# Recent advances in nanodentistry: a special focus on endodontics

*Fatemeh Mohammadi*[1,2], *Abbas Abbaszadegan*[3], *Ahmad Gholami*[4] ✉

[1]*Biotechnology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*
[2]*Department of Medical Nanotechnology, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran*
[3]*Department of Endodontics, Dental School, Shiraz University of Medical Sciences, Shiraz, Iran*
[4]*Pharmaceutical Science Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*
✉ *E-mail: Gholami@sums.ac.ir*

Published in Micro & Nano Letters; Received on 15th December 2019; Revised on 13th March 2020; Accepted on 7th June 2020

Root canal ecosystem is a complex environment due to its anatomy and persistence of microorganisms; those may reside within the canal after therapeutic efforts and cause subsequent complications and treatment failure. Nanomaterials with unique physicochemical properties have high accessibility to untouched areas of the intracanal ecosystem. Therefore, they have attracted the attention of researchers on the efficacy of nanodentistry in endodontics. This Letter reviews the recent advances in nanodentistry, especially in root canal treatment. In addition, it focuses on the application of nanoparticles in treatment and prevention of a variety of post-treatment infections in endodontics, treatment of antibiotic resistance and bacterial biofilm structures. In addition, it points out applications of nanoparticles in endodontic materials, restorative materials, dental adhesives, implants, prostheses and dentures. At last, the Letter elaborates on how nanoparticles used for targeted endodontic drug delivery and their efficiently controlled releases.

**1. Introduction:** Nanodentistry is rapidly advancing towards diagnosing and treating diseases including caries, infections, periodontal disease and restorative dentistry. Nanodentistry also helps with performing surgeries more efficiently, and preventing later complications of common approaches in oral health, dental care and post-treatment disease. Nanodentistry research studies mainly focus on producing new materials with specific characteristics or manipulating the current materials to improve their function and physical properties. These nanomaterials can mimic the natural processes or act as nanorobots to improve common dentistry procedures. For this purpose, various nanostructures are applied in the forms of nanoparticles (NPs), nanospheres, nanotubes, nanofibres, nanorods, dendrimers, and dendritic copolymers.

Various applications of nanomaterials in nanodentistry have studied in the past decades containing restorative dental materials, dental adhesives, elastomeric prostheses, dental implants and dentures.

In endodontics, nanomaterials have been used as filler materials in the form of sealers, Gutta Percha and cement, and as disinfectants in form of irrigants or medicaments. None of the current endodontic irrigants or medicaments has all the required properties and each of them can cause some complications, such as toxicity, a decrease of dentine strength or unpleasant taste. Furthermore, these common disinfection irrigants cannot affect difficult-to-reach regions and can be inactivated by organic components [1]. Therefore, some nanomaterials and nanostructures have designed as disinfectants and their properties have improved as much as possible to achieve a perfect treatment. The following section elaborates further on the application of nanomaterials for endodontic purposes.

1.1. Silver NP: The antibacterial activity of AgNPs as endodontic sealers and irrigants has been investigated in previous studies. These NPs could improve the antibacterial efficacy [2, 3] and can affect physiochemical properties of dentin [4]. Bruniera *et al.* [5] evaluated a formulation containing 75% AgNPs (w/w) suspension as intracanal disinfectants and concluded that AgNPs could be label as a potential disinfectant in root canal treatments. In another study, Fan *et al.* used Ag-loaded mesoporous bioactive glasses and mesoporous calcium-silicate NPs as intracanal medicaments in root canal therapy. Mesoporous structures could penetrate into dentinal tubules and induced a sustained release of Ag ions over time. This caused longer and controlled existence of AgNP in root canal space and helped to optimise the antibacterial effects of Ag on bacterial strains without significant cytotoxicity [6].

Ertem *et al.* evaluated the core-shell structure of AgNPs applied as endodontic irrigation. They demonstrated that core-shell AgNPs had an acceptable antibacterial effect on oral biofilm, even longer than that of AgNPs alone, possibly due to the increasing presence of soluble Ag ions over time. Therefore, endodontic irrigations containing core-shell AgNPs might be a good choice for those applications which need a long-term antimicrobial activity [7].

