REVIEW ARTICLE

AODMR

Antibacterial Nanoparticles in Endodontics

Lija Issac[1], Mali G Nair[2], Anulekh Babu[3], Sajith Chandran[1], Mohammed Akber[1]

[1]Junior Resident, Government Dental College, Thiruvananthapuram; [2]Head of Department, Department of Conservative Dentistry and Endodontics, Government Dental College, Alappuzha; [3]Associate Professor, Department Of Conservative Dentistry and Endodontics, Government Dental College, Trivandrum.

.

Address for Correspondence:
Dr. Lija Issac, Junior Resident, Government Dental College, Thiruvananthapuram, India.

ABSTRACT:

Nanotechnology has been playing a very important role in creating novel materials for biological applications, including dental biomaterials and devices for short and long-term applications, for which their antimicrobial effect and biocompatibility are demanded. Nanoparticles with their enhanced and unique physicochemical properties hold new prospects for the treatment and prevention of dental infections. The near future potential of nanoparticles in clinical endodontics warrants sound research based on scientific and clinical collaborations. The goal of the present article is to review the current state of nanoparticles used for antimicrobial purposes in root canal infections.

Keywords: Antibacterial, Bioactive glass, Chitosan, Nanoparticles, Silver.

INTRODUCTION

Bacteria persisting in the root canal environment after endodontic treatment or re-colonizing the already filled root canal systems play a very major role in development of persistent endodontic infections.[1] Clinical studies have revealed persistence of bacteria within the root canal system in spite of proper cleaning, shaping and application of highly efficient antimicrobial agents.[1] The general emergence of truly pan-drug resistant bacteria due to bacterial mutations from the inappropriate overuse of antibiotics and the complex anatomy of the root canal system which allows bacteria to localize in the inaccessible areas have rendered the bacteria less susceptible for antimicrobial agents. Moreover, the efficacy of antibacterial agents is restricted by factors like concentration, time and volume within the root canals.[2]

WHAT ARE NANOPARTICLES?

The science of manipulation of matter at the atomic or molecular level is referred to as nanotechnology. A nanoparticle (NP) denotes a natural or manufactured material containing particles in an unbound state or as an aggregate or agglomerate in which 50% or more of the particles in number, size, distribution, or 1 or more external dimensions is in the size range of 1–100 nm.[3] They offer unique physicochemical properties such as ultrasmall sizes, large surface area/mass ratio and increased chemical reactivity compared with their bulkier counterparts.[4] These advantages may be exploited to design highly specific materials and devices to interact with at the molecular and subcellular level in the human body in order to achieve maximal therapeutic efficacy with minimal side effects.[5] The dental applications of nanotechnology have led to the emergence of a new field called nanodentistry which aims to provide practically ideal oral health with the use of nanomaterials and nanotechniques in almost all the aspects of dentistry.[6] The scope of such strategies includes a wide variety of oral health–related issues such as biofilm elimination, diagnosis and treatment of oral cancers, treatment of dentin hypersensitivity, bone replacement materials, and so on. In the field of endodontics, the development of nanoparticles is focused on steps that would improve antimicrobial efficacy, mechanical and physical integrity of previously diseased dentin matrix and tissue regeneration.[7]

Antibacterial nanoparticles

The increasing incidence of oral microbial infections together with drug resistance to

antimicrobial agents has become one of the challenging issues.[8] Development of novel antimicrobial delivery systems to improve the pharmacological characteristics of the applied antibacterial agents has been considered as one of the solutions to this problem.[9]

The antibacterial activity of various compounds has been used to control infections in dentistry and to manage the oral biofilms.[5] Their efficacy has been shown to improve as a result of treatment with nanotechnology. The combination of particular physiochemical properties of NPs together with the antimicrobial effects has gained attention in scientific circles leading to the introduction of more beneficial generations of traditional antimicrobials.[10] These systems can greatly improve the therapeutic efficacy of antimicrobial drugs by producing more favorable drug bioavailability, serum stability and pharmacokinetics. The nano-based formulations have shown to provide better penetration and allow slow and controlled release of active ingredients at target sites.[11]

Nanoparticles are generally classified based on the composition as either naturally occurring or synthetic. They are also categorized as inorganic or organic in nature (inorganic, polymeric or metallic). Based on the shape, they are classified as particles, tubes, spheres, plates, rods and so on. This review aims to provide comprehensive information on the scientific knowledge that is available for the use of nanotechnology toward antibacterial applications in endodontics.

