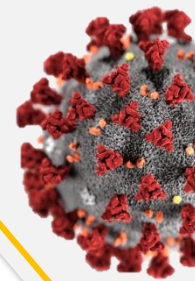




ANTIMICROBIAL NANO-SILVER SANITIZER SPRAY



PURPOSE

To provide brief information on the safety, effectiveness and cost-effectiveness of Antimicrobial Nano-Silver Sanitizer Spray based on request from the Director General of Health, Ministry of Health Malaysia following proposal by a company to provide and distribute 500,000 Antimicrobial Nano-Silver Sanitizer Spray to the public, beginning with Ministry of Health Malaysia hospitals and clinics to prevent COVID-19 transmission.

BACKGROUND

Nanoparticles include particles ranging in size from one to 100nm in diameter.¹ Silver nanomaterials are fine particles of metallic silver that have at least one dimension less than 100nm.² Due to their unique size, they tend to possess novel physical, chemical and biological properties that make this material superior. Silver nanoparticles (AgNP) and titanium dioxide nanoparticles (TiO₂NP), are among the top NPs in the pharmaceutical product, building materials and other consumer products, pivotal in the development of nanotechnology.³ Silver was known for its antibacterial effect and silver-based compounds have been used in many antimicrobial applications.^{4,5}

By converting bulk silver to nanosized silver, its effectiveness for controlling bacteria and viruses was increased multifold.² Due to their bactericidal properties, silver nanoparticles (AgNP) are the most frequently applied nanomaterials, attracting much interest and has the highest degree of commercialisation.^{5,6,7} The unique property of nanosilver is mainly attributed to the high surface area to volume ratio.² They are used in textiles, cosmetics, as product for domestic cleaning, air cleaners, food packaging, coating for refrigerators, water disinfection, and in every application where bacteria may exert harmful effect.⁸ Medical application for nanocrystalline silver include cardiovascular implants such as heart valves, central venous catheters, neurosurgical catheters, bone cement or wound dressing.⁹ Nanotechnology offers promising progress in diagnostics and therapy strategies e.g. drug delivery devices, cancer targeting, tumor reduction and tissue engineering.⁷ In recent years, AgNP was considered for the production of new class of antimicrobials.⁵

Physical, chemical and biological methods were the ways depicted to synthesize silver nanoparticles.⁴ The AgNP properties result from the unique physicochemical characteristics connected with their small size.¹⁰ The AgNP have at least one dimension in the range from one to 100nm, and as particle size decreases, the surface area-to-volume ratio greatly increases.⁵

Because of numerous practical application of AgNP, they may enter living organism including the human body, in food, through skin or respiratory system and even the blood-brain barrier.¹¹ Inhalation and ingestion appear to be the main route while there are various potential routes of exposure.¹²

The nano silver particles used in the Antimicrobial Nano Silver Sanitizer Spray produced by Rus Aurum Global was claimed to be 100,000 times smaller than diameter of human hair of one billionth of a meter, suspended in distilled water.

All nanoparticles are taken up by cells by pinocytosis, endocytosis dependent on caveolae and lipid raft composition, clathrin-dependent endocytosis and phagocytosis.¹³ The mechanism of AgNP uptake, transport pathways inside the cell and cellular target are as in Figure 1. When NPs come in contact with cells, they are taken up by a variety of mechanism that can lead to activation of cellular signalling processes producing reactive oxygen species (ROS), inflammation and finally cell cycle arrest or death.¹⁴ Nanosilver when in contact with bacteria and fungus, adversely affect the cellular metabolism of the electron transfer system and the transport of substrate in the microbial cell membrane.² The effect at cellular level of AgNP is as illustrated in Figure 2.⁶

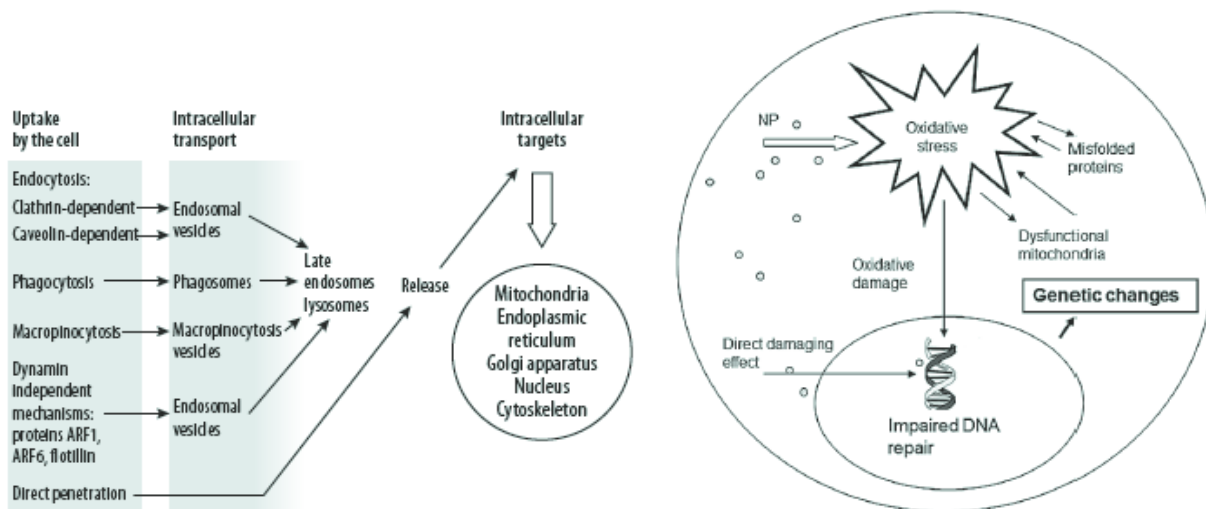


Figure 1 (left): Diagram showing AgNP uptake, transport pathways inside the cell and cellular targets.
 Figure 2 (right): Effect of AgNP at cellular level