Although a few studies showed increasing antibacterial effects by adding NPs to conventional materials, some other studies were unable to confirm such findings. Alabdulmohsen and Saad showed that the composite of AgNPs has a less antibacterial effect against *Enterococcus faecalis* (*E. faecalis*) compared to conventional materials [8]. Wu *et al.* also evaluated antibacterial effects of AgNPs as an irrigant or medicament in root canal therapy. They reported that AgNP as a medicament was able to eliminate bacterial films, however, this effect was not observed when AgNP was used as an irrigant [9].

1.2. Zinc: In addition to AgNPs, zinc oxides (Zn) NPs also considered as important and practical NPs investigated as an endodontic disinfectant. ZnNP can eliminate bacterial films; therefore, it could be used for enhancing the antibacterial effects of endodontic materials. These NPs have shown to demonstrate an effective bactericidal activity by enhancing tissue regeneration and improving wound healing [10, 11]. Kishen *et al.* evaluated the antibacterial activity of cationic ZnNPs added to endodontic sealers and suggested that ZnNPs could inhibit the adherence of bacteria to treated dentin and hence, was capable to improve antibacterial properties without changing in flow characteristics [12].

1.3. Metal oxide NP: Most metal oxide NPs, such as Zn NP, iron oxide NP, $TiO_2$ NP and Mg NP are good choices for clinical applications because of their appropriate antibacterial activities




doi: 10.1049/mnl.2019.0747

and biocompatibility with human cells [13–15]. As metal oxide NPs has high physicochemical activity, they show a wide range of reactions with bacteria. In addition, these NPs withstand temperature changes and harsh conditions making them capable of remaining active in the root canal system and continuing their antimicrobial effects. Mg NP aqueous solution is reported as an endodontic irrigant with longer antibacterial activity than sodium hypochlorite [16].

1.4. Chitosan NP: Chitosan (Cs) NPs reported to have the potential to use in endodontic disinfection [17]. The potency of CsNP to eliminate or disrupt bacterial films assessed and the results showed that antibacterial properties of these NPs retained even after 90 days [18].

1.5. Poly lactic-co-glycolic acid (PLGA) NP: In recent studies, photodynamic therapy was experimented using photosensitiser methylene blue (MB) to inactivate microorganisms; however, it did not demonstrate sufficient efficacy [19]. Polymer-based NPs, such as poly lactic-co-glycolic acid (PLGA) NP, have been used for improving MB delivery and release and revealed that PLGA conjugated MB mainly concentrated on the cell walls of microorganisms, penetrated well and reduced the number of bacteria during the planktonic phase [20].

1.6. Quaternary ammonium polyethylenimine (QPEI) NP: Quaternary ammonium salt is a cationic surface-active agent with potential clinical applications. It has shown to have high antimicrobial activity against bacteria, some viruses, yeast, fungi, and protozoans. This insoluble NP has also shown a prolonged antimicrobial activity experimented in vivo and in vitro conditions [21]. Beyth *et al.* tested a combination of QPEI NP and an epoxy-based endodontic sealer. This incorporation provided a bactericidal surface with appropriate physical properties, especially good flow rate [22]. In addition, Kesler Shvero *et al.* evaluated the antibacterial effects of endodontic sealers incorporated with QPEI as an insoluble cationic NP. The results of this study showed that the modified epoxy resin-based endodontic sealer trapped bacteria and promoted bacterial cell death. This nanocomposite showed stable and significant antibacterial properties at low concentrations [21].

1.7. Nanocarbon materials: Nanocarbon materials have a wide range of applications in medicine. A few studies have shown that graphene, nanotubes of carbon, fullerene, and diamond NPs could improve mechanical properties of some biomaterials, provide colloidal stability, sustain the release of some biological agents, and have antibacterial activities [23]. Recently, carbon nanotube (CNT) has received considerable attention due to its unique properties in biomedical applications, especially dentistry. It improves the strength of implants and composite materials, proliferation, cell adhesion, and antibacterial activity. Akasaka *et al.* evaluated the effects of multi-walled CNT coating on tooth slices. The results showed that CNT adhered selectively and easily to the surfaces of dentin and cementum without causing any changes in tensile bond strength of dental adhesives. It is probably due to its strong interaction with collagen. This unique feature makes CNT application in improving endodontic and restorative materials promising [24].

