Nanomaterials as an alternative for preservative and biocidal substances

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Abstract

Silver and silver compounds have been used for many years, its antibacterial effect is used in medicine and cosmetic and many other cathegories of science. Silver (Ag) is metal IB group of Periodic Table of Elements. It is a precious metal. It is a minimal chemical activity and its effect is only a physical activity. Silver has strong bactericidal and fungicidal properties known since antiquity. For this reason, it is very difficult for bacteria to create defense mechanisms. Silver was already used in Ancient Greece and Rome to prevent infection. The healing properties were described by Hippocrates, and the Phoenicians stored water and wine in vessels made of silver. In the Middle Ages, Silver was used for disinfection of water and foodstuff preservation, as well as to treat burns and ulcers. Since the 17th century, Silver has been used for disinfection of water and is described as a universal medicament. In 2008, the antimicrobial activity of nanosilver on anthrax was also published. Nano silver is also used as an additive in textiles used for people with post-burn wounds, ulcers or various types of atopy of the skin. Many surgical instruments are silver coated, including dialysis instruments (catheters), wherever it is necessary to reduce the risk of bacterial infections. The best silver effect is obtained when it is in the form of nanoparticles, then its active surface increases and the ability to affect microorganisms as well.

Key words:

antibacterial activity, nanosilver, safety to use, biocidal efect

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In the face of ever-changing legislation, including a reduction in the amount of preservatives used in cosmetics, as well as a problem in which bacterial strains are formed that are able to create mechanisms for inactivation of biocides, including preservatives or antibiotics, it seems to be a very important search for alternatives. One of the most interesting and promising areas currently used in products is nanotechnology, the growing resistance of microorganisms to metal ions and antibiotics, researchers from different areas of science have become interested in the antimicrobial properties of nano-silver [1], recognizing them as a new generation of antibacterial agents [2].

Nano-silver is the most popular and widely researched metal and from the perspective of the use of nanomaterials, it is also an important a preservative and biocidal. Nano-silver combines features of a precious metal (chemical passivity) and high fragmentation, i.e. it shows minimal chemical activity and its effect is limited to physical activity. This, among other things, makes it very difficult for bacteria to produce defence mechanisms [3].

The evaluation of nanomaterials is carried out by scientific committees both in Europe and around the world, including ECHA – European Chemicals Agency, NMWG – (ECHA) Working Group on Nanomaterials, GAARN – (ECHA) Evaluation Group Registered Nanomaterials, OECD – Organization for Economic Cooperation and Development, SCCS- Scientific Committee on Consumer Safety.

According to the definition of Regulation 1223/2009 / EC on cosmetic products, „A nanomaterial means an insoluble or biopersistent and intentionally produced material having at least one external dimension or internal structure on a scale of 1 to 100 nm [4]". There are no specific requirements for nanomaterials under REACH and CLP regulation, but under the Biocides Regulation (BPR) nanomaterials are materials or chemicals that are manufactured and used on a very small scale. In addition, 50% of particles must have a size of 1-100 nm particles which are in the free state or in the form of an aggregate or agglomerate. The particles obtained in this way have a very developed active surface, which allows for a significant increase in efficiency with a small amount of nano. It is directly visible in price of the used material. Nano-silver combines features of a precious metal (chemical passivity) and high fragmentation, i.e. it shows minimal chemical activity and its effect is limited to physical activity. It is known that the effectiveness of nano-silver is related to, among, size [5], but also from the shape. Triangular nanoparticles are more reactive than spherical particles [6].

The variety of obtained and produced nanomaterials of various physicochemical forms depends, among other things, on production methods, which is why it is necessary for the European Commission to cooperate with the industrial sector in the research and implementation of nanomaterials. It is very important for industry to agree with research units so that products placed on the market are well-defined, researched and, above all, safe for human health.

The unique properties of silver have been known from centuries. Metallic silver was used as well as its compounds (silver nitrate or silver sulphadianisin), using their antibacterial action in medicine and cosmetology. When the pharmaceutical industry developed the production of antibiotics on a large scale, that the more expensive and less accessible became less frequently used.

Many antimicrobial substances (including antibiotics) have proved irritant and toxic effects, that's way it's neccecery search new solutions which are safer for humans and the environment and more accessible to the general public [7,8,9].