EVIDENCE/INFORMATION SUMMARY

A total of 20 titles were retrieved from the scientific databases such as Medline, EBM Reviews, EMBASE via OVID, Pubmed from 2010 onwards and from the general search engines [Google Scholar and US Food and Drug Administration (USFDA)] were found on nano silver. No evidence retrieved from the databases on nano silver sanitizer spray. A Technology Review published by Malaysian Health Technology Assessment Section on Bionano Clean and Bionano Care (Sanitizer and disinfectant spray) was retrieved, in which the active ingredient was nano silver ion. One article on nano silver was found to be relevant and included in this review which comprised of laboratory study.

EFFECTIVENESS/EFFICACY

Bouryabaf et al. (2017) conducted a study to assess the antibacterial and biofilm removal properties of agar hydrogel prepared by incorporation of different concentration of silver nanoparticles (SNP), and to investigate the sanitising activity of SNP hydrogels against *Staphylococcus aureus* and *Salmonella typhimurium*. Agar dilution method was selected to determine the minimal inhibitory concentration (MIC) of SNP against *S aureus* and *S typhimurium*. Agar hydrogels was prepared by adding five grams of agar into distilled water. The final solution was autoclaved at 121⁰C for 15minutes. The SNP at different concentration was poured in molten agar at 50⁰C achieving final hydrogel with 0.5MIC, MIC and two MIC of SNP. Control hydrogels were developed identically without the addition of SNP. Sanitising effects of SNP agar hydrogel were investigated according to Phongphakdee & Nitisinprasert (2015). Bacterial cultures (1x10⁷ CFU/ml)(0.5ml) were added to tubes containing 4.5ml of either agar hydrogel or hydrogel with SNP at a final concentration of 0.5MIC, MIC and two MIC. Tubes without hydrogel were used as control. All plates were incubated for 24 hour at 37⁰C and CFU counted. The MIC value was 125µg/ml for both bacteria. All SNP hydrogels represented antibacterial activity against *Staphylococcus aureus* and *Salmonella typhimurium* on agar culture, significantly compared to control (silver sulfadiazine cream). The developed biofilm of *S aureus* and *S typhimurium* were 85% and 60% reduced by SNP hydrogels during 15 minutes contact time respectively. A 2.3log₁₀ CFU/ml was obtained on *S typhimurium* using agar hydrogel containing SNP at two MIC concentration. A dose dependent biofilm reduction was not demonstrated when different SNP concentration was tested. They concluded SNP incorporated agar hydrogel as an effective biofilm removal sanitizer.¹⁶

Earlier in 2010, a Technology Review was published by Malaysian Health Technology Assessment Section on Bionano Clean and Bionano Care (Sanitizer and disinfectant spray). The assessment found no retrieved evidence on its efficacy, safety and cost-effectiveness, although it contained nano silver ion which is the active ingredient in the product. There was insufficient and poor level of evidence on nano silver ion to determine its efficacy. Hence, Bionano Clean and Bionano Care (Sanitizer and disinfectant spray) was not recommended to be used in clinical setting such as Ministry of Health hospitals, until there is sufficient high quality scientific evidence to demonstrate its safety, efficacy and cost-effectiveness. Its usage in non-clinical setting could not be determined.¹⁷

SAFETY

Silver was registered in the United States (US) as a pesticide in 1954. In 1991, the US Environment Protection Agency (EPA) established an oral reference dose of 0.005 mg/kg/day for silver. Maximum contaminant level was issued by USEPA Office of Water for silver in 1991 based on the ability of silver to cause argyria.² There was no retrievable evidence on US FDA approval or CE mark for Nano-Silver Sanitizer Spray.¹⁸ The antimicrobial nano silver sanitizer spray produced by Rus Aurum Global was entirely manufactured in Malaysia, and claimed to have SIRIM and Halal certification.

COST-EFFECTIVENESS

There was no evidence retrieved on cost-effectiveness of Nano-Silver Sanitizer Spray to prevent COVID-19 transmission.

CONCLUSION

There was no retrieved evidence on the efficacy, safety and cost-effectiveness of Nano-Silver Sanitizer Spray to prevent COVID-19 transmission, although it contained nano silver which is the active ingredient in the product. There was very limited evidence on nano silver demonstrating its efficacy as *Staphylococcus aureus* and *Salmonella typhimurium* biofilm removal sanitizer in non-clinical setting.

Hence, the efficacy, safety and cost-effectiveness of Nano-Silver Sanitizer Spray in clinical setting could not be determined.

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Based on available evidence up to 18 March 2020

Disclosure: The authors of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia.

Disclaimer: This rapid assessment was prepared to provide urgent evidence-based input during COVID-19 pandemic. The report is prepared based on information available at the time of research and a limited literature. It is not a definitive statement on the safety, effectiveness or cost effectiveness of the health technology covered. Additionally, other relevant scientific findings may have been reported since completion of this report.

Malaysian Health Technology Assessment Section (MaHTAS),
Medical Development Division,
Ministry of Health, Malaysia.