The results of a study reported proper antimicrobial activity for single-walled nanotubes applied as surface coatings and water filtration; [25] therefore CNT materials could be used in dental equipment and dental water filtration systems due to their antimicrobial properties [26]. Graphene-based materials, such as graphene, graphene oxide (GO), and reduced GO improve the physical, chemical and antibacterial properties of biomaterials with low toxicity. Graphene sheets, for instance, have shown high surface area and mechanical strength with the ability to affect stem cell differentiation [27]. Dybowska–Sarapuk *et al.* reported that graphene and graphene-nanosilver layers which are graphene coated with AgNPs could prevent bacterial biofilm formation [28].

GO is a derivative of graphene with various applications in medical and biological sciences. In many studies, the antimicrobial properties of GO, especially against dental bacteria, have been shown [29, 30]. He *et al.* evaluated the antibacterial effects of GO nanosheets against dental pathogens. The results suggested that these nanosheets effectively inhibited the growth of these microorganisms by damaging bacteria membrane and cell walls by compromising their integrity [31]. In addition, Lee *et al.* reported that GO nanosheets incorporated PMMA, widely applied as dental materials, can have antibacterial effects on microbial species by sustained antiadhesion properties [32]. Incorporation of antibacterial materials into fillers could prevent reinfection in the root canal system. Lee *et al.*, added nanodiamond to Gutta Percha to improve the antibacterial effects of this common filler material in endodontic treatment. This modified Gutta Percha was able to eliminate existing microorganisms sufficiently [33].

1.8. Silica NP and its derivatives: Silica NP is an important material in nanotechnology due to its antibacterial activity in many biological applications. In addition, silica NP acts as an antibiotics carrier due to its good biocompatibility, high chemical and thermal stability, and high surface area. Modifications made on the surface of the NPs could also help to target drug delivery and provide prolonged and efficient drug interaction with the target tissues. Therefore, the modified NP can facilitate optimal antibiotic concentration access to the diseased tissue resulting in reducing dosage frequency, side effects, fluctuation of drug, and overcoming antimicrobial resistance.

Mesoporous silica (MSN) NP could also be a good choice for drug delivery application. The properties of MSN, such as high stability and surface area, tunable size, and large volume of the pore, makes it suitable for intracellular controlled release of drugs, genes, and other agents [34]. Tian *et al.* introduced MSN structure, which encapsulated calcium and phosphates for the treatment of dentin surfaces and tubular sealing. Obstruction of dentinal tubules with MSNs as a means to achieve deeper sealing could be an effective strategy for the treatment of dentin hypersensitivity. Due to their nanoscale size, these structures could penetrate into deeper areas, about 105 μm into the dentinal tubules. Dentin hypersensitivity is a common complication, which may occur after some dental treatments for the patients. Furthermore, these nanostructures could act as sources of calcium and phosphate to improve remineralisation [35]. Mesoporous calcium-silicate nanoparticles (MCSNs) can also apply as an endodontic disinfectant. AgNP and ZnNP incorporated MCSNs can adhere to the walls of root canal well and penetrate into dental tubules along with maintaining mechanical properties of dentin such as elasticity or flexural strength [36].

Bioactive glass NP is another form of silica-based material showing antibacterial effects against oral aerobic bacteria responsible for periodontal diseases and caries. Bioactive glass nanopowders could also bind to surrounding living tissues and help to maintain osteoplastic phenotype, growth and maturation of osteoblast-like cells on their surface [37].