A. METALLIC NANOPARTICLES AS ANTIMICROBIALS

Metals like silver, copper, gold, titanium, zinc and their oxides have gained particular attention as antimicrobial agents, each having different properties and spectra of action. The mechanisms for antibacterial effect of metal NPs are the free metal ion toxicity arising from dissolution of the metals from surface of the nanoparticles and oxidative stress via the generation of reactive oxygen species (ROS). They adhere to the surface of the cell membrane and drastically disrupt its functions such as cellular respiration and permeability. They are able to penetrate into the bacteria and cause further damage by interactions with sulfur and phosphorus-containing compounds such as DNA.[12] It has been found out that the bacteria are much less likely to develop resistance to metal nanoparticles when compared to conventional antibiotics. This is because metals can act on a wide range of microbial targets and more than mutations would have to occur for the microbes to resist their antimicrobial activity.

Silver Nanoparticles

Among metal nanoparticles, silver has unique properties allowing it to be one of the most commonly used metal NPs in dental application.[13] In dentistry, silver and its nanoparticles have been studied for application as endodontic retrograde filling material, dental restorative material, dental implants and caries inhibitory solution.[14] Silver NPs in different formulations have also shown mostly encouraging results as an antibacterial component.

Mechanism of Action

Silver exerts an antibacterial effect by acting on multiple targets. Silver NPs induce pits in the bacterial membrane and further destabilize the bacterial membrane and increase permeability, leading to leakage of cell constituents and fragmentation of the cell.[15] Silver ions also interact with sulfhydryl groups of enzymes, proteins and DNA that lead to disruption of metabolic processes which in turn cause the cell death.[16] They also intefere with the respiratory chain, cell-wall synthesis and cell division.[17]

Current Applications

Samiei et al. and Wu et al. in their separate studies showed appropriate antimicrobial actions of Silver NPs (Ag-NPs) after prolonged contact with E. feacalis.[18] Their studies showed that the efficacy of Ag-NPs was significant when applied as a medicament

and not as an irrigant as there is a prolonged interaction between positively charged Ag-NPs and negatively charged biofilm bacteria/ structure. These results suggest that silver NPs can be embedded in root canal sealers due to its sustained antimicrobial activity. 0.02% Ag-NP gel as medicament for 7 days was found to be significantly better in disruption of E. faecalis biofilm compared with calcium hydroxide groups. Ag-NP suspension in combination with calcium hydroxide showed significantly reduced E. faecalis from root canal dentin.[19] Mesoporous bioactive glass loaded with silver nanoparticles(Ag-MBG) showed significant disruption of the biofilm when compared with mesoporous bioactive glass and calcium hydroxide. This is due to sustained Ag ions released from the mesoporous structure.[20]

Two main issues associated with Ag-NPs are the possibility of discoloration of dentin and toxicity towards cells. The toxic concentrations of Ag-NPs have found to be 10–100 mg/L for eukaryotic cells.[21] However, the prolonged interaction time required by Ag-NPs for effective bacterial killing needs to be considered and its use should ideally be limited to medicament rather than as an irrigant. Researches have now been directed toward modifying Ag-NPs with specific antibacterial activity along with lower cytotoxicity to host cells.

