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Silver nanoparticles – a material of the future…?

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Abstract: The paper presents properties of nanomaterials and methods of their principal applications. Environmental aspects of using nanomaterials and reasons for their toxicity are also reviewed. The vast part of the paper is devoted to properties, application and market of silver nanoparticles. Their biocidal activity is clarified. However, silver nanoparticles may cause environmental pollution. Reasons for their toxicity have been also described.

Keywords: nanotechnology, silver nanoparticles, biocidal activity, environment pollution

1 Introduction

Nanotechnology is a rapidly growing field of science, which is particularly interesting for researchers since the early 90s of the last century. This area has become an integral part of modern technology [1]. Nanotechnology is said to be a “key technology of the 21st century”, which is the result of its interdisciplinary nature [2].

Nanomaterials are increasingly becoming a part of our daily lives. They are characterized by new properties that do not accompany to their counterparts existing at the macro scale. Therefore, nanomaterials are used in innovative products and processes [3]. According to the recommendations of the European Commission 2011/696/EU, nanoparticles (also called nanocrystals or nanopowders) are defined as “natural, randomly created or manufactured materials containing particles in a free state or as an aggregate or agglomerate, wherein at least 50% of the particles has one or more dimensions in the range 1–100 nm. In certain cases, justified on grounds of environmental protection, health, safety or competitiveness, one can take a value between 1–50%”. The recommendation 2011/696/EU also states that: “Where technically feasible and requested in specific legislation, compliance with definition may be determined on the basis of the specific surface area by volume. A material falls under the definition if its specific surface area by volume is greater than 60 m^2 cm^{-3}” [4].

The vast majority of manufactured nanomaterials are available in different shapes and sizes. It is expected that their use will significantly increase in the next decade. Currently, nanomaterials are produced in the hundreds of thousands of tons. They are used in a variety of products, including consumer electronics, automobiles, aerospace, sporting goods, household, hygiene, construction and medical. According to the definition, nanoparticles occur naturally or can be prepared intentionally. The latter group is divided into the following categories [3]:

1. Non-metallic inorganic nanoparticles (TiO_2, SiO_2, ZnO, $Al(OH)_3$, Fe_2O_3, Fe_3O_4, CeO_2, ZrO_2, CaO, ITO, ATO)
2. Metals and metal alloys (Au, Ag, Pt, Pd, Cu, Fe, Ni, Co, Al, Mn, Mo)
3. Nanomaterials based on carbon (fullerenes, carbon nanotubes, carbon nanofibers, graphene)
4. Nanopolymers and dendrimers (polymeric nanoparticles, polymer nanotubes, nanowires and nanorods, nanocellulose, nanostructured polymer films)
5. Quantum dots (cadmium telluride, cadmium selenide, quantum dots free of cadmium).

Production of nanomaterials may be carried out by three types of methods:

1. biological (production of nanoparticles by microorganisms),
2. chemical (e.g. chemical vapour deposition CVD, chemical reduction),
3. physical (e.g. physical vapour deposition, PVD, production of thin films).

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2 Properties of nanomaterials

The properties and behaviour of materials at the nanoscale differ significantly when compared to microscale. The nanoparticles show enhanced electrical, optical and magnetic properties. There are two basic factors which cause that nanomaterials behave differently than macromaterials. These are surface effects (properties of surface atoms fraction) and quantum effects. These factors affect the chemical reactivity of materials, as well as they determine their mechanical, optical, electrical and magnetic properties [5].

Compared to microparticles, the fraction of surface atoms in nanoparticle is increased. In relation to microparticles, nanoparticles are characterized by increased mass of surface particles. The ratio of surface area to mass in nanometric particles is 1000-fold greater than in micrometric particles [3]. The nanometric particles are thus characterized by increased chemical reactivity, which is approximately 1000-fold higher compared to micromaterials. Quantum dots are the materials which in greatest extent use the quantum effects [6]. Their electron behaviour is similar to the behaviour of single atoms or small molecules. Quantum dots are described as artificial atoms. Another result of the quantization effect is the appearance of magnetic moments in nanoparticles, while they do not occur in bulk materials such as gold, platinum or palladium. Magnetic moments are due to the presence of several unpaired electron spins formed by a few hundred atoms. Quantum effects also affect the ability to accept or donate electrical charge, which determines the catalytic ability [3].

3 Application and market

Favourable modification of the properties of materials by changing their size is also possible, enhancing their profitability. Today, nanotechnology is used in a broad spectrum of scientific fields (biotechnology, medicine, pharmacy, ecology, electronics and others). The possibility of applying nanomaterials for use in agriculture, veterinary medicine, the food industry and cosmetology is also being explored [7]. The group of materials of particular interest includes: nanoparticles of silver, gold, zinc, selenium, titanium dioxide and carbon nanotubes [8]. In addition, it is expected that in the near future, the scope of research will enable materials to be obtained with previously unknown properties. Medical bioengineering is an area where nanotechnology has found many applications [9]. In this area, nanotechnology is mainly used in the field of diagnostic tests – as a tool for the detection of diseases and their imaging and monitoring of pharmacological therapy (mainly the system of drug delivery and disposition in the human body) [10]. Nanomaterials are increasingly an integral part of orthopaedic implants and scaffolds for tissue bioengineering. The main advantage of such solutions is the ability to manipulate the properties of biomaterial surfaces on a nanometric scale. That results in the unmistakable increase in the level of biocompatibility of implants used [11]. The beauty industry is another sector in which nanotechnology is used [12,13]. In this field, it is very important to protect the products against microbial contamination which may occur during production of cosmetics or their storage. Before nanotechnology permanently penetrated the cosmetic industry, organic compounds such as parabens [14] and phenoxyethanol [15] had been used to control unwanted microbial flora. Studies revealed the irritant effects of these types of preservatives, especially parabens, in relation to epidermis [16]. What is more, their increased susceptibility to UV light has been confirmed [17,18]. The harmful preservatives have been partially replaced by metal nanoparticles, in particular silver nanoparticles [19]. Nanotechnology is also used in information technology. In recent decades a term “computers of new generations” has become a common phenomenon. These are the computers which are produced with the use of nanomaterials as component elements that increase efficiency and energy savings of these devices. In 2007 IBM’s research team published the results of using self-assembling nanostructures in the production of chips. It was found that such a novel solution allows an increase the current flow of up to 35% in the chips. The company estimates that a similar application of nanomaterials will quadruple the number of chip transistors, so that future computers will work more efficiently [20]. The properties of nanomaterials also allow using them in the energy sector. The application of a new generation of catalysts, whose construction is based on nanostructures, results in a significant reduction in energy consumption. Studies carried out during the production of biomass fuels revealed that the use of nanoporous membranes facilitates an increased efficiency of the process. It was noted that no other ways of reducing processing costs and increasing the yield of energy processes are as efficient as using nanostructured materials [20].

