Journal of Bacteriology and Virology 2012. Vol. 42, No. 2 p.177 – 179
http://dx.doi.org/10.4167/jbv.2012.42.2.177

Letter to the Editor

Silver Nanoparticles as a Smart Antimicrobial Agent

Eun-Jeong Yang, Jiyoung Jang, Seungjae Kim and In-Hong Choi*

Department of Microbiology, Yonsei University College of Medicine, Seoul, Korea 50 Yonsei-ro, Seodaemun-gu, Seoul, Korea

In modern medicine the resistance to conventional antibiotics is becoming a serious concern due to high instances of mortality. Several metallic nanoparticles are suggested as promising anti-microbial agents against multidrug-resistant bacteria and some viruses. Among the nanoparticles mentioned, we review the recent finding which demonstrate the impact of silver nanoparticles on antimicrobial activities and recommend them as a potential candidate for restraining infections.

Key Words: Silver nanoparticles, Antimicrobial agent

A recent report has shown that methicillin-resistant *Staphylococcus aureus* was detected in high proportions between 28～63% in hospitals of Asia and South Africa (1), the number of infection-related hospitalizations with antibiotic resistance has also increased 359% during the 10-year period in the United States (2). The various and complicated mechanisms of antibiotics resistance make conventional treatment difficult for the eradication of such infections. Therefore, other strategies are required to overcome drug resistant microorganisms.

Historically silver salts have been used for infections such as syphilis and gonorrhea (3) and nowadays the use of silver has extended to treat a range of other microorganism including human pathogens. Recently, due to the advancement of nanotechnology, size-controlled silver nanoparticles have been produced in a large scale at industrial sites or laboratories, which has leads to the wide application of silver nanoparticles as broad spectrum antimicrobial agents. Contrary to the effects of ionic silver, the antimicrobial activity of silver particles is determined by the dimensions of the particles. Small particles have greater antimicrobial effect than large particles. One recent paper shows that the minimum inhibitory concentration (MIC) of silver nanoparticles (mean diameter of 9 nm) against Gram positive *S. aureus* and Gram negative *Escherichia coli* were 180 μg/ml and 15 μg/ml, respectively (4). When compared, silver sulfadiazine silver nanoparticles were more effective with a significantly lower risk for percutaneous absorption of silver ions (5). The other report shows that the MIC of smaller silver nanoparticles (mean diameter of 9~14 nm) have lower MIC (14~28 μg/ml) to *E. coli*, *Pseudomonas aeruginosa* and *S. aureus* than those of larger particles (mean diameter of 24~30 nm), which are 215~258 μg/ml (6). But the assay methods also influence the bactericidal activities. When the same 10 nm silver nanoparticles were used, *E. coli* was more sensitive than *Bacillus subtilis* in the growth inhibition and colony forming unit (CFU) assays, whereas *B. subtilis* was more sensitive than *E. coli* in the liquid-to-plate assay (7).

The exact mechanisms of antimicrobial or toxicity

Received: May 10, 2012/ Revised: May 29, 2012
Accepted: June 4, 2012
*Corresponding author: In-Hong Choi. Department of Microbiology, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea.
Phone: +82-2-2228-1821, Fax: +82-2-392-7088
e-mail: inhong@yuhs.ac
**This work is supported by Nano Material Technology Development Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2011-001916 and 2012-0006195).

activities by silver nanoparticles are still in investigation. The positive charge on the Ag ion is suggested crucial for antimicrobial activity. Some literature shows that the electrostatic attraction between negatively charged bacterial cells and positively charged nanoparticles is responsible (8). These nanoparticles have been shown to accumulate inside the membrane and can subsequently penetrate into the cells causing damage of cell wall or cell membranes (9). Other mechanisms involving interaction of silver molecules with biological macromolecules such as enzymes and DNA through an electron-release mechanism (10) or free radical production (11) have been proposed. Some literatures suggest inhibition of cell wall synthesis as well as protein synthesis has been shown to be induced by silver nanoparticles with the proteomic data showing evidence of accumulation of envelope protein precursor or destabilization of outer membrane, which finally leads to ATP leaking (12).