**2. Advances in nanomaterials and nanotechnologies in endodentics:** Endodontics has made remarkable progress in material and technologies. These advances could be categorised in the fields of endodontic imaging, procedures of regenerative endodontics, root canal preparation, root canal filling and endodontic disinfection [38]. Nanotechnology has widely emerged as a promising scientific field to solve many longstanding problems in these areas and has brought about promising improvements in endodontics. Most of these studies have focused on antibacterial effects of NPs; since the main challenge in endodontics is the failure of current procedures in overcoming bacterial resistance [39]. It is vital to eliminate bacteria completely from root canal space and prevent its reinfection; therefore, effective disinfectants are necessary for a successful root canal treatment. Additionally, some studies applied medicinal herbs such as Zataria Multiflora and Aloe vera [40] and Cinnamomum zeylanicum essential oil [41] as medicaments in root canal treatment, which presented acceptable antibacterial efficacy compared to common endodontic materials, especially in prolonged exposure time.

Moreover, various NPs have studied in the form of solution for irrigation, medication, and as additive materials to sealers to give them improved antibacterial properties. Functionalisation of NPs using photosensitisers and antibiotics helps to increase their antibacterial effects [42].

2.1. Properties of NPs: Physicochemical properties of NPs are major factors regarding their antibacterial activities. These significant properties include particle size, charge and morphology of surface, zeta potential and crystal structure; however, there are some other factors, such as bacterial species, exposure frequency, and environmental condition, which should not be ignored either [43, 44]. Various NPs have widely been used as antimicrobial agents because of their unique characteristics. Studies have shown that each NP has specific effects on specific microorganisms. These effects might be different due to NPs' specific characteristics and different performances.

Abbaszadegan *et al.* evaluated the antimicrobial activity of AgNPs using negative, positive and neutral surface charges. The study showed that the surface charges of bacteria were an important factor in the antibacterial activity of Ag NPs. The results indicated that positively charged AgNPs showed better antibacterial efficacy against planktonic *E. faecalis* with acceptable cytocompatibility [45]. The same antimicrobial effects of positive charge at the surface are also seen in QPEI [43]. Electrostatic interactions between the cationic surface of NPs and multiple anionic sites on bacterial cell surface might be the reason for the success of QPEI in eliminating bacterial resistance [22]. In addition to different kinds of electrical surface charges, the amount of charges is also effective in antimicrobial activity of NPs [46]. In addition, the size of NPs is one of the main determining factors in antibacterial efficiency of NPs, where the smaller sizes can induce unique properties such as more interaction with bacterial cells. These properties help to improve antibacterial efficacy of NPs and makes their application controllable [43].

2.2. Filler materials: Apart from the progress made in developing novel irrigants and enhancement of their mode of delivery, to achieve an acceptable treatment, filler materials also need to be improved. Root-filler materials are expected to provide an effective barrier against pathogens while being ecofriendly and easy to control. However, common materials used for filling root canal system could not meet these expectations [38], thus either various NPs such as QPEI and zinc are added to these materials or the same materials undergo nanomodification to be used as endodontic fillers capable of bactericidal activities. Hydrophobic properties and a positive charge of QPEI increase its antibacterial activity [47]. Adding titanium dioxide NPs also prevents microorganism adhesion and biofilm formation by increasing the hydrophilic activity of materials [48]. Silica NPs could also increase the flexural strength, thermal and strength stability of materials [49] Gerasymchuk *et al.* confirmed the antimicrobial activity of graphite oxide-based composite containing silver NPs. These NPs could be added to endodontic fillings as an effective bactericidal agent because of their high and prolonged antimicrobial activity [50]. Additionally, nano-modifications of materials such as WMTA could improve some features of common materials. Nanomodified WMTA caused the release of calcium, which is an external supply of minerals and elevation of the pH, that both of which are among important factors regarding the antibacterial activity. Furthermore, it helped to promote the healing process in dental tissues [51].