Nanomaterials have also found an application in the industry of paints and coatings. For example, paints and coatings containing nanomaterials are used in the aerospace, automotive, construction and hygiene

Table 1: Market for nanomaterials - global production in 2014 [3].

Production	Nanoparticles	Minimum global production volume [tons]	Maximum global production volume [tons]
High volume production	Titanium dioxide	60,000	150,00
	Zinc oxide	32,000	36,000
	Silicon dioxide	185,000	1,400,000
	Aluminium oxide	5,000	10,100
	Carbon nanotubes	1,550	1,950
	Nanoclays	25,000	51,000
	Cerium oxide	880	1,400
Low volume production	Quantum dots	4.5	9
	Antimony tin oxide	120	225
	Copper oxide	290	570
	Silver	135	420
	Nanocellulose	400	1,350
	Bismuth oxide	35	55
	Cobalt oxide	5	<10
	Dendrimers	0.3	1.25
	Fullerenes & POSS	40	100
	Graphene	60	80
	Gold	1	3
	Iron oxide	9	45
	Magnesium oxide	15	30
	Manganese oxide	2	3.5
	Nickel	5	20
	Zirconium oxide	80	300

industries. By introducing nanoparticles in the structure of materials, it is possible to give products antibacterial and anticorrosion properties and protection against UV radiation. The resultant structures can also be easier to clean. Sigma Aldrich is currently the leading supplier of nanomaterials. BASF and Evonik Degussa are its close competitors, in particular in the offer of nanomaterials in cosmetics and personal hygiene. According to a statement issued by the European Commission, the global amount of manufactured nanomaterials is close to 11.5 million of tonnes, which is equivalent to their market value reaching 20 billion per year (this estimate also applies to soot and amorphous silica). It is estimated that the current global market for nanomaterials is from 300 000 tons up to 1.6 million tons. The Asian region accounts for largest market share (approx. 34%), followed by North America (approx. 31%) and Europe (approx. 30%) (Table 1, Fig. 1) [3].

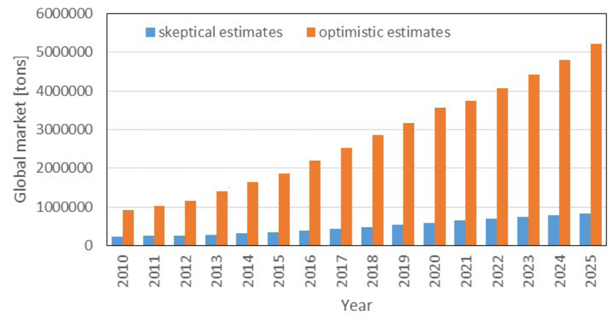

Figure 1: The global market for nanomaterials [3].

4 Environmental aspects of the use of nanomaterials

Global demand for nanomaterials increases year by year. It is related with inevitable penetration of nanoparticles into the environment. It may have a substantial impact on the functioning of living organisms. The Commission to the European Parliament, the Council and the European Economic and Social Committee claims that monitoring the presence of nanoparticles in the environment is a major technical challenge. The small size of nanomaterials, and their low, and sometimes trace level, abundance in environmental samples is the main problem. Despite the fact that science has some methods of controlling environmental pollution by nanomaterials, the current state of development assumes that they are not fully verified. That makes it difficult to compare the available data and does not allow for a thorough analysis of the problem [8]. There is no doubt that the presence of nanoparticles in many consumer products generally improves the quality of life, providing numerous benefits and economic utility. The nanoparticles have been introduced in the formulation of different types of products. Because of the nanometric particles size, one may not observe their chemical and physical effects on living matter [21]. Penetration of nanomaterials into environment and its specific reactivity can cause degradation effects. Therefore, there is a need to develop techniques to monitor potential risks [22]. The impact of nanoparticles on the environment can take many forms. It is worth noting that weather factors such as temperature or humidity can also affect the physical properties of nanoparticles (size and stability). These processes are lengthy, but one should be aware that nanoparticles once introduced into the environment affect pollution of soil, surface water and groundwater as well as flora and fauna. Living organisms may be not exposed to nanomaterials during their life, but toxicological concerns can be a problem in the future when the processes of penetration of nanomaterials reach the stage of direct contact with successive generations of living matter [1].

Mostly, the toxicity of the product is determined as a function of its mass. In the case of nanomaterials this assumption is incorrect and one must use a different technique for risk assessment. Nanoparticles can penetrate into living organisms by means of swallowing, inhalation, absorption and penetration through the skin. Understanding the life cycle of nanoparticles in the environment and their chemical stability is an important step in the process of determining their influence on living organisms. Despite the lack of thorough research, a framework to conduct analysis has been developed. It involves:

- physicochemical characteristics of particles which may have a negative effect on living matter,
- familiarity with the life cycle of nanomaterials and the mode of their penetration into living organisms,
- selection of appropriate techniques to measure the degree of an organisms exposure to the nanomaterials,
- defining the rules governing deployment of nanoparticles in different parts of living organisms,
- developing mechanisms for inducing conditions [1].