During the past decade, the application of silver nanoparticles in wound dressing has dramatically increased as a preferred treatment for infected wounds, including burn wounds (13, 14). Silver infused wound dressing shows efficient bactericidal activities against routine isolates from burn wounds. Forty-nine antibiotic-resistant bacteria including vancomycin-resistant *Enterococcus faecium*, methicillin-resistant *S. aureus*, multidrug-resistant (MDR) *P. aeruginosa*, MDR Vibrio *spp*., extended-spectrum β-lactamase producing *Salmonella spp*., ESBL producing *Klebsiella pneumoniae*, ESBL producing *Proteus mirabilis*, ESBL producing *E. coli* and MDR *Acinetobacter baumannii* show susceptibility to the antimicrobial activities over all pH ranges although all of which are more susceptible in instances of higher pH acidity levels (15). Some dressings have been modified to work more efficiently. A biological dressing containing silver-impregnated polyelectrolyte multilayers was revealed to reduce bacterial burdens significantly in murine skin wounds (16). Dressings with chitosan-based composite sponge containing silver nanoparticles have also proven to possess bacteriostatic and bactericidal properties against *S. aureus*, *E. coli* and *P. aeruginosa* (17). Furthermore biocomposite films composed of chitosan sago starch and silver nanoparticles showed faster healing patterns compared to the untreated control, which suggests that this film may be applicable not only as a dressing material for wound healing but also for bactericidal purpose (18). These wound healing results are supported by our report that silver nanoparticles induce angiogenesis with induction of vascular endothelial growth factor and nitric oxide in the animal model (19). Some silver nanoparticles are more effectively modified when prepared in thermosensitive gel (20) or in a disc carrier (21) to improve their medical applications.

In addition to their antibacterial activities, silver nanoparticles are also reported to have antiviral properties. Silver nanoparticles are known to bind envelope protein gp120 of human immunodeficiency virus to interfere viral binding to $CD4^{+}$ T cells (22). Silver nanoparticles also bind extracellular virions of hepatitis B viruses or inhibit RNA synthesis of these viruses (23). The inhibitory effect of silver nanoparticles for replication of influenza virus by inhibiting fusion of viral membranes (24) and inhibition of early phase replication of Tacaribe virus (25) have also been reported.

In conclusion, the importance of silver nanoparticles is clearly demonstrated by their broad-spectrum antimicrobial activity; their wide application as a topical agent applied to cervical tissues or to mucous membrane is also promising.

REFERENCES

1) Mainous AG, 3rd, Diaz VA, Matheson EM, Gregorie SH, Hueston WJ. Trends in hospitalizations with antibiotic-resistant infections: U.S., 1997-2006. Public Health Rep 2011;126:354-60.
2) Westh H, Zinn CS, Rosdahl VT. An international multicenter study of antimicrobial consumption and resistance in *Staphylococcus aureus* isolates from 15 hospitals in 14 countries. Microb Drug Resist 2004; 10:169-76.
3) Alexander JW. History of the medical use of asilver. Surg Infect (Larchmt) 2009;10:289-92.
4) Amato E, Diaz-Fernandez YA, Taglietti A, Pallavicini P, Pasotti L, Cucca L, *et al*. Synthesis, characterization and antibacterial activity against Gram positive and

Gram negative bacteria of biomimetically coated silver nanoparticles. Langmuir 2011;27:9165-73.