2.3. Beyond the antibacterial effect of NPs: In addition to antibacterial activity, nanocomponents have other important impacts on dentistry. MSNs could be applicable to dentinal tubule occlusions due to their small size, high reactivity and solubility. The application of sealers containing MSNs during dentin hypersensitivity treatments has examined. Some NPs such as MSNs penetrate effectively to deeper areas, which are often inaccessible. If MSNs encapsulated calcium and phosphates, they could act as a sustained release source of these ions and facilitate the remineralisation process [35]. Hence, MSNs might be a good choice for drug delivery in root canal treatment. As graphene and its derivatives are modified and functionalised with several biomolecules for medical applications, they also might be a useful media for medicaments and substrates particularly in endodontics [27]. MCSNs used for controlling drug delivery and mineralisation. Fan *et al.* described a controlled release device composed of Ag–MCSNs which could be used to deliver several biomolecules and, therefore, might serve as a good candidate to synthesise developed multifunctional biomaterials [52].

In addition, adding some NPs to common endodontic materials could cause a controlled release of essential ions, such as $Ca^{2+}$ or fluoride those are essential factors in dental tissue regeneration, remineralisation and prevention of recurrent caries. Moreover, nanomodification of some dental materials can be helpful in root canal therapy. Zand *et al.* reported that nanoparticle calcium hydroxide, used as an intracanal medicament, penetrated into dental tubules more deeply than conventional calcium hydroxide and subsequently showed more antimicrobial activity due to the longer presence time [53]. In addition, several NPs, such as titanium, zinc, or cerium nano-oxides are investigated with respect to their improving effect over mechanical properties of maxillofacial prostheses [54]. Moreover, Xia *et al.* reported that functionalisation of calcium phosphate cement scaffold with iron oxide NPs [55] or gold NPs [56] can improve bone regeneration by effecting on dental pulp stem cells.

**3. Concerns about nanomaterials:** As nanomedicine and nanodentistry are rapidly developing worldwide, several issues including public acceptance, regulation, ethics and human safety must be addressed before NPs' widespread use; especially since their application in dentistry is directly related to human cells.

Although the increasing size-dependent absorption of NPs is a significant advantage for the delivery of materials to unreachable areas, it might, as well, because of a number of unwanted effects on cells and organs such as lung, brain etc. In addition, due to their very slow degradability, NPs interference with biological processes is a serious concern. NPs could massively attack into cell structures and react with DNA, RNA or other intracellular components which may even lead to gene mutations [57].

To induce and assess health risks, NPs should be absorbed in significant quantities and evaluated individually in each new material. In addition, there are engineering challenges, such as the complexity cost of synthesis and user safety in need of consideration. There are also concerns about the toxicity of chemical agents used in the synthesis and manufacturing of bio-friendly nanomaterials. For this reason, in several studies, biological synthesises of NPs, such as green synthesis, have been developed to reduce risks for environment and laboratory users [58]. In line with nanodentistry and its increasing development, massive studies and clinical trials are essential to confirm the safety of nanomaterials.

One of the main concerns regarding the use of NPs is toxicity. Despite the effectiveness that nanomaterials have shown in nanodentistry, nanosafety remains a controversial issue. Some studies



*Micro & Nano Letters*, 2020, Vol. 15, Iss. 12, pp. 812–816
doi: 10.1049/mnl.2019.0747

have suggested that NPs could result in cytotoxicity, neurotoxicity or genotoxicity [59, 60]. Nanotoxicity depends on many factors including concentration or size of NPs, surface charge [61], method of synthesis [62], exposure time and cell lines [1, 63]. Different cell lines used in toxicity assays include fibroblast cell lines such as 3T3 mouse fibroblast [64], L929 mouse fibroblast [46], osteoblast like cells [65], human liver hepatocellular carcinoma cell line [59, 63], human peripheral blood lymphocytes [66], human periodontal ligament stem cells [67], proliferation of macrophage [68] etc. It is possible for one NP not to be cytotoxic to some cell lines while having toxicity on some others [69]. Temporary usage of NPs can significantly prevent the toxicity of these materials. Therefore, specific assays on individual dental cell lines are crucial for each new material designed or developed in dentistry.