5 Mechanisms of toxic effect of nanomaterials on organisms

In the literature one can find two main hypotheses explaining the toxic effects of nanoparticles on living organisms [23]. The first hypothesis that the harmful activities of nanoparticles is due to the release of metal ions [23,24]. The second states that the toxicity is induced by formation of ROS (reactive oxygen species). The resulting free radicals are able to damage any components of the cell, and initiate the production of ever-increasing numbers of reactive oxygen species [25]. For example, generated free radicals are able to oxidize the double bonds of fatty acids in cell membranes, resulting in increased permeability of membranes, and increased permeability contributes to the osmotic stress [26]. ROS may also inhibit the activity of enzymes by binding to them and changing the helix of DNA, which can lead to cell death. The formation of larger amounts of reactive oxygen species is induced by the higher surface area of nanoparticles as compared to their larger analogues [26]. Nanomaterials may also damage the cell membrane, oxidize proteins, be genotoxic as well as interfer with the conduction of energy [25].

Balancing the risks and benefits of nanomaterials is essential in carrying out safe and responsible studies of their development. There is a general belief that research on the toxicity of nanomaterials are lagging behind the desire for their commercial use [27]. There is an urgent need to standardize safety evaluation of nanomaterials, which would facilitate the assessment of exposure to nanomaterials and risks arising from their use. The aim of such an action is a safe assimilation of nanotechnology in society. Environmental organizations and public opinion treat silver nanoparticles as a key factor in campaign against the use of nanomaterials [3].

6 Silver nanoparticles

Living organisms are exposed to bacteria, viruses and fungi. Silver nanoparticles, thanks to their unique properties, are seen as a leader in the fight against pathogenic microbial activity. Silver has a strong effect of slowing their activity down. Compared to the solid form of silver, the increased surface area of silver nanoparticles is feature responsible for their behaviour in this regard [28]. This results in better contact with microorganisms, and more effective biocidal activity [29]. Silver nanoparticles are effective against a broad spectrum of Gram-negative and Gram-positive bacteria, including some antibiotic-resistant strains [30]. The group of Gram-negative bacteria, against which the biocidal activity of silver nanoparticles has been confirmed, includes: *Acinetobacter* [31], *Escherichia* [32], *Pseudomonas* [33] and *Salmonella* [34]. The effective action of silver nanoparticles was also reported against Gram-positive bacteria: *Bacillus* [35], *Enterococcus* [36], *Listeria* [37], *Staphylococcus* [38] and *Streptococcus* [39]. Recent studies have shown that the use of silver nanoparticles in combination with certain antibiotics such as penicillin G, amoxicillin, erythromycin, clindamycin and vancomycin, creates a synergic effect in the fight against *Escherichia coli* and *Staphylococcus aureus* [40]. Research has shown that silver nanoparticles can also be an effective weapon in the fight against viruses [41] by inhibiting their replication. Their activity has been confirmed even against the HIV-1 [42] and influenza virus [43].

The efficiency of processes leading to destruction of viruses strictly depends on the shape and size of nanoparticles [42]. Silver nanoparticles are also not indifferent to certain fungi. Studies have shown that they are effective and fast-acting agent that destroys different types of fungi such as *Aspergillus* [44], *Candida* [45] and S*accharomyces* [30].

Table 2: The use of silver nanoparticles - a commercialization level [3].

Applications	Research	Applied research & development	Demonstration	Commercial
High Volume Applications				
Anti-microbials in wound care				
Anti-microbial medical devices				
Anti-microbial textiles				
Water purification				
Conductive inks and films				
Low Volume Applications				
Food packaging				
Novel Applications				
Smart glass				

7 Application of Silver nanoparticles

Progress in the development of nanotechnology, particularly in the development of new methods of acquiring silver nanoparticles, meant that the introduction of silver nanoparticles to a variety of consumer products has become very popular (Table 2) [3,46]. The unique properties of silver nanoparticles attracted the attention of many industries, particularly those in which an antiseptic effect is particularly desirable. This applies to food, textile, construction, medicine, cosmetology, pharmacy and other branches of industry [47,48]. Silver nanoparticles are also used in the power industry [49] and in biomedicine, in which they act as receptors in labelling of biological materials[50]. Fig. 2 illustrates the most common use of silver nanoparticles in various areas.

A particularly important issue is the use of silver nanoparticles in therapy. A process for preparing synthetic materials impregnated by silver nanoparticles which may be used for production of catheters has been developed. The coating containing silver nanoparticles has antibacterial and disinfectant properties. In *in vitro* tests confirmed the inhibition of bacterial flora , with the effect maintained for a further 72 hours [51].

A group of market products containing silver nanoparticles includes, among others, Acticoat Wound Care with nanocrystalline silver, and I-Flow SilverSoaker Nanosilver catheters. SilvrSTAT ABL™ from ABL Medical during laboratory testing within a few minutes causes the destruction of *Staphylococcus aureus* (MRSA) - a strain resistant to methicillin and *Enterococci bacteria* - resistant to vancomycin [3].

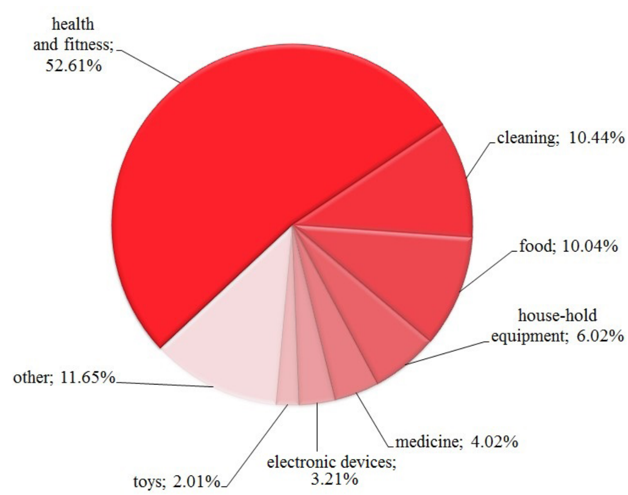

Figure 2: Categories of products containing silver nanoparticles [51].