5) Brandt O, Mildner M, Egger AE, Groessl M, Rix U, Posch M, *et al*. Nanoscalic silver possesses broad-spectrum antimicrobial activities and exhibits fewer toxicological side effects than silver sulfadiazine. Nanomedicine 2012;8:478-88.
6) Guzman M, Dille J, Godet S. Synthesis and antibacterial activity of silver nanoparticles against gram-positive and gram-negative bacteria. Nanomedicine 2012;8:37-45.
7) Kim SW, Baek YW, An YJ. Assay-dependent effect of silver nanoparticles to *Escherichia coli* and *Bacillus subtilis*. Appl Microbiol Biotechnol 2011;92:1045-52.
8) Kim JS, Kuk E, Yu KN, Kim JH, Park SJ, Lee HJ, *et al*. Antimicrobial effects of silver nanoparticles. Nanomedicine 2007;3:95-101.
9) Sintubin L, De Gusseme B, Van der Meeren P, Pycke BF, Verstraete W, Boon N. The antibacterial activity of biogenic silver and its mode of action. Appl Microbiol Biotechnol 2011;91:153-62.
10) Sharma VK, Yngard RA, Lin Y. Silver nanoparticles: green synthesis and their antimicrobial activities. Adv Colloid Interface Sci 2009;145:83-96.
11) Park J, Lim DH, Lim HJ, Kwon T, Choi JS, Jeong S, *et al*. Size dependent macrophage responses and toxicological effects of Ag nanoparticles. Chem Commun (Camb) 2011;47:4382-4.
12) Li WR, Xie XB, Shi QS, Duan SS, Ouyang YS, Chen YB. Antibacterial effect of silver nanoparticles on *Staphylococcus aureus*. Biometals 2011;24:135-41.
13) Hermans MH. Silver-containing dressings and the need for evidence. Adv Skin Wound Care 2007;20:166-73; quiz 74-5.
14) Toy LW, Macera L. Evidence-based review of silver dressing use on chronic wounds. J Am Acad Nurse Pract 2011;23:183-92.
15) Percival SL, Thomas J, Linton S, Okel T, Corum L, Slone W. The antimicrobial efficacy of silver on antibiotic-resistant bacteria isolated from burn wounds. Int Wound J 2011.
16) Guthrie KM, Agarwal A, Tackes DS, Johnson KW, Abbott NL, Murphy CJ, *et al*. Antibacterial efficacy of silver-Impregnated polyelectrolyte multilayers immobilized on a biological dressing in a murine Wound Infection Model. Ann Surg 2012.
17) Li D, Diao J, Zhang J, Liu J. Fabrication of new chitosan-based composite sponge containing silver nanoparticles and its antibacterial properties for wound dressing. J Nanosci Nanotechnol 2011;11:4733-8.
18) Marie Arockianathan P, Sekar S, Kumaran B, Sastry TP. Preparation, characterization and evaluation of bio-composite films containing chitosan and sago starch impregnated with silver nanoparticles. Int J Biol Macromol 2012;50:939-46.
19) Kang K, Lim DH, Choi IH, Kang T, Lee K, Moon EY, *et al*. Vascular tube formation and angiogenesis induced by polyvinylpyrrolidone-coated silver nanoparticles. Toxicol Lett 2011;205:227-34.
20) Chen M, Yang Z, Wu H, Pan X, Xie X, Wu C. Antimicrobial activity and the mechanism of silver nanoparticle thermosensitive gel. Int J Nanomedicine 2011;6:2873-7.
21) Ebert M, Assadian O, Hubner NO, Koburger T, Kramer A. Antimicrobial efficacy of the silver wound dressing Biatain Ag in a disc carrier test simulating wound secretion. Skin Pharmacol Physiol 2011;24:337-41.
22) Lara HH, Ixtepan-Turrent L, Garza Trevino EN, Singh DK. Use of silver nanoparticles increased inhibition of cell-associated HIV-1 infection by neutralizing antibodies developed against HIV-1 envelope proteins. J Nanobiotechnology 2011;9:38.
23) Lu L, Sun RW, Chen R, Hui CK, Ho CM, Luk JM, *et al*. Silver nanoparticles inhibit hepatitis B virus replication. Antivir Ther 2008;13:253-62.
24) Xiang DX, Chen Q, Pang L, Zheng CL. Inhibitory effects of silver nanoparticles on H1N1 influenza A virus *in vitro*. J Virol Methods 2011;178:137-42.
25) Speshock JL, Murdock RC, Braydich-Stolle LK, Schrand AM, Hussain SM. Interaction of silver nanoparticles with Tacaribe virus. J Nanobiotechnology 2010;8:19.