The health risk of using nanosilver depends on the potential exposure, if there is no systemic absorption, the potential risk is possibly associated with exposure to the site of exposure, i.e. lung, liver or skin. The capture of nanomaterials and absorption through the skin is either very low or absent. The systemic effect of oral nanomaterials is also considered to be much lower than for example water-soluble molecules. The limited absorption of nanomaterials makes it very difficult to assess the distribution of molecules into organs and, consequently, toxokinetics [10]. The probable antimicrobial mechanism of nano-silver does not dependt on a chemical reaction, but on the ability to transfer or store atomic oxygen or through a bielectric action. Absorbed oxygen creates cavities in cell membranes, which increases their permeability and

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generates free radicals that destroy cell membranes [11]. According to some researchers, nanoparticle silver binds with sulfonic groups of peptidoglycan found in bacterial cell membranes, penetrates deep into the cell, is embedded in bacterial DNA chain and prevents its replication [12,13] and blocks the reaction in the respiratory chain, which directly leads to cell death [14,15,3,16]. Murein, the main component of peptidoglycans, is a building material of a bacterial cell wall and does not occur in animal cells, which prevents the penetration of nano-silver into undamaged human or animal cells.

Nano silver has a two-track anti-inflammatory effect:

- inhibits pro-inflammatory factors;
- activates apoptosis in inflammatory cells without induction into healthy cells.

There is no serious report about silver allergy [17], but the possible silver toxicity expressed by argyria is possible in the presence of a large open wound and a high concentration of metal ions and not nanometric particles. Many studies on nanoparticle silver suggest a lack of toxicity [18] fear of nanoparticles is probably due to their small size and variable properties, which could suggest that they are dangerous, although this is not confirmed [19].

In medicine, antibacterial properties of nano-silver have been used for a long time, for example in the coating of implants, catheters [20,21,22] as an addition to bone cement [23], antibacterial gel for disinfection [23,24].

Studies on animals treated with silicone valves coated with nano-silver confirm good biocompatibility [25]. The use of nano-silver incorporated into the structure of the polymer significantly delayed the formation of the biofilm [26], in-vivo mouse-testing in 10-day tests also confirmed the absence of toxicity [27]. Next step, after such an exellent is to conduct extensive in-vivo clinical trials on humans.

In medicine, nano-gels or nanocrems are very often used, which have a great impact on the regeneration of wounded or burned skin.

Nano-silver and antibacterial properties are seen as good, safe and non-toxic. It is used for coating medical materials to form an antibacterial coating on their Surface [28]. Antibacterial properties of nano-silver mainly on Staphylococcus aureus, Pseudomonas aeruginosa, Staphylococcus epidermidis was observed while using used for coating catheters which are used in brain surgery [29,30]. No nano-silver toxicity has been observed in this type of surgical applications [31] and the risk of a bacterial infection has been eliminated [32].

Nano-silver is used as an additive in polymeric bone cement (PMMA- poly(methyl methacrylate), which is used in hip and knee joint operations [23]. The antibacterial properties of nano-particles reduce the risk of infection or rejection. The risk of complications due to bacterial infections in this type of operations is quite high and amounts to 1-4%, the use of bone cement antibiotics reduces the risk of infection to 0. 4-1. 8%. However, the use of an antibiotic is not beneficial due to the high risk of bacteria becoming resistant to the active substances in the antibiotic used [33].

Although very successful studies confirming the lack of toxicity of nanosilver and its wide application in medicine [34], care and hygiene products [35,36] used mainly for burns, Steven-Johanson's syndrome, pemphigus [37], toxic skin necrosis, chronic ulcers [38] the subject is still being treated with great concern. There is no serious report of silver allergy to [17], whereas possible argyria-based silver toxicity is possible in the presence of a large open wound and at a high concentration of metal ions rather than nanometric particles.

Many studies on nanoparticle silver suggest that there is no toxicity [39] concern that arises from nanoparticles is probably due to their small size and variable properties, which could suggest that they are dangerous, although this is not confirmed [19]. In-vitro studies on various types of cells suggest cytotoxic effects of nanosilver and reaction to e. g. cell mitochondrial or cytotoxic effects associated with ROS production [40]. However, inhalation and oral administration studies in 28-day rat trials do not confirm the toxicity effects [41].

Each nano-material must be considered individually and the potential risks of nano-materials must be taken into account when assessing toxicity.

The particle size may be the same as/compatible with the molecular gap in the DNA chain, which may entail the risk of a possible nanoparticle being built

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into the DNA helix, which may directly lead to chain destruction or denaturation of proteins and enzymes and produce free radicals [42].

The Scientific Committee on Emerging and Newly Identified Health Risks considers that there is no consistent causal link between the size of nanomaterials and risk for humans. In order to be able to assess the safety of nanoparticles, it is important to know whether nanoparticles of substances can actually pass through any of the body's barriers (respiratory tract, skin, digestive tract).

The studies carried out show that there is no systemic absorption of silver nano, therefore the health risk of using silver nano is possibly related to the effects at the exposure site, such as lungs (inhalation), liver (oral administration) or skin (dermal contact). In the case of skin, the uptake of nano-materials and absorption through the skin is either very low or non-existent. This is also confirmed by the experience and opinions of the scientific committees concerning the nano-titanium oxide or nano-zinc oxide. The systemic effect of nano-materials after oral dosage is also considered much lower than in the case of e.g. water-soluble molecules. Limited absorption of nano-materials makes it very difficult to assess the distribution of molecules to organs and thus toxicokinetic evaluation [43].