In US Patent 6379712 B1 Yan and Cheng described a process for preparing granules coated with silver nanoparticles acting as an antibacterial and antifungal agent. This product inactivates a broad range of bacteria, such as *Staphylococcus aureus*, *Chlamydia trachomatis*, *Providencia stuarti*, *Vibrio vulnificus*, *Bacillus subtitilis* and *Streptococcus paratyphi*. The composition of the matrix granules allows their use as a component of various types of hygiene preparations, such as ointments, lotions, mouth washes, eye or other infected part of the body [52].

The properties of a polylactide composite with silver nanoparticles were also examined. Its biocidal activity was observed against two bacterial strains – *Escherichia coli* and *Staphylococcus aureus*. A 5% concentration of silver nanoparticles was sufficient to reduce bacterial growth by about 70%. The authors report that the material may be an ingredient of a fibrous membrane used as a scaffold for tissue engineering [53]. Silver nanoparticles are also used in the materials applied in wounds and burns dressings. Nanostructured silver particles are embedded in the hydrophilic coating as a part of a fibre composite. This layer is in direct contact with the surface of the skin and its main task is to disinfect wounds and absorb body fluids [54]. The use of silver nanoparticles in order to reduce the attachment of bacteria to the surface of dental implants (to prevent biofilm formation, which causes the risk of infection around the implant surface) is also known. The presence of silver nanoparticles in dental materials helps to avoid contamination and infection [55,56]. Nadworny and co-workers attempted to clarify the mechanism of action of silver nanoparticles with anti-inflammatory properties. Evaluation of such activity was based on the reaction of the skin tissue after treatment with the silver nanoparticles. The skin derived from pigs was used in studies. It was found that silver nanoparticles inhibit the development of inflammation. This was confirmed by reduced levels of TNF-α – a protein belonging to the group of cytokines, which increased amount states of inflammation state [57].

Cosmetic products are exposed to bacteria and fungi, in particular during their manufacture or storage. Since cosmetics have a direct contact with human body, it is important to prevent their contamination with pathogenic microorganisms. In addition, the biological purity in the final products should be also ensured. For this purpose silver nanoparticles have been also used. Ha et al in their patent provide a method of using silver nanoparticles as an ingredient in cosmetics dyeing mixture. The colour is dependent on the nanometal structure. In the case of silver nanoparticles a yellow colour is mostly achieved. The authors report that one can use a combination of nanoparticles of silver and gold and thus get a yellow-red colour. The product can be used in dyeing of cosmetic foundations, eye shadows, powders, lipsticks, inks, varnishes or eyebrow pencils. According to Ha et al, the products with metal nanoparticles, unlike the conventionally used metallic pigments, are not harmful to human health, and may even have health benefits [58]. A soap incorporating silver nanoparticles is also known and in 2013 the method for its preparation was patented [59]. The authors report that thanks to the presence of silver nanoparticles, the product also has anti-inflammatory activity and protects the skin against the adverse effects of the microorganisms. Silver nanoparticles can penetrate deep into the skin and remove from it any bacterial contamination, which inhibits the formation of acne [59]. Silver nanoparticles have also been used in the production of toothpaste or oral care gels. Silver as an ingredient of such products at a concentration of 0.004% w/w is an effective factor in preventing the growth of bacteria that cause unpleasant oral smells and dental cavities. The authors stipulate that the best biocidal effect is achieved when the average size of nanoparticles is less than 15 nm [60].

One way of using silver nanoparticles is to use them as a biocidal component of building materials. In US patent application 0272542 A1, a method of their incorporation in the structure of the building materials, in particular polyurethane foam, is described. These materials may be used as roofing, insulation, siding, upholstery and other applications. The authors of the patent indicate that silver nanoparticles present in these type of materials inactivate bacteria, fungi or algae, which can cause significant damage to clean materials [61]. A paint containing silver nanoparticles is also known. Kwon et al. described a method of obtaining such a formulation, which, thanks to the presence of silver nanoparticles, has biocidal properties [62]. Incorporation of silver nanoparticles in the structure of building materials provides many new opportunities for the application of well-known construction and finishing materials.

Prashant and Pradeep describe a method of enriching polyurethane foam with silver nanoparticles by physical adsorption of the nanoparticles on the foam surface. The authors suggest that their resulting material can be used as a filter for drinking water, in which the bacterial flora contamination poses a threat to human health. The microbiological tests demonstrate high biocidal activity of the material obtained, which enables a wide range of applications [63].

An important issue is maintaining antiseptic conditions in industrial facilities which, due to the nature of the production, are particularly vulnerable to microbial contamination. An innovative approach is the use of silver nanoparticles to purify the air in meat plants. The air blown into the production halls is an agent that transfers microorganisms to meat products may provide an environment conducive to their growth. Microorganisms can penetrate into meat products during slaughter, storage or their processing. Therefore, the blowing air must be filtered. In order to avoid the risk of microbial growth, a method of impregnating the air filter with silver nanoparticles has been developed. Results of microbiological tests confirmed that the impregnation of baghouse with silver nanoparticles allows for almost total elimination of microbiological contamination of the air [64].

The current problem is to optimize the conditions for rearing and farm animals breeding [65]. Animal droppings and feed are a source of air pollution, especially with odours such as ammonia and hydrogen sulphide. The air gas present in the air is highly dangerous for the environment. There are studies whose aim was to determine the level of ammonia emissions from the sheep droppings after treatment with the mineral sorbent with silver nanoparticles. The results confirmed a lower emission of the gas compared to untreated sorbent [66].

Nia has described an example of silver nanoparticles application in the rural area, particularly in activities that improve the plant growth. The behaviour of various plants after contact with silver nanoparticles has been studied. The group of tested plants included citrus, grains, fruits and oleaceae trees. In the course of the experiment it was established that spraying the plants with silver nanoparticles resulted in their rapid growth and formation of longer roots. Furthermore, studies have shown that the use of silver nanoparticles inhibited diseases that commonly attack the roots [67].