**4. Conclusion:** Nanodentistry creates an opportunity to improve dental material efficacy and reduces failures. In this new therapeutic approach, optimising physicochemical properties of NPs for targeted tissues are crucial. Numerous nanostructures and nanomaterials have studied in endodontics, which represents specific features such as high stability with optimal therapeutic activity, antimicrobial functionality and possibility of penetrating to deeper unreachable areas such as dentinal tubules. In addition, some surface-modified NPs could act as carriers for chemicals and medicines. These modifications also help intracellular controlled release of drugs. Various NPs, such as AgNP, ZnNP and QPEI, applied in forms of irrigants, medicaments or as additives to sealers and restoratives materials often act as antimicrobial agents in root canal treatment. According to the recent studies each NP have a specific range of antimicrobial activity on a particular panel of microorganisms, therefore, each newly designed nanomaterials should be assessed individually.

Regarding nanosafety issues, public acceptance, regulations, ethics and human safety are among those items to be taken into consideration before NPs' widespread applications. Endodontic studies have shown that NPs may cause cytotoxicity, neurotoxicity and genotoxicity depending on several factors including NP type, amount of concentration, size, exposure time, type of cell lines and the method of synthesis. This has emphasised the necessity to develop nanosafety researches further to keep up with rapid nanodentistry advances.