Conclusion

The literature review confirmed the wide use of nano-silver. The results of the application are very good and the applied preparations containing nano-silver do not have any defects of the antibiotics used. No evidence was found, even in cases of argyria, that silver in any form, let alone nano-silver, has a negative or toxic effect on the human body and its systemic effects [43] In vitro studies have shown the harmful effect of nano-silver particles, however, many Samberg researchers [44], Nymark, Walmslay, Park [45], agrees that genotoxic additives may be added to prevent e.g. agglomerations and that this risk can be eliminated by thorough leaching.

In vivo studies the toxicity of nanosilver has not been confirmed [46,47].

References

1. Ping G., Li H, Yang X., Preparation and antibacterial activity of Fe3O4@ Ag nanoparticles, Nanotechnology 2007; 18, 604-611
2. Chen X, Schluesener HJ. Nanosilver: a nanoproduct in medical application, Toxicol Lett, 2008, 176, 1-12
3. Morones J., Elechiguerra J., Camacho A. The bactericidal effect of silver nanoparticles Nanotechnology. 2005, 16(10):2346-53
4. Dz. Urz. UE L 342 z 29.12.2009 r., str. 59
5. Raimondi F., Scherer GG., Kötz R., Nanoparticles in energy technology: examples from electrochemistry and catalysis Angew Chem Int Ed Engl. 2005, 8;44(15):2190-2209
6. Pal S., Tak YK., Song JM. Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the Gram-negative bacterium Escherichia coli, Appl Environ Microbiol. 2007,73(6):1712-1720
7. Sondi I., Salopek-Sondi B., Silver nanoparticles as antimicrobial agent: a case study on E. coli as a model for Gram-negative bacteria., J. Coll. Int. Sci. 2004, 275, 177-182
8. Fresta M., Puglisi G, Giammona G, Cavallaro G, Micali N, Furneri PM., Pefloxacine mesilate- and ofloxacin-loaded polyethylcyanoacrylate nanoparticles: characterization of the colloidal drug carrier formulation J Pharm Sci. 1995, 84(7):895-902.
9. Hamouda T., Hayes MM, Cao Z, Tonda R, Johnson K, Wright DC, Brisker J, Baker JR Jr A novel surfactant nanoemulsion with broad-spectrum sporicidal activity against Bacillus species J Infect Dis. 1999, 180(6):1939-1949
10. SCENIHR opinion of 12 grudnia 2013
11. Kim JS., Kuk E, Yu KN. Antimicrobial effects of silver nanoparticles, Nanomedicine. 2007, 3(1):95-101.
12. Siddhartha S., Tanmay B., Arnab R. Characterization of enhanced antibacterial effects of novel silver nanoparticles, Nanotechnology 2007, 18, 225
13. Yang W., Shen C, Wang J. Food storage material silver nanoparticles interfere with DNA replication fidelity and bind with DNA, Nanotechnology. 2009, 25;20(8):085102.
14. Feng QL., Wu J., Chen GQ. A mechanistic study of the antibacterial effect of silver ions on Escherichia coli and Staphylococcus aureus, J Biomed Mater Res. 2000, 15;52(4):662-8.

