Journal of Oral Research

EDITORIAL

DOI: *10.17126/joralres.2016.030*

Antimicrobial Nanoparticles in Dentistry. A fad or a real therapeutic option?

The recent discovery of a plasmid-borne colistin resistance gene heralds the emergence of truly pan-drug resistant bacteria. In that scenario, search for some alternatives to these microbes is a great responsibility for researchers, and antimicrobial nanoparticles appear like a therapeutic alternative. The explosion in the number of bacteria that have become resistant to a variety of these drugs is not related to antibiotic molecules themselves. Instead, the problem is in the way drugs are used. The inappropriate overuse of antibiotics has resulted in a critical situation due to bacterial mutations developing resistant strains. This is also true for antimicrobial nanoparticles.

Nanoparticles are particles with a size not greater than 100nm, with spherical, cubic and needle-shaped forms[1]. They are formed from metallic or polymeric materials and their active surface area, chemical reactivity and biological activity, are different from larger size particles. It is suggested that bacteria are much less likely to develop resistance to metal nanoparticles in comparison to conventional antibiotics. This is because metals can act on a wide range of microbial targets, and many mutations would have to occur for the microorganisms to resist their antimicrobial activity. Metals have been used for centuries as antimicrobial agents. Silver, copper, gold, titanium, zinc have gained particular attention, each having different properties and spectra of action. An inverse relationship between the size of the nanoparticles and antimicrobial activity has been clearly demonstrated, where particles in the range of 1-10nm in size have demonstrated greater killing activity against bacteria compared to larger particles. Adhering to the surface of the cell membrane, they drastically disrupt its functions, such as permeability and cellular respiration. They are able to penetrate into the bacteria and cause further damage by possible interactions with sulfur and phosphorus-containing compounds such as DNA. They release ions, which will make an additional contribution to the bactericidal effect of nanoparticles[2].

Bacterial susceptibility to nanoparticles depends on several factors such as the bacterial strain, the type and size of nanoparticles, the nature of the initial growth media and cell concentration. In general, Gram-negative organisms are more resistant to the ion effect of copper nanoparticles than Gram-positive bacteria[3].

There is growing interest in the application of nanoparticles as oral antimicrobials to control various infections, for their biocidal properties and anti-adhesive capabilities against biofilms. In dentistry there are some studies reporting the use of antimicrobial nanoparticles as components of prosthetic coatings, and topical agents within dental materials, and a few reports about their use in endodontics[4].

With respect to metallic nanoparticles, the antimicrobial properties of copper are among the most described[5]. Compared to traditional antibiotics, nanoparticles are effective at concentrations 1000 times lower. Periodontal pathogens like *Porphyromonas gingivalis, Fusobacterium nucleatum, Prevotella intermedia* and *Aggregatibacter actinomycetemcomitans* were found to be susceptible to silver nanoparticles and copper oxide (CuO) in anaerobic conditions, with minimum bactericidal concentrations (MBC) ranging from 0.025 to 2.5mg/ml[6]. However, copper is cheaper than silver, readily miscible with polymers, and relatively stable chemically and physically.

Other alternatives developed to synthesize metal nanoparticles are the use of polymers, for example, polyvinylpyrrolidone, polyethylene glycol, and chitosan. Nanoparticles stabilized by biopolymers prolong their release time, which improves, among other things, their antimicrobial properties. Chitosan is the second most abundant biopolymer of natural origin after cellulose and is obtained by removing an acetyl group from chitin. It consists of glucosamine units and N-acetylglucosamine. It is a biocompatible, biodegradable, non-toxic polymer, and has various applications in pharmaceutical and biomedical fields. It presents positive charge and is soluble in acidic to neutral solution, allowing it to bind to mucosal surfaces. These

properties make chitosan a good candidate for medical applications and research[7].

Chitosan-copper nanoparticle surfaces are covered by fragments of chitosan that protect against aggregation and oxidation, increasing the release time of the compound. It was shown that the size of nanoparticles could be controlled by manipulating the concentrations of chitosan and silver, and copper nitrate used in their synthesis. Particle size could be increased either by decreasing the concentration of chitosan or increasing the concentration of metal ions. Nanoparticles produced had a positive surface charge and chitosan used in their synthesis contributed to the stability of suspensions of such particles and had a bactericidal effect[8]. Although antimicrobial irrigants (without incorporation of chitosan) currently used to disinfect root canals in treating endodontic infections are able to kill *Enterococcus faecalis*, they often fail in endodontic restorations. An *in vitro* study by Kishen *et al.*[9] showed that the root canal surfaces treated with cationic antibacterial nanoparticles combined with chitosan significantly reduced the adhesion of *E. faecalis* to dentin. In theory, such surface treatment may prevent bacterial recolonization and biofilm formation.

Although more research on the effectiveness of antimicrobial nanoparticles in dentistry is required, the antimicrobial potential of metal nanoparticles, together with its high availability and low cost, make it worthy of consideration as a therapeutic alternative.

The growing phenomenon of bacterial resistance, caused by the use and abuse of antibiotics and the simultaneous decline in research and development of new antimicrobial drugs, is now threatening to take us back to the pre-antibiotic era[10]. Antimicrobial nanoparticles are a real therapeutic alternative in the field of dentistry as long as we do a responsible and appropriate use of them.

GABRIELA SÁNCHEZ-SANHUEZA. DDS, MEd, PhD(c).
Assistant Editor
Journal of Oral Research.

REFERENCES.

1. Allaker RP, Memarzadeh K. Nanoparticles and the control of oral infections. Int J Antimicrob Agents. 2014;43(2):95–104.
2. Lok CN, Ho CM, Chen R, He QY, Yu WY, Sun H, Tam PK, Chiu JF, Che CM. Silver nanoparticles: partial oxidation and antibacterial activities. J Biol Inorg Chem. 2007;12(4):527–34.
3. Yang M, He J, Hu M, Hu X, Yan C, Cheng Z. Synthesis of copper oxide nanoparticles and their sensing property to hydrogen cyanide under varied humidity conditions. Sensors Actuat B: Chemical. 2015;213:59–64.
4. Kishen A. Advanced therapeutic options for endodontic biofilms. Endod Topics. 2010;22(1):99–123.
5. Re G, Hu D, Cheng EW, Vargas-Reus MA, Reip P, Allaker RP. Characterisation of copper oxide nanoparticles for antimicrobial applications. Int J Antimicrob Agents. 2009;33(6):587–90.
6. Prado JV, Vidal AR, Durán TC. [Application of copper bactericidal properties in medical practice]. Rev Med Chil. 2012;140(10):1325–32.
7. Usman MS, Ibrahim NA, Shameli K, Zainuddin N, Yunus WM. Copper nanoparticles mediated by chitosan: synthesis and characterization via chemical methods. Molecules. 2012;17(12):14928–36.
8. Mallick S, Sharma S, Banerjee M, Ghosh SS, Chattopadhyay A, Paul A. Iodine-stabilized Cu nanoparticle chitosan composite for antibacterial applications. ACS Appl Mater Interfaces. 2012;4(3):1313–23.
9. Kishen A, Shi Z, Shrestha A, Neoh KG. An investigation on the antibacterial and antibiofilm efficacy of cationic nanoparticulates for root canal disinfection. J Endod. 2008;34(12):1515–20.
10. Cars O, Högberg LD, Murray M, Nordberg O, Sivaraman S, Lundborg CS, So AD, Tomson G. Meeting the challenge of antibiotic resistance. BMJ. 2008;337:a1438.