A common use of silver nanoparticles is to incorporate them in the structure of textile materials [68]. This enables their use in the production of sterile materials used to prevent or minimize bacterial infections. Based on a biological synthesis method, Durán et al. prepared silver nanoparticles and have built them into fibres of cotton and studied their antimicrobial activity against *Staphylococcus aureus*. Incorporation of silver nanoparticles in the fibre structure was achieved by immersion of cotton in an aqueous suspension of nanometal. In the next step the sample was dried at elevated temperature and it was subjected to microbiological tests. The reduction of bacterial colonies was estimated to be 99.9%. It has been found that the addition of silver nanoparticles enriches the fibres with biocidal properties [69]. Similar studies were conducted by Montazer et al. In the course of their work they checked biocidal properties of silver nanoparticles aqueous suspensions of varying concentrations and their impact on the colour change of material samples which were clippings of nylon carpet. A reduction of bacteria *Staphylococcus aureus* and *Escherichia coli* by 99% and 79%, respectively, was reported. This was confirmed in another report, that noted silver nanoparticles are an effective agent against Gram-positive bacteria. The authors report that silver nanoparticles coating of nylon fibres used for making floor coverings helps to secure them against odors and the growth of pathogenic microorganisms [70].

In 2010 a coating layer lining that contains nanoparticles of silver was patented. The layer was designed to cover the underside of the carpet, since in high humidity conditions it is exposed to the growth of mold (saprophytic fungi). Authors mention the numerous advantages resulting from the use of this type of carpet protection, of which the most important are: preventing the formation of mold, reducing the degree of bacterial growth and low production and maintenance costs [71].

Another way to use the valuable properties of silver nanoparticles is the patented manufacturing of socks, trousers and other fabrics which stay in direct contact with skin. The presence of silver nanoparticles in these type products protects against the development of bacteria that would cause odour and bacterial symptoms. The authors also indicate that socks with silver nanoparticles have not only prophylactic properties, but also pro-health properties since they can be used in the treatment of diseases caused in particular by *Staphylococcus aureus*, *Escherichia coli* strains as well as by *Candida albicans* fungus [72].

Silver nanoparticles have also found applications in the paper industry. DocuGuard uses paper with silver nanoparticles to protect medical records against the growth of bacteria. The company also offers letterheads, envelopes, brochures, book binding materials, to which silver nanoparticles are added.

Wires doped with silver nanoparticles are treated as an alternative to sputter deposited indium tin oxide. Conductive materials containing silver nanoparticles have an extremely high conductivity and are used in organic light-emitting diodes (OLED) and in optoelectronics [3].

8 Silver nanoparticles market

The group of companies participating in the development of silver nanoparticles includes Blue Nano, Cambrios, Agfa, Blue Nano, Carestream Advanced Materials, Cima Nanotech, Dow Chemical, PolyIC, Ferro, Saint-Gobain, Sigma Technologies, Suzhou NanoGrid Technology and Sumitomo Metals and Mining, Nano Silver Manufacturing Sdn Bhd, NovaCentrix, Advanced Nano Products Co. Ltd., Ames Goldsmith Corporation, Creative Technology Solutions Co. Ltd., Applied Nanotech Holdings, Inc., NanoMas Technologies, Inc., ras materials, SILVIX Co., Ltd. and Bayer MaterialScience AG [3].

Prices of silver nanoparticles are listed in Table 3. The size of silver nanoparticles global market is shown

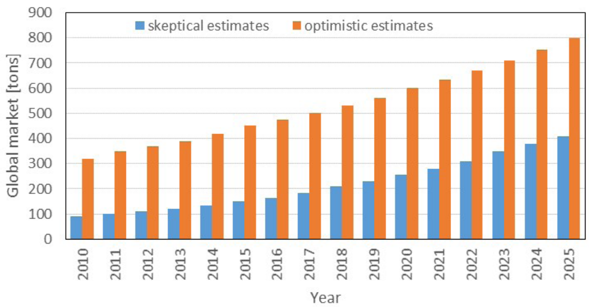

Figure 3: The global market for silver nanoparticles [3]

Table 3: Prices of silver nanoparticles [3].

Company	Size [nm]	Price [$/kg]
NaBond Technologies Co., Limited	<60	160
Inframat	50 – 80	179
SkySpring Nanomaterials, Inc.	40	472
Sigma Aldrich	<50	3,200
Sun Innovations	25	18,000
Plasmachem GmbH	40	4,500

Table 4: Summary of silver nanoparticles global market [3].

Class of offered particles	• silver nanoparticles: 3~7 nm • silver + inorganic particle: 0.4 μm • silver + inorganic particle: 100 nm • silver + inorganic particle: 10 nm
Application	• in the final products, conductive paste is supported with a curable resin • mixed into in the structure of the resin or fibres also dispersed in paints • without surface treatment
Advantages	Silver nanoparticles: • conductivity in a small amount • form microcircuits • silver + inorganic particle: at expansion in the surface region, antimicrobial effect is enhanced
Market estimates	Total world production of silver: 14000-31250 tons • *Nanofate*: 33.4 tons/year in Europe • *EC:* Total world production of silver for antimicrobial purposes, estimated for 2010: 22 tons • *Hendren CO, et al.:* 2.8-20 tons in the USA • *Silver Nanotechnology Working Group:* 250–312 tons • *SRI Consulting*: 20 tons/year • *Silver Institute:* 400-500 tons/year • *Keller et al:* 400 tons in 2010
Global consumption in tonnes in 2014	North America: 54 tons Far East: 43.2 tons Europe: 35 tons RoW: <3 tons
Main current use	• Connecting/wiring material in electronic devices • antimicrobial activity • textiles: clothing, bedding, masks, etc. • paints, coatings and cleaning materials • conductive paint • cosmetics • package • antimicrobial coating

in the Fig. 3. Table 4 summarizes the characteristics and statistics on the silver nanoparticles production.