Zinc oxide nanoparticles

Zinc oxide NPs (ZnO-NP) have also attracted attention of the researchers due to their antimicrobial efficiency. Zhang et al. showed the potential benefits of using ZnO-NP to improve the antibacterial capabilities of endodontic sealers and to inhibit re-colonization of bacteria in root canals. One proposed mechanism for the antimicrobial mechanism of ZnO is the generation of reactive oxygen species causing membrane dysfunction and cell damage. Moreover, interruption of transmembrane electron transportation has also been seen with ZnO-NP.[22]

Copper nanoparticles

Copper has been found to be cheaper than silver, readily miscible with polymers, and relatively stable chemically and physically. They can be considered as potential candidate as antibacterial nanoparticles. Periodontal pathogens like *Porphyromonas gingivalis, Fusobacterium nucleatum, Prevotella intermedia* and *Aggregatibacter actinomycetemcomitans* were found to be susceptible to copper oxide (CuO) in anaerobic conditions, with minimum bactericidal concentrations (MBC) ranging from 0.025 to 2.5mg/ml[6.23]

B. BIOACTIVE INORGANIC NANO-PARTICLES AS ANTIMICROBIALS

Bioactive glass (BAG) has received considerable interest toward various orthopedic and dental applications mainly because of its osteoinductive effect and antibacterial properties. BAG consists of SiO_2, Na_2O, CaO_2, and P_2O_5 at different concentrations and depends on the local physiological changes for its antibacterial effects.

Mechanism of Action

Bioactive glass exerts antimicrobial activity in aqueous solutions via the release of their ionic compounds over time.The antibacterial activity of BAG depends on the following factors acting simultaneously.[24] –

1. High pH: The release of sodium and calcium ions and the incorporation of protons into the glass lead to a high-pH environment in the root canal systems, which is a harsh environment for microbiota. This will inturn raise the osmotic pressure (above 1%) is inhibitory for many bacteria.
2. Ca/P precipitation: Release of calcium, sodium, phosphate and silicate induces mineralization on the bacterial surface and also promotes dentin mineralization.

Current Applications

BAGs in micro- and nanoforms have been tested to improve root canal disinfection. The nanometric BAG used by Zehnder et al

showed a significantly less antibacterial effect compared with calcium hydroxide in preventing residual bacterial growth.[25] Waltimo et al suggested that a preparation of 45S5 BAG suspensions composed of spherically highly agglomerated NPs having 30 nm (bioactive glass) and 8 nm (zirconium oxide) had killing efficiency substantially higher against all the tested strains of Enterococci from persistent root canal infections.[26]

Even though the nanometric BAG had the higher specific surface area, the micrometric counterpart had a considerably higher alkaline capacity and eliminated biofilms significantly better.[26] Planktonic bacteria were killed significantly better compared with biofilm bacteria. The conflicting evidence on BAG microparticles and nanoparticles to generate a significant antibacterial effect warrants further research before clinical application.

Tetracycline loaded calcium deficient hydroxyapatite nanoparticles

Madhumathi and Kumar in 2014 developed an osteoconductive drug delivery system composed of apatitie nanocarriers capable of providing sustained delivery of tetracycline in the periodontium. They synthesized calcium deficient hydroxyapatite (CDHA) nanoparticles with different Ca/P ratios. It showed increased antibacterial activity and increased cellular proliferation of human periodontal ligament fibroblast cells. The CDHA nanoparticles could be considered as osteoconductive bone substitutes with antibacterial and proliferative cell properties for local periodontal applications.[27]

Bioactive mesoporous calcium silicate nanoparticles

Wu and colleagues prepared injectable bioactive mesoporous calcium–silicate (MCS) NPs with high specific surface area and pore volume for potential application of filling an apical part of the root canal. It has shown to induce apatite mineralization with no cytotoxicity with enhanced the osteogenic differentiation of periodontal ligament cells (PDLCs). It also showed antibacterial activity and sustained delivery of ampicillin.[28]

C. POLYMERIC NANOPARTICLES AS ANTIMICROBIALS

Antimicrobial loaded polymeric NPs have also been investigated for antimicrobial delivery in endodontics as well. Nanoparticles are stabilized by biopolymers which prolong their release time, thus improving antimicrobial properties of polymeric nanoparticles. The polymers considered in nanotechnology include polyvinyl pyrrolidone, polyethylene glycol, alginate and chitosan.