**5. Acknowledgments:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## 6 References

[1] Chan E.L.K., Zhang C., Cheung G.S.P.: 'Cytotoxicity of a novel nano-silver particle endodontic irrigant', *Clinical, Cosmet Investig Dent*, 2015, **7**, pp. 65–74
[2] Haghgoo R., Ahmadvand M., Nyakan M., ET AL.: 'Antimicrobial efficacy of mixtures of nanosilver and zinc oxide eugenol against *Enterococcus Faecalis*', *J. J Contemp Dent Pract*, 2017, **18**, (3), pp. 177–181
[3] Suzuki T.Y.U., Gallego J., Assuncao W.G., ET AL.: 'Influence of silver nanoparticle solution on the mechanical properties of resin cements and intrarradicular dentin', *PLOS One*, 2019, **14**, (6), p. e0217750
[4] Abbaszadegan A., Ghahramani Y., Farshad M., ET AL.: 'In vitro evaluation of dynamic viscosity, surface tension and dentin wettability of silver nanoparticles as an irrigation solution', *Iran. Endod. J.*, 2018, **14**, (1), pp. 23–27
[5] Bruniera J.F.B., Silva-Sousa Y.T.C., Lara M.G., ET AL.: 'Development of intracanal formulation containing silver nanoparticles', *Braz. Dent. J.*, 2014, **25**, pp. 302–306
[6] Fan W., Wu D., Ma T., ET AL.: 'Ag-loaded mesoporous bioactive glasses against *Enterococcus Faecalis* biofilm in root canal of human teeth', *Dent. Mater. J.*, 2015, **34**, (1), pp. 54–60
[7] Ertem E., Gutt B., Zuber F., ET AL.: 'Core-shell silver nanoparticles in endodontic disinfection solutions enable long-term antimicrobial effect on oral biofilms', *ACS Appl. Mater. Interfaces*, 2017, **9**, (40), pp. 34762–34772
[8] Alabdulmohsen Z., Saad A.: 'Antibacterial effect of silver nanoparticles against *Enterococcus Faecalis*', *Saudi Endod J*, 2017, **7**, (1), pp. 29–35
[9] Wu D., Fan W., Kishen A., ET AL.: 'Evaluation of the antibacterial efficacy of silver nanoparticles against *Enterococcus Faecalis* Biofilm', *J. Endod.*, 2014, **40**, (2), pp. 285–290
[10] Kozuszko S.N., Sánchez M.A., de Ferro M.I.G., ET AL.: 'Antibacterial activity and biocompability of zinc oxide and graphite particles as endodontic materials', *J. Hard Tissue Biol*, 2017, **26**, (4), pp. 311–318
[11] Toledano M., Osorio E., Aguilera F.S., ET AL.: 'Polymeric nanoparticles for endodontic therapy', *J. Mech. Behav. Biomed. Mater.*, 2020, **103**, p. 103606
[12] Kishen A., Shi Z., Shrestha A., ET AL.: 'An investigation on the antibacterial and antibiofilm efficacy of cationic nanoparticulates for root canal disinfection', *J. Endod.*, 2008, **34**, (12), pp. 1515–1520
[13] Huang L., Li D.-Q., Lin Y.-J., ET AL.: 'Controllable preparation of nano-MgO and investigation of its bactericidal properties', *J. Inorg. Biochem*, 2005, **99**, (5), pp. 986–993
[14] Gholami A., Rasoul-Amini S., Ebrahiminezhad A., ET AL.: 'Magnetic properties and antimicrobial effect of amino and lipoamino acid coated iron oxide nanoparticles', *Minerva. Biotecnol.*, 2016, **28**, pp. 177–186
[15] Alhadrami H.A., Baqasi A., Iqbal J., ET AL.: 'Antibacterial applications of anatase $TiO_2$ nanoparticle', *Am. J. Nanomater.*, 2017, **5**, pp. 31–42
[16] Monzavi A., Eshraghi S., Hashemian R., ET AL.: 'In vitro and ex vivo antimicrobial efficacy of nano-MgO in the elimination of endodontic pathogens', *Clin. Oral Investig.*, 2015, **19**, (2), pp. 349–356
[17] Loyola-Rodriguez J.P., Torres-Mendez F., Espinosa-Cristobal L.F., ET AL.: 'Antimicrobial activity of endodontic sealers and medications containing chitosan and silver nanoparticles against *Enterococcus Faecalis*', *J. Appl. Biomater. Funct. Mater.*, 2019, **17**, (3), p. 2280800019851771
[18] Shrestha A., Shi Z., Neoh K.G., ET AL.: 'Nanoparticulates for antibiofilm treatment and effect of aging on its antibacterial activity', *J. Endod.*, 2010, **36**, (6), pp. 1030–1035
[19] Fontana C.R., Abernethy A.D., Som S., ET AL.: 'The antibacterial effect of photodynamic therapy in dental plaque-derived biofilms', *J. Periodontal Res.*, 2009, **44**, (6), pp. 751–759
[20] Pagonis T.C., Chen J., Fontana C.R., ET AL.: 'Nanoparticle-based endodontic antimicrobial photodynamic therapy', *J. Endod.*, 2010, **36**, (2), pp. 322–328
[21] Kesler Shvero D., Zaltsman N., Weiss E.I., ET AL.: 'Lethal bacterial trap: cationic surface for endodontic sealing', *J. Biomed Mater Res A*, 2016, **104**, (2), pp. 427–434
[22] Beyth N., Kesler Shvero D., Zaltsman N., ET AL.: 'Rapid kill-novel endodontic sealer and *Enterococcus Faecalis*', *PLoS One*, 2013, **8**, (11), p. e78586
[23] Padovani G.C., Feitosa V.P., Sauro S., ET AL.: 'Advances in dental materials through nanotechnology: facts, perspectives and toxicological aspects', *Trends Biotechnol.*, 2015, **33**, (11), pp. 621–636
[24] Akasaka T., Nakata K., Uo M., ET AL.: 'Modification of the dentin surface by using carbon nanotubes', *Biomed. Mater. Eng.*, 2009, **19**, (2–3), pp. 179–185
[25] Dong L., Henderson A., Field C.: 'Antimicrobial activity of single-walled carbon nanotubes suspended in different surfactants', *J. Nanotechnol.*, 2012, **2012**, p. 928924
[26] Vahabi S., Mardanifar F.: 'Applications of nanotechnology in dentistry: a review', *J. Dental School Shahid Beheshti Univ. Med. Sci.*, 2014, **32**, (4), pp. 228–239
[27] Xie H., Cao T., Rodriguez-Lozano F.J., ET AL.: 'Graphene for the development of the next-generation of biocomposites for dental and medical applications', *Dent. Mater.*, 2017, **33**, (7), pp. 765–774
[28] Dybowska-Sarapuk L., Kotela A., Krzeminski J., ET AL.: 'Graphene nanolayers as a new method for bacterial biofilm prevention: preliminary