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15. Sondi I., Salopek-Sondi B. J., Silver nanoparticles as antimicrobial agent: a case study on E. coli as a model for Gram-negative bacteria J Colloid Interface Sci. 2004, 1;275(1):177-82.
16. Juan L., Mo A., Zhimin Z. Antibacterial titanium plate deposited by silver nanoparticles exhibits cell compatibility, Int J Nanomedicine. 2010; 5: 337–342.
17. Leaper D., Silver dressings: their role in wound management, Int Wound J. 2006;3(4):282-94.
18. Rai M., Yadav A., Gade A. Silver nanoparticles as a new generation of antimicrobials, Biotechnol Adv. 2009;27(1):76-83
19. Braydich-Stolle L., Schlager J., Hofmann Marie--Claude, In Vitro Cytotoxicity of Nanoparticles in Mammalian Germline Stem Cells, Toxicol Sci. 2005; 88(2): 412–419.
20. Samuel U., Guggenbichler JP. Prevention of catheter-related infections: the potential of a new nano-silver impregnated catheter., Int J Antimicrob Agents. 2004;23 Suppl 1:S75-8.
21. Roe D., Karandikar B., Bonn-Savage N., Antimicrobial surface functionalization of plastic catheters by silver nanoparticles, J Antimicrob Chemother. 2008, 61(4):869-766
22. Vonberg RP., Gastmeier P.J. Hospital-acquired infections related to contaminated substances, J Hosp Infect. 2007, 65(1):15-23.
23. Alt V., Bechert T., Steinrücke P., An in vitro assessment of the antibacterial properties and cytotoxicity of nanoparticulate silver bone cement, Biomaterials. 2004, 25(18):4383-4391.
24. Kumar A., Vemula PK., Ajayan PM. Silver-nanoparticle-embedded antimicrobial paints based on vegetable oil Nat Mater. 2008, 7(3):236-241.
25. Jamieson W., Seven-year results with the St Jude Medical Silzone mechanism prosthesis, J. Thorac. Cardiovasc. Surg. 2006, 137, 1109-1115
26. Samuel U. Preventation of catheter – related infectons: the potential of a new nano-silver impregnated catheter, Int. J. Antimicrob. Agents 2004, 23, 75-78
27. Roe D., Karandikar B., Bonn-Savage N., Antimicrobial surface functionalization of plastic catheters by silver nanoparticles, Chemother. 2008, 61, 869-876
28. Chaloupka K., Malam Y., Seifalian AM. Nanosilver as a new generation of nanoproduct in biomedical applications, Trends in Biotechnology, 2010, 28,11, 580-588
29. Whitby M., Pessoa-Silva Cl., McLaws M. Behavioural considerations for hand hygiene practices: the basic building blocks, J. Hosp. Infect. 2007, 65, 39-42
30. Orsi G., Scorzolini L., Franchi C. Hospital-acquired infection surveillance in a neurosurgical intensive care unit, J. Hosp. Infect. 2006, 64, 23-29
31. Lackner P., Beer R. , Broessner G., Efficacy of silver nanoparticles-impregnated external ventricular drain catheters in patients with acute occlusive hydrocephalus, Neurocrit. Care 2008, 8, 360-365
32. Galiano K., Pleifer C., Engelhardt K., Silver segregation and bacterial growth of intraventricular catheters impregnated with silver nanoparticles in cerebrospinal fluid drainages., Neurol. Res. 2008, 30, 285-287
33. Jiranek W., Hanssen A., Greenwald A., Antibiotic--loaded bone cement for infection prophylaxis in total joint replacement., Bone Jt. Surg. Am. 2006, 88, 2487-2500
34. Chen X., Schluesener H., Nanosilver: a nanoproduct in medical application, Toxicol. Lett, 2008, 176, 1-12
35. Impellitteri C., Tolaymat T., Scheckel K., The speciation of silver nanoparticles in antimicrobial fabric before and after exposure to a hypochlorite/detergent solution, J. Environ. Qual. 2009, 38, 1528-1530
36. Reijnders L., Cleaner nanotechnology and hazard reduction of manufactured nanoparticles, J. Cleaner Prod. 2006, 14, 124-133
37. Vlachou E., Chipp E., Shale E. The safety of nanocrystalline silver dressings on burns: a study of systemic silver absorption, Burns 2007, 33, 979-985
38. Sibbald R., Contreras-Ruiz J., Coutts P., Bacteriology, inflammation, and healing: a study of nanocrystalline silver dressings in chronic venous leg ulcers, Adv. Skin Wound Care 2007, 20, 549-558
39. Rai M., Yadav A., Gade A., Silver nanoparticles as a new generation of antimicrobials, Biotechnology Advances 2009, 27, 76-83
40. Carlson C., Hussain S., Schrand A., Unique cellular interaction of silver nanoparticles: size-dependent generation of reactive oxygen species, J. Phys. Chem. B 2008, 112, 13608-13619
41. Carlson C., Hussain S., Schrand A., Unique cellular interaction of silver nanoparticles: size-dependent generation of reactive oxygen species, Inhal. Toxicol. 2008, 20, 575-983

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42. Hsin Y., Chen C., Huang S. The apoptotic effect of nanosilver is mediated by a ROS- and JNK-dependent mechanism involving the mitochondrial pathway in NIH3T3 cells, Toxicol. Lett. 2008, 179, 130-139
43. SCENIHR opinion of 12 grudnia 2013
44. Samberg M., Orndorff P., Monteiro-Riviere N., Antibacterial efficacy of silver nanoparticles of different sizes, surface conditions and synthesis methods, Nanotoxicology, 5, 244-53
45. Kim W., Kim J., Park J., Ryu H. Histological study of gender differences in accumulation of silver nanoparticles in kidneys of Fischer 344 rats, J Toxicol Environ Health A. 72, 1279-1284, 2009
46. Asghari S., Johari S., Lee J. Toxicity of various silver nanoparticles compared to silver ions in Daphnia magnaJournal of Nanobiotechnology 2012 10:14. doi:10.1186/1477-3155-10-1
47. Asare N., Instanes C., Sandberg W., J Cytotoxic and genotoxic effects of silver nanoparticles in testicular cells. Toxicology 2012, 291, 65-72

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