Chitosan Nanoparticles

Chitosan (poly [1,4-b-D-glucopyranosamine]) is a biocompatible, biodegradable polymer and is the second most abundant biopolymer of natural origin after cellulose. It consists of N-acetyl glucosamine units and is obtained by removing an acetyl group from chitin. It has positive charge and is soluble in acidic to neutral solution, allowing it to bind to mucosal surfaces. Chitosan has received significant interest in biomedicine[29] because of its versatility in various forms such as powder (micro- and nanoparticles), films, scaffolds, capsules, hydrogels, bandages, and beads. Chitosan has a structure similar to extracellular matrix components and is therefore used to reinforce the collagen constructs.[30]These properties make chitosan a good candidate for medical applications and research.

Nanoparticles of chitosan have been developed mainly for antibacterial and drug/gene delivery applications. Chitosan has excellent antibacterial, antiviral, and antifungal properties.[30] In case of bacteria, gram-positive bacteria were found out to be more susceptible than gram-negative ones. The minimum inhibitory concentrations ranged from 18–5000 ppm depending on the organism, degree of deacetylation (DD), pH, molecular weight,

chemical modifications, and presence of lipids and proteins.[31]

Mechanism of Action

The proposed mechanism of action of chitosan nanoparticles is contact-mediated killing which involves the electrostatic attraction of positively charged chitosan with negatively charged bacterial cell membranes. This leads to altered permeability of the cell wall, eventually resulting in the rupture of cells and leakage of the proteinaceous and other intracellular components.[32] When examined under transmission electron microscopy, the bacterial cells were noted to be completely enveloped in the chitosan, forming an impermeable layer.[33] This could result in the prevention of transport of essential solutes leading to cell death. Chitosan as an antifungal was hypothesized to enter the cell and reach the nucleus, bind with DNA, and inhibit RNA and protein synthesis.

Current Applications

Kishen *et al.* 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.[34] The antibacterial efficacy of CS-NPs and zinc oxide in disinfecting and disrupting E. faecalis biofilms was evaluated later on.[35] These nanoparticles eliminated biofilms on a concentration- and time dependent manner and also retained their antibacterial properties after aging for 90 days. CS-NPs can be delivered within the dentinal tubules and anatomic complexities of an infected root canal to enhance root canal disinfection using ultrasonics.[36] CS-NPs when used in combination chlorhexidine provided a significantly greater reduction of colony-forming units in agar culture plates and infected collagen membranes.[37]

Shrestha et al studied the antibacterial effect of a photosensitizer, rose Bengal functionalized chitosan NPs [CSRBnp] against planktonic E. faecalis in the presence of different inhibiting agents. CSRBnp demonstrated residual effect and eliminated the bacteria after 24 hours of interaction after photodynamic therapy. The higher affinity of cationic chitosan antibacterial NPs to bacterial cell surfaces and singlet oxygen release after photoactivation of RB offered a synergistic mechanism even in the presence of tissue inhibitors. They concluded that CSRBnp are a novel antibacterial agent with potential advantages in root canal disinfection.[2]

The incorporation of CS-NP and zinc oxide nanoparticles in a zinc oxide–based root canal sealer and resin-based root canal sealer improved the antibacterial property and ability to diffuse the antibacterial component.[34] The addition of nanoparticles did not deteriorate the flow characteristics of the root canal sealer. Another recent study added CS-NPs to epoxy resin sealer resulting in enhanced antibacterial ability.[38]

A challenge in using antibacterial agents inside the root canal space is the neutralizing effect of different tissue inhibitors.[39] The tissue inhibitors such as serum albumin and pulp inhibited the antibacterial effect of CS-NPs significantly, whereas dentin, the dentin matrix, and lipopolysaccharides did not affect the efficacy of CS-NPs.[40] The effect of tissue inhibitors and the prolonged treatment time required to achieve effective bacterial elimination presented as major setbacks to CS-NPs. This warranted methods to overcome these shortcomings in future research toward the application of CS-NPs.