9 Factors affecting the antimicrobial activity of silver nanoparticles

Silver nanoparticles are currently used in the form of colloids, consisting mainly of diffused nanometric silver particles, stabilizing substance and a solvent. The biological activity of silver nanoparticles depends on the morphology and physicochemical properties of the nanoparticles, as well as the specific characteristics of microorganisms which are treated by silver nanoparticles [73]. One can distinguish a number of factors affecting the antimicrobial activity, such as shape, size and zeta (ζ) potential of metal particles which influence the surface properties of the particles and the stabilizer, the pH of the suspension, ionic strength contaminants etc. [74-77].

10 The mechanism of silver nanoparticles activity

The mechanism of silver nanoparticles antimicrobial activity is not completely understood. There are many scientific theories which do not exclude a number of mutually supportive interactions [78,79].

One of the most common mechanisms of silver nanoparticles antibacterial activity is based on their natural affinity for bonding with a thiol group that is present in cysteine, which is a building block of the protein bacterial cell wall. Consequently, the enzymatic function of proteins is disturbed and the chain of cellular respiration is interrupted. At the same time other enzymes such as NADH and succinate dehydrogenase are destroyed [80]. Studies on silver nanoparticles biocidal activity against Gram-negative and Gram-positive bacteria has been carried out. The study involved the following bacteria: *Escherichia coli*, *Staphylococcus aureus* and *Salmonella typhus*.

It has been estimated that silver nanoparticles are more effective against Gram-negative bacteria, which is related to differences in the construction of cell walls of both groups of bacteria. Gram-negative bacteria have lipopolysaccharide layer positioned on the outside of the cell wall beneath which a thin layer of peptidoglycan is located. The lipopolysaccharide layer structure is characterized by a lack of rigidity and strength. A negative charge, located on lipopolysaccharides attracts the positively charged particles of silver nanoparticles, whose presence is explained by silver ions depositing on the particle surface. However, only a thin layer of peptidoglycan, which creates a rigid three-dimensional structure, is the main component of cell walls of Gram-positive bacteria. Its structure comprises polysaccharide cross-linked short chains of protein molecules. The stiffness and geometry of these layers are not conducive to penetration of silver nanoparticles through the cell wall of Gram-positive bacteria. However, it has been proved that silver nanoparticles are able to penetrate both types of cell wall and enter into the cell, resulting in the uncontrolled tyrosine phosphorylation. The phosphorylation process consists of binding of a phosphate residue to a nucleophilic atom (in this case the oxygen atom of the tyrosine –OH group) and consequently the bacterium is unable to survive [81,82] The presence of silver nanoparticles causes changes in regulation of expression of gens that encode proteins belonging to all complexes of phosphorylation pathway [83].

Cho et al. investigated the antibacterial efficacy of silver nanoparticles against *Staphylococcus aureus* (Gram positive bacteria) and *Escherichia coli* (Gram-negative bacteria). A suspension of silver nanoparticles characterized by an average size of 10 nm was used. It was found that the suspension significantly inhibited the growth of both *S. aureus* and *E. coli*. The impact of stabilizing agents i.e. poly(N-vinyl-2-pyrrolidone) (PVP), and sodium dodecyl sulphate (SDS) was evaluated. It was found that silver nanoparticles stabilized by poly(N-vinyl-2-pyrrolidone) have a higher antibacterial activity against both strains. The minimum effective concentration of silver nanoparticles in the suspension was equal to 50 mg dm^{-3} for *Staphylococcus aureus*, and 100 mg dm^{-3} for *Escherichia coli* [75].

An important issue is the activity of silver nanoparticles against viruses. Elechiguerra et al. presented a possible mechanism of antiviral activity of silver nanoparticles against HIV-1 [42]. In order to better explain the mechanism of destroying viruses by silver nanoparticles, the structure of HIV-1 is first outlined here: The outer layer of HIV-1 virus is coated with a lipid shell, with glycoprotein tabs. They consist of two types of subunits: glycoprotein subunit (gp120) and transmembrane subunit (gp41). It should be noted that the glycoprotein subunit is the most protruding part of virus, so it is highly accessible to potential attacking factors [84]. It was found that gp120 subunits have nine disulphide bridges in their structure. These S–S bonds can be broken and used for the creation of new connections. Leonard et al suggested that it is most likely that silver nanoparticles combine with sulphur present in the subunits of gp120 [85]. It was found that silver binds with HIV-1 through interaction with sulphur present in disulphide bridges [86,87]. It should be noted that the geometry of HIV-1 virus limits the possibilities of binding silver nanoparticles. The ideal size of bonded silver nanoparticles is 14 nm. When the size of silver nanoparticles is significantly different from the model one, the bond strength is much lower. The essence of the mechanism for virus deactivation is the introduction of silver nanoparticles selectively binding the gp120 subunit, which results in blocking of virus connectivity with “host” cell [42]. Studies on silver nanoparticles activity against influenza virus has been also carried out. In this case, the mechanism is similar. The coating of influenza virus is composed of two lipid layers from which glycoprotein (HA - hemagglutinin and NA – neuraminidase) subunits protrude [88]. Hemagglutinin is responsible for combining virus with the cell “host” cell. The structure of HA also contains disulphide bridges. The natural tendency of silver to connect with sulphur, suggests that silver nanoparticles are able to block the point of attachment to healthy cells by connecting to the HA subunit [43].

The mechanism of silver nanoparticle activity against fungi is not specifically described, although it is known that silver nanoparticles exhibit biocidal activity against such strains as *Candida albicans*, *Candida tropicalis*, *Saccharomyces cerevisiae* and *Aspergillus fumigatus* [30]. Lee et al. published a comparison of antifungal activity of silver nanoparticles at a concentration of 60 mg dm^{-3} as well as other antimicrobial agents. The treatment was directed against selected fungal strains. A comparison of results relating to minimum inhibitory concentrations of agents inhibiting fungal growth in 80% ($IC_{80\%}$) is shown in Fig. 4 [89].

