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Editorial

Silver Ions Vs Silver Nanoparticles as Antibacterial Factor

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Definitions

Nanotechnology – one of the fastest developing sciences in the last years; the aim of this science is designation, production and application the nanoparticles with size below 100 nm.
Nanoparticles – products of nanotechnology with size below 100 nm.
Nanocompounds – compounds built from at least two components, where one of those is in nanoscale (below 100 nm).

Silver as antibacterial agent has been known for ages, used as silver nitrate and silver sulfadiazine. Mentioned compounds, a focus of antibacterial silver ions, were used mainly in medicine to treatment (e.g. wounds, ulcers) and prevention the bacterial growth (e.g. tooth lapis). In the past the silver coins were used to prevent bacterial growth in water too (in royal house or spaceship by NASA and MIR) [1]. Thanks to oligodynamic effect of silver ions they indicate a high efficacy against gram positive and gram negative bacteria [2]. The development of nanotechnology has given us possibilities of using silver in new formulations as antibacterial agent, e.g. silver nanoparticles or silver in nanocompounds. Nanotechnological modifications of silver ions are achieved by the conversion of the silver ions into silver nanoparticles or the immobilization of silver (ions or nanoparticles) on an inorganic carrier (e.g. silica, titanium dioxide, graphene) [3-7] to increase the antibacterial efficacy. The reason for this interest is that the physical and chemical properties of particles on the nanoscale can be different from those of larger particles or dissolved compounds [8]. The parameter which makes nanoparticles better than microstructures is its highly developed surface which causes improved activity, hardness and biocompatibility of particles on the nanoscale [9,10]. It is worth emphasizing that silver nanoparticles never perform alone due to their tendency to aggregate with each other and they are always connected by stabilizers such as organic acids, inorganic compounds, e.g. TiO2, thus forming nanomaterials (nanocompounds, nanocomposites).

In recent years the popularity of antibacterial silver (especially silver nanoparticles and nanocompounds) has grown outside of the clinic as well and is incorporated into a variety of domestic and personal products (e.g. food containers, sportswear, underwear, towels, carpets, assorted electronics, mobile phones, household goods, toilet seats) [1,11], lens [12].

The antibacterial mode of action of silver ions and their mechanisms of bacterial resistance to silver ions are well known (especially in Gram-negative bacteria) [1], but the mode of action and resistance mechanism of silver in nanoscale form still remains unclear. Randall., *et al.* [2] described endogenous and exogenous mechanisms of resistance to silver ions in Gram-negative bacteria and showed that silver ions provided selective pressure to enrich a population of silver resistant bacteria. After 6 days of exposure to subinhibitory concentrations of silver ions, *E. coli* BW25113 became resistant to them. Endogenous silver resistance has been associated with a loss of porins from the outer membrane (that are required for the up taken of silver ions to the cell with major porins OmpF, OmpC), and up-regulation of the native Cus efflux mechanism (that is capable of transporting silver out of a bacterial cell).

The exogenous resistance of bacteria to silver ions is associated with the sil genes carried on the pMG101 plasmid that encodes the Sil proteins located in the cell envelope that are connected with an efflux of silver ions [2].

While silver ions do not have different physico-chemical properties (antibacterial mode of action was reviewed by Kedziora., *et al.* [1]), silver nanoparticles are very different among themselves. Silver nanoparticles, have been usually considered as one kind of silver nanoproduct, with the same mode of action and the same mechanism of resistance. Based on our observations, we know that all silver nanoparticles and silver nanocompounds (even with the same inorganic compounds as a carrier) should be considered separate products with different physico-chemical properties, a different mode of action and in fact different interactions with a bacteria cell and different cyto and genotoxicity on eukaryotic cells. Karami Mehrian S and De Lima R [13] reviewed cyto and genotoxicity in plants and emerged 3 different entry mechanisms of silver nanoparticles to the cell: 1) directly move across the membrane, 2) endocytosis and 3) channels and membrane transporter proteins. Above mechanisms depend on the physico-chemical properties of nanoparticles such as: size, shape, composition, charge, time of exposure. Riaz., *et al.* [14] developed (from the literature data) size-dependent effects of AgNPs *in vitro*. In general, the smaller nanoparticles the higher toxicity effect on eukaryotic metabolism, structure and physiology. They showed significance of physico-chemical properties on the interpretation of *in vitro* cytotoxicity studies. On the other hand Dziendzikowska., *et al*. [15] proved a potential negative effect of silver nanoparticles (20 nm and 200 nm) on the hormonal regulation of reproduction in male rats, regardless of the silver nano particles size and dose.

In our previous study we checked the sensitivity of gram negative (*E. coli, K. pneumonia, E. aerogenes*) bacteria to long-term exposure to silver nanomaterials: silver nanoparticles (pure, commercially available) and silver nanocompounds (silver ions and silver nanoparticles immobilized on titanium dioxide, made ourselves [6,7]). We have observed that a strain becomes resistant to some silver modifications but stays susceptible to other modifications [16]. We suspect that there may be mechanisms of resistance and changes in the antibacterial mode of action different than $AgNO_3$ and between nanocompounds that result from the physico-chemical properties of silver nanocompounds.

In summary, silver nanoparticles (nanomaterials, nanocompounds) with its high efficacy can be applied as an alternative to antibiotics for killing pathogens, but every nanoproduct should be considered a separate antibacterial factor due to different mode of action, resistance mechanism, cyto and genotoxicity.

Conflict of Interest

There is any conflict of interest exist.

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