Methylene blue loaded polylacticoglycolic acid nanoparticles

Polylacticoglycolic acid is a non toxic biopolymer which has also gained interest for its application in biomedical field. Pagonis et al. studied the in vitro effects of polylactico-glycolic acid (PLGA) NPs loaded with the photosensitizer methylene blue (MB) using light against E. faecalis biofilms in the root canals. The results showed a synergistic effect of light and MB-loaded NPs in reduction of bacterial counts in both planktonic phase and biofilm phase.[41]

Triclosan loaded polylacticoglycolic acid nanoparticles

Triclosan is an antimicrobial agent which is non cationic in nature. It has well-known efficacy against several plaque-forming bacteria. Pinon-Segundo et al. found that there is quick release of TCS from NPs attributed to the large surface area of NPs and also suggested that TCS-NPs could help decrease gingival inflammation in periodontal treatment.[42]

PHOTODYNAMIC THERAPY USING NANOPARTICLES

The concept of photodynamic therapy (PDT) using nanoparticle based antimicrobial agents has been the subject of several researches in recent years. PDT is based on the utilization of producing free radicals by activation using a low energy light (such as singlet oxygen). The highly reactive singlet oxygen targets various bacterial sites such as cell wall, membrane proteins and nucleic acid. However, the antibacterial activity of PDT was found to be limited. This was attributed to the interaction of photosensitizers with the tissue inhibitors which in turn led to decreased half-life of the singlet oxygen produced on photoactivation reduced binding to the bacterial cell and reduced uptake into bacterial cells.[2]

Ongoing researches in PDT have recently focused their attention on the utilization of polymer-based NPs for photosensitizer delivery and release systems. These delivery systems have several benefits over untreated photosensitizing molecules namely larger critical mass (concentrated package of photosensitizer), target therapy by localized delivery agents and limiting the efflux system of target cells (thus reducing the possibility of multiple drug resistance).

DRAWBACKS OF THE ANTI-BACTERIAL NANOPARTICLES

In addition to the beneficial properties of NPs, understanding their shortcomings is crucial. Increasing use and demand for NPs will lead to their accumulation in the environment[43]. Probable cellular effects such as the inhibition of cell growth[44] and induction of apoptosis, genotoxicity, neurological and respiratory damage should be considered in the use of the NP.[45] Nanoparticles have shown greater lung deposition and rapid systemic translocation.

Regarding the possible unexpected effects of NPs, nanotechnology research should proceed with risk assessments and suitable quality control procedures process.[46] Furthermore, overcoming the general restrictions of NPs, such as incomplete in vivo release and incomplete degradation is of critical importance and should be also taken into account.[47]

CONCLUSION

It is well known that nanotechnology will fundamentally improve healthcare with the development of novel methods for disease diagnosis and prevention. It is also expected to modernize clinical dental practice as well. Utilization of NPs to fight root canal infections has become a focus of interest to researchers due to their biocidal, anti-adhesive and delivery capabilities. However, it is also necessary to understand their shortcomings and their probable cellular effects and toxicity as well as environmental effects. The future and success of these promising approaches lies in the development of efficient antimicrobial nanoparticles with better delivery techniques and minimal toxicity.

REFERENCES

1.Nair PNR., Henry S, Cano V, Vera J. Microbial status of apical root canal system of human mandibular first molars with primary apical periodontitis after ‘one-visit’ endodontic treatment. *Oral Surg Oral Med Oral Pathol* Oral Radiol Endod 2005;99:231-52.

2.Shrestha A, Kishen A. Antibacterial Efficacy of Photosensitizer Functionalized Biopolymeric Nanoparticles in the Presence of Tissue Inhibitors in Root Canal. Journal of Endodontics 2014;40:566-70.