The research team confirmed the possibility of destroying the yeast cell membrane, which was indicated by the fact that silver nanoparticles were able to penetrate to the interior of the cell. The immediate consequence of silver nanoparticles penetration into the fungal cell is the leakage of ions and other compounds, such as glucose and trehalose. Trehalose prevents inactivation and denaturation of proteins which may be caused by temperature changes or the effects of oxidizing agents. At the same time, the electric potential within the membrane is disturbed and the fungus is not able to grow normally [89].

11 Risks associated with the use of silver nanoparticles

In order to identify emerging threats from silver nanoparticles one should take into account four factors: hazard identification, assessment of toxicity degree, assessment of exposure and hazard characteristics. The state of silver nanoparticles toxicity may be influenced by their physicochemical properties such as size, particle shape, and variations in the intensity of its biological reactivity [90].

Silver nanoparticles may be seen as an eco-toxic biodegradable threat or as a product bio-accumulating in the trophic chain [91]. The US Environmental Protection Agency (EPA) reports that the penetration of silver nanoparticles into the food chain is possible even as a result of the operation of cosmetic formulations containing silver nanoparticles, such as suntan lotions that can easily get into the water. This is the shortest way of silver nanoparticles penetration into living organisms [92].

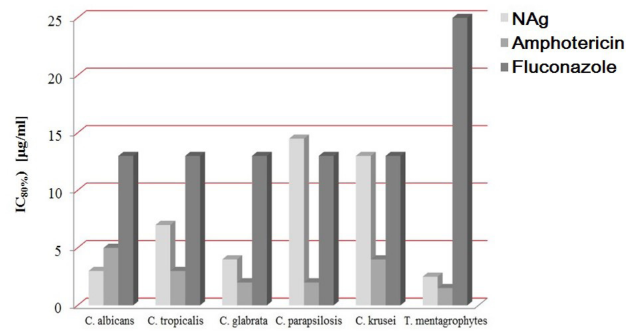

Figure 4: Comparison of antifungal activity of some biocidal factors [90].

It is very important to know the whole “life cycle” of products containing nanomaterials. Existing data show how processed nanomaterials accumulate in the environment, and what is more, every year their number drastically increases. For example, the amount of silver nanoparticles derived from various sources in 2005 was equal to 4 tonnes per year, while in 2008 it increased to 563 tonnes per year.

Model and experimental data suggest that nanomaterials may concentrate on the surface of water. The rapid increase in the concentration of nanoparticles in water is due to their increasing use, which implies an increased level of their emissions [93]. A model approach provides a starting point for assumptions about the “life cycle” of products containing silver nanoparticles and the concentration at which they are released and accumulated in the environment [93].

Following a probability based on putative life cycle of products containing nanomaterials, it has been shown that currently projected accumulation in the environment in European high and low quartile (Q0.15 and Q0.85) is equal to 0.5–2 ng L^{-1} (on the water surface), 32–111 ng L^{-1} in the outflow from the sewage treatment plant and 1.3–4.4 mg kg^{-1} in the sludge [94]. It has also been predicted that there will be a high annual increase in the concentration of silver nanoparticles in most components of the environment. However, also in this case there is no data confirming the model assumptions [93].

It is very difficult to estimate the amount of production, which releases silver nanoparticles to the environment because there is lack of full inventory of products containing silver nanostructures. However, it is possible that the use of silver nanoparticles will result in a massive increase in its concentration, which may lead to environmental threats. The main drawback in modelling of environmental hazards resulting from the use of Ag nanoparticles is the lack of analytical methods and instrumental techniques, which would be able to *in situ* identify and characterize the concentration of silver nanoparticles (or any other nanomaterial) [93].

The widespread use of silver nanoparticles means that they may penetrate into the environment, polluting waters, soil and air. After entering the ecosystem, silver nanoparticles could pose a serious threat to living organisms.

12 The impact of silver nanoparticles on living organisms

Water is the fastest medium to spread contamination out of large areas. After the silver nanoparticles accumulate in reservoirs, there is a risk of their transfer to a vast area, which poses a threat not only to aquatic organisms, but also organisms whose natural habitat is coastal areas. This is particularly dangerous, since water is the habitat of many organisms constituting the first state of food chains and silver nanoparticles can easily get into the higher points in the hierarchy of trophic chain [95].

For example, silver nanoparticles embedded in textiles, as a result of their laundry, get into the waste water. That poses a threat of their leakage and their impact with living organisms. Blaster et al have provided analysis whose results have contributed to the assessment of the impact of silver nanoparticles released from plastics and textiles on the ecosystem in the river Rhine. As a result of the work it was possible to establish that silver nanoparticles were bound by mud and sewage, what, in the future, may result in the risk of its spreading on agricultural fields, and this in turn can lead to its bioaccumulation and toxicological threat [96].

Asghari et al. studied the effects of silver nanoparticles on daphnia, a genus of small planktonic crustaceans that are the basis of the trophic chain of aquatic ecosystems. Any changes in their quantity or quality may affect the populations of other aquatic organisms. After exposure of daphnia to silver nanoparticles, their body discoloration has been noted. It indicated that silver nanoparticles had accumulated under the armor. Moreover, the presence of nanoparticles has been found in the gastrointestinal tract of daphnia, indicating the consumption of nanoparticles. In some cases, the intake was significant enough to result in inhibition of normal seaworthiness. An irregular track movement was observed. In later stages, daphnia migrated to the bottom of the test vessel. Such disorders were induced by various dispersions of silver nanoparticles whose test concentration was equal to 0.002 mg dm^{-3}. In particular, the authors tested three different suspensions of silver nanoparticles. They were purchased from various commercial sources and their stock concentrations were as follows: nAg1 – 200000 mg dm^{-3}, nAg2 – 4000 mg dm^{-3} and nAg3 – 400 mg dm^{-3}. The minimum concentration of silver nanoparticles causing 100% mortality of daphnia, followed by 48 hours, was equal to 0.00325, 0.006 and 0.275 mg dm^{-3}, respectively [97].

