11.  Nanoparticulate silver is neither in the United States nor in other countries generally restricted or subject to mandatory reporting. If used in medical products, the use of nanosilver is governed by rather strict rules demanding the approval and the demonstration of their safety and efficacy. However, nanosilver as a component of items of clothing, personal care products, as fortifying agents for plants, or as dietary supplements can be used without the requirement of registration or a pre-market demonstration of its safety.

12.  The European regulation REACH provides an over-arching legislation applicable to the manufacture, placing on the market, and use of chemical substances. Nanomaterials are covered by the definition of a chemical ‘substance’ in REACH, even though there is no explicit reference to nanomaterials. REACH stipulates that industrial users and importers of substances need to ensure that the chemicals it manufactures and puts on the market do not adversely affect human health or the environment. REACH is based on the precautionary principle. When a chemical substance is introduced in nanoform, an update of the registration dossier is required. A communication from the European Commission concludes that current legislation may have to be modified in light of new information and mentions the need for a rapid improvement of the scientific knowledge basis to support regulatory work.

13.  Silver has been included on the U.S. Environmental Protection Agency (USEPA) priority pollutant list since 1977. Silver is one of 136 chemical substances whose discharge into lakes and streams is subject to special restrictions. The European Union does not list silver on its list of substances of very high eco-toxicity. In high concentrations and under special conditions, the toxicity of silver may be enhanced; it can be bio-persistent and can bioaccumulate in aquatic organisms. Currently, only limited information is available about the effects and final destination of silver nanoparticles in the environment.

14.  In the European Union, the regulation of products containing nanosilver does not cover all products – a legal loophole exists for so-called ‘plant tonics’ used as fertilizer. In Germany, a nanosilver spray is freely available on the market, which has even been included on the list of plant tonics issued by the German Environmental Agency (UBA). The advertisement claims for this product mention its possible ‘off-label’ use for the treatment of psoriasis, fungal skin infections, and as a bactericide, but does not present data backing up the efficiency of this product. In their public report, the experts of the German ‘Nano-Kommission’ criticized the availability of this product even before proofs concerning the safety with respect to human health and the environment had been presented.

15.  In the United States, silver is regarded as a pesticide. Silver, as well as other insecticides and rodenticides, must first be registered before it can be distributed or sold. Products that advertise their bactericidal properties without being registered with the EPA are in violation of the FIFRA – Federal Insecticide Fungicide and Rodenticide Act. Therefore, the EPA watches only those products that are being advertised as bactericidal. If the companies refrain from mentioning the bactericidal properties of those products that have not been registered, they can continue to offer and distribute them.

16.  The US Food and Drug Administration (FDA) issued in 1996 a warning that no drug products containing colloidal silver ingredients for internal or external use are recognized as safe or effective. A final FDA ruling in 1999 pointed out the lack of reliable data concerning the safety and efficiency of these products for the treatment or prevention of any disease.

17.  The European Food Safety Authority (EFSA) published a scientific statement concerning the safety of silver hydrosol in food supplements. As the toxicological data provided by the producer dealt only with ionic silver, the experts concluded that they were not sufficient to establish the safety of silver hydrosol.
Data on the toxicity profiles of silver in nanoform are not available, and they cannot be inferred from data on their equivalent non-nanoforms. Therefore, the scientists declared their inability to assess the safety of this product.46

A number of nanosilver products have been withdrawn from the market on a voluntary basis. The washing machines containing a mechanism that added silver ions during the wash cycle were temporarily made unavailable in Sweden, and the Swedish association of pharmacies (“Apoteket AB”) decided in 2006 to discontinue the sale of silver-coated wound dressings.47

In spring of 2008, a coalition of consumer and environmental NGOs (Greenpeace, Consumers Union, Friends of the Earth, ICTA) submitted a legal petition to the EPA concerning the health and environmental risks of nanosilver products. It requested that EPA classify nanoscale silver as a new pesticidal substance that differs from silver and silver compounds currently being used. This new classification would require nanosilver products to undergo pre-market approval, and the producers could be asked to submit nano-specific testing data. The petition also demanded that EPA assesses the potential health and environmental risks of nanosilver.48

Products containing nanosilver have not been subject to approval or regulation, and there are no international agreements covering this area. For the expert group of the UK Royal Commission on Environmental Pollution, the greatest concerns at present relate to nanosilver and carbon nanotubes.49 They strongly recommend a more directed and co-ordinated research effort, an amendment of the REACH regulations to facilitate their effective application to nanomaterials, and the implementation of an early warning system.

Conclusions

In the hospital setting, nanosilver is used to manage wounds and reduce infection. Silver promises to be an effective antimicrobial agent against many different bacteria, including those that have acquired immunity against other antibiotics. The current widespread use of nanosilver-based products in many areas as a powerful antimicrobial has led to concerns. The benefits of these applications are often unclear, and it is not possible to reliably rule out potential health risks to humans and the environment.

In clinical studies, bacterial resistance to silver has been observed. The emergence of this resistance can be minimized if the level of silver ions released from the product is high and the bactericidal activity rapid. An inappropriate and indiscriminate use of antimicrobial silver products in low doses could, however, contribute to the increased occurrence of resistant bacteria. In order to preserve their important role in infection control, biocides should be used appropriately and prudently. Knowledge about the toxicity and fate of silver nanoparticles in the environment is still very limited. They may behave differently than regular silver particles, depending on their surface structure. Studies indicate a higher toxicity for silver nanoparticles than silver ions or silver compounds. They also act as a reservoir of silver ions and may release Ag+ continuously. The persistence of this nanomaterial and its potential for bioaccumulation is poorly understood. A body of work will be necessary for definitive conclusions regarding the risks that nanosilver poses for natural ecosystems.

The governmental agencies in charge of health and environmental issues are confronted with the formidable challenge of regulating the numerous, widely available consumer products containing nanosilver. Our knowledge with respect to the potential health risks of these products is still fragmentary. As more and more products enter the market, adequate resources for research, correlation between research and decision making, and monitoring systems for the detection of threats are more necessary than ever in order to reap the potential benefits while limiting the unnecessary risks of nanotechnology.

Notes and References

1 Bourne Research, in “Nanotechnology News” (19. Apr. 2006): “Silver nanoparticles one of the fastest growing product categories in the nanotechnology industry”.


9 SCENIHR Opinion of 19 January 2009


15 www.biogate.de.


Final repart. Ressourcen Management Agen- tur (RMA) commissioned by Magistratsabteilung 22 – Umweltschutz der Stadt Wien.


Meeting of the EPA-Committees concerning pesticides, Nov. 8, 2006 (p. 323).

US Federal Register, Vol. 64, N. 158 (Aug. 17, 1999), Department of Health and Human Serv- ices/Food and Drug Administration: Over-the Counter Drug Products Containing Colloidal Silver Ingredients or Silver Salts.


Ergänzung zu Dossier Nr. 010, Stand: November 2010


Addendum for Dossier No. 010, Version: November 2010

At the end of 2009, the German Federal Institute for Risk Assessment (BfR – Bundesinstitut für Risikobewertung) recommended "to avoid the use of nanoscaled silver or nanoscaled silver compounds in foods and everyday products … until such time that the data are comprehensive enough to allow a conclusive risk assessment which would ensure that products are safe for consumer health." The President of the Institute endorsed this position in a press release in June 2010 stressing that nanosilver has no place in food, textiles or cosmetics.