3.Kishen A. Nanotechnology in Endodontics: Current and Potential Clinical Applications. (Springer 2015).
4.Curtis A, Wilkinson C. Nano-techniques and approaches in biotechnology. Trends Biotechnol 2001;19:97-101.
5.Venugopal J et al. Nanotechnology for nanomedicine and delivery of drugs. Curr Pharm Des 2008;14:2184-200.
6.Bhardwaj A et al. Nanotechnology in dentistry: Present and future. J Int Oral Health 2014;6:121-6.
7.Costerton JW et al. Biofilms, the customized microniche. J Bacteriol 1994;176:2137-42.
8.Foster HA, Ditta IB, Varghese S, Steele, A. Photocatalytic disinfection using titanium dioxide: spectrum and mechanism of antimicrobial activity. Appl. Microbiol. Biotechnol 2011;90:1847-68.
9.Kishen A. Advanced therapeutic options for endodontic biofilms. Endod Topics 2010;22: 99-123.
10.Besinis A, De Peralta T, Handy RD. The antibacterial effects of silver, titanium dioxide and silica dioxide nanoparticles compared to the dental disinfectant chlorhexidine on Streptococcus mutans using a suite of bioassays. Nanotoxicology 2014;8:1-16.
11.Dizaj SM, Lotfipour F, Barzegar-Jalali M, Zarrintan MH, Adibkia K. Antimicrobial activity of the metals and metal oxide nanoparticles. Mater Sci Eng C Mater Biol Appl 2014;44:278-84.
12.Lok CN et al. Silver nanoparticles: partial oxidation and antibacterial activities. J Biol Inorg Chem 2007;12:527-34.
13.Castellano JJ et al. Comparative evaluation of silver-containing antimicrobial dressings and drugs. Int Wound J 2007;4:114–122.
14.García-Contreras R et al. Perspectives for the use of silver nanoparticles in dental practice. Int Dent J 2011;61:297-301.
15.Sondi I, Salopek-Sondi B. Silver nanoparticles as antimicrobial agent: a case study on E. coli as a model for Gram-negative bacteria. J Colloid Interface Sci 2004;275:177-82.
16.Egger S, Lehmann RP, Height MJ, Loessner MJ, Schuppler M. Antimicrobial properties of a novel silver-silica nanocomposite material. Appl Environ. Microbiol 2009;75:2973-6.
17.Sotiriou GA, Pratsinis SE. Antibacterial activity of nanosilver ions and particles. Environ Sci Technol 2010;44:5649-54.
18.Wu D, Fan W, Kishen A, Gutmann JL, Fan, B. Evaluation of the antibacterial efficacy of silver nanoparticles against Enterococcus faecalis biofilm. J Endod 2014;40:285-90.
19.Javidi M, Afkhami F, Zarei M, Ghazvini K, Rajabi O. Efficacy of a combined nanoparticulate/calcium hydroxide root canal medication on elimination of Enterococcus faecalis. Aust Endod J 2014;40:61-5.
20.Fan W, Wu D, Ma T, Fan B. Ag-loaded mesoporous bioactive glasses against Enterococcus faecalis biofilm in root canal of human teeth. Dent Mater J 2015;34:54-60.
21.Chernousova S, Epple M. Silver as antibacterial agent: ion, nanoparticle, and metal. Angew Chem Int Ed Engl 2013;52: 1636-53.
22.Hajipour MJ et al. Antibacterial properties of nanoparticles. Trends Biotechnol 2012;30: 499-511.
23.Prado JV, Vidal AR, Durán TC. Application of copper bactericidal properties in medical practice. Rev Med Chil 2012;140: 1325-32.
24.Stoor P, Soderling E, Salonen JI. Antibacterial effects of a bioactive glass paste on oral microorganisms. Acta Odontol Scand. 1998;56:161-5.
25.Zehnder M, Luder HU, Schatzle M, Kerosuo E, Waltimo T. A comparative study on the disinfection potentials of bioactive glass S53P4 and calcium hydroxide in contra-lateral human premolars ex vivo. Int Endod J 2006;39: 952-8.
26.Waltimo T et al. Fine-tuning of bioactive glass for root canal disinfection. J Dent Res 2009;88:235-8.
27.Madhumathi K, Sampath Kumar TS. Regenerative potential and anti-bacterial activity of tetracycline loaded apatitic