Bilberg et al. studied the effect of silver nanoparticles on the effectiveness of Eurasian perch breathing. The average diameter of nanoparticles was 81 nm. The gills of fish have naturally direct contact with the surrounding water, making them a potential target for silver nanoparticles. The researchers examined the degree of oxygen consumption during exposure of perch to silver nanoparticles. The final results revealed that exposure to silver nanoparticles causes weakening tolerance to hypoxia, or oxygen deficiency [98].

Massarsky et al. evaluated the effects of silver nanoparticles (average size of approximately 9 nm) on zebrafish embryos, which are a freshwater fish of the carp family. They used aqueous suspensions of silver nanoparticles at a concentration ranged from 0.03 to 1.55 μg cm^{-3}. It was observed that the increased silver concentration implies its higher toxic activity, which manifests in increased mortality of embryos. In exposure conditions, a lower percentage of fish hatching was observed. In addition, it was also noted that exposure to silver nanoparticles reduces embryos heart rate. It is disturbing that the researchers noticed a physical distortion of embryos manifested especially in higher concentration of silver nanoparticles. They concerned sprains of notochord, pericardial edema and degeneration of the body. Despite the fact that the mechanism of the toxic effect of silver nanoparticles on fish is not completely understood, the team suggests that the indirect reason of the observed anomaly may be caused by oxidative stress induced by silver nanoparticles [99].

Silver nanoparticles can penetrate into the soil, e.g. due to leaching of its particles from building materials [100]. Leaching is conditioned by unfavourable weather conditions and insufficient bonding of nanoparticles with the material.

Kaegi et al. assessed the intensity of silver nanoparticles realised from paint covering building facades, specifically for this purpose. It was found that after 12 months approx. 30% of silver nanoparticles with particle size less than 15 nm was transferred into the environment [101].

Silver nanoparticles present in soil can penetrate into the tissue of plants, which in turn may then be provided as food for humans and animals. Furthermore, silver nanoparticles may also penetrate the tissue of animals, such as annelids, which are eaten by other organisms placed above in the trophic chain.

Loghman et al. investigated the toxicity of silver nanoparticles (average diameter of 18 nm) in relation to broiler chickens. A suspension of silver nanoparticles was added daily to their feed. Histopathological examination of their liver samples showed several types of changes. In the case of silver nanoparticles at a 4 ppm concentration, they were accumulated in hepatocytes, which were also swollen and hyperaemic. Higher concentrations of silver nanoparticles (8 ppm) resulted in a further extension of central vein and change of the lipid profile. In the case of silver nanoparticles at a 12 ppm concentration, the growth of fibrous tissue and focal necrosis of hepatocytes (pathological apoptosis) was also observed [102].

Koohi et al. studied toxicity of silver nanoparticles against rabbits. They investigated nanoparticles whose average size was 10, 20 and 30 nm. The first stage of the study concerned the assessment of the nanoparticles impact on their skin, and in the next step they studied the reaction of other organs, including liver, kidney, heart and brain. In the case of 10 and 20 nm particles, skin erythema and edema were diagnosed. Skin hyperkeratosis and the appearance of abnormal epidermal warts, as well as fibrosis, congestion, redness, swelling, and glazing of intracellular collagen in the dermis were also observed. Liver function testing revealed the death of its cells, pathological changes in fatty and central venous congestion. Spleen hyperaemia was also diagnosed. Scientists have also noted the occurrence of cerebral edema and changes in the meninges. It has been concluded that exposure of rabbits to the silver nanoparticles causes more adverse effects than with larger particles [103].

Silver nanoparticles can be released into the air from different types of devices that are used to clean air. Silver nanoparticles present in the air may easily penetrate into organisms via the respiratory process. Scientists have a limited knowledge of the effects of inhalation of silver nanoparticles by humans. However, studies on the effects of silver nanoparticles after entering into the animal respiratory system have been carried out.

Stebounova et al. studied the effects of inhalation of silver nanoparticles (with an average size of 5 ± 2 nm) by mice. The authors observed that exposure of mice to silver nanoparticles causes pulmonary inflammation [104].

Kim et al investigated the genotoxicity of silver nanoparticles (with an average size of 18 nm) to female laboratory rats. It was noted that silver nanoparticles accumulate mainly in the lungs and liver of rats, but no evidence of silver nanoparticle genotoxicity was found [105]. Sung's team performed a similar study, using the dsame sized nanoparticles. As the result of exposure, a significantly reduced lung volume was observed. It was concluded that with increasing concentration of silver nanoparticles, a large number of pneumonia incidences occurred. Alveolar inflammation and other changes in the physical appearance of rats were also noted [106].

Roberts et al. evaluated threats to the respiratory and circulatory systems of rats that could result from inhalation of silver nanoparticles with an average size of approximately 35 nm. It was observed that after a short time of inhalation, silver nanoparticles did not cause significant changes in the studied parameters and only increased heart rate values were observed. However, the accumulation of silver nanoparticles in the bodies of rats was confirmed [107].

14 Summary

In recent years, the number of available products containing nanoparticles, in particular metallic silver significantly increased. Nanoparticles can penetrate into the human body through the skin, respiratory and digestive systems. Silver nanoparticles tend to accumulate in various organs, especially in the liver, kidneys, and lungs. The presence of silver nanoparticles in the liver may be particularly dangerous. The alleged accumulation of silver nanoparticles in the lungs can also have negative effects which are likely to manifest in the future.

Undoubtedly, it is necessary to conduct further research on the toxicity of silver nanoparticles in relation to living organisms. Full scientific information is not yet available, as developed conclusions are incomplete. It is necessary to implement the full cycle of research, on the basis of which it will be possible to determine the actual amount of silver nanoparticles penetrating into the environment. In the next stage, it is also necessary to perform tests to determine the degree of silver accumulation in living matter. Implementation of a full cycle of research will form the basis for further action aimed primarily at protecting the environment. If the alarming data are confirmed, it will be also necessary to provide a method of environment renaturalization and protect it against a possible threat from nanomaterials that may accumulate in the future.

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