nanocarriers for the treatment of periodontitis. Biomed Mater 2014;9:035002.
28.Wu C, Chang J, Fan W. Bioactive mesoporous calcium–silicate nanoparticles with excellent mineralization ability, osteostimulation, drug-delivery and antibacterial properties for filling apex roots of teeth. J Mater Chem 2012;22:16801-9.
29.Agnihotri SA, Mallikarjuna NN, Aminabhavi TM. Recent advances on chitosan-based micro- and nanoparticles in drug delivery. J Control Release 2004;100:5-28.
30.Rabea EI, Badawy MET, Stevens CV, Smagghe G, Steurbaut W. Chitosan as antimicrobial agent: applications and mode of action. Biomacromolecules 2003;4:1457-65.
31.No HK, Park NY, Lee SH, Meyers SP. Antibacterial activity of chitosans and chitosan oligomers with different molecular weights. Int J Food Microbiol 2002;74:65-72.
32.Qi L, Xu Z, Jiang X, Hu C, Zou X. Preparation and antibacterial activity of chitosan nanoparticles. Carbohydr Res 2004;339:2693-700.
33.Muzzarelli R et al. Antimicrobial properties of N-carboxybutyl chitosan. Antimicrob Agents Chemother 1990;34:2019-023.
34.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;34:1515–20.
35.Shrestha A, Shi Z, Neoh KG, Kishen A. Nanoparticulates for antibiofilm treatment and effect of aging on its antibacterial activity. J Endod 2010;36:1030-5.
36.Shrestha A, Fong SW, Khoo BC, Kishen A. Delivery of antibacterial nanoparticles into dentinal tubules using high-intensity focused ultrasound. J Endod 2009;35:1028-33.
37.Barreras US et al. Chitosan nanoparticles enhance the antibacterial activity of chlorhexidine in collagen membranes used for periapical guided tissue regeneration. Mater Sci Eng C Mater Biol Appl 2016;58:1182-7.
38.Del Carpio-Perochena A, Kishen A, Shrestha A, Bramante CM. Antibacterial Properties Associated with Chitosan Nanoparticle Treatment on Root Dentin and 2 Types of Endodontic Sealers. J Endod 2015;41:1353-8.
39.Portenier I et al. Inactivation of root canal medicaments by dentine, hydroxylapatite and bovine serum albumin. Int Endod J 2001;34: 184-8.
40.Shrestha A, Kishen A. The effect of tissue inhibitors on the antibacterial activity of chitosan nanoparticles and photodynamic therapy. J Endod 2012;38:1275-8.
41.Pagonis TC et al. Nanoparticle-based endodontic antimicrobial photodynamic therapy. J Endod 2010;36:322-8.
42.Piñón-Segundo E, Ganem-Quintanar A, Alonso-Pérez V, Quintanar-Guerrero D. Preparation and characterization of triclosan nanoparticles for periodontal treatment. Int J Pharm 2005;294:217-32.
43.Gajjar P et al. Antimicrobial activities of commercial nanoparticles against an environmental soil microbe, Pseudomonas putida KT2440. J Biol Eng 2009;3:9.
44.Horie M, Kato H, Iwahashi H. Cellular effects of manufactured nanoparticles: effect of adsorption ability of nanoparticles. Arch. Toxicol 2013;87:771-81.
45.Tsuji JS et al. Research strategies for safety evaluation of nanomaterials, part IV: risk assessment of nanoparticles. Toxicol Sci 2006;89:42-50.
46.Yah CS, Simate GS, Iyuke SE. Nanoparticles toxicity and their routes of exposures. Pak J Pharm Sci 2012;25:477-91.
47.Peng H et al. Preparation of hierarchical mesoporous CaCO3 by a facile binary solvent approach as anticancer drug carrier for etoposide. Nanoscale Res Lett 2013;8:321.

How to cite this article: Parackal LI, Nair MG, Babu A, Chandran S, Akber M. Antibacterial Nanoparticles in Endodontics. Arch of Dent and Med Res 2017;3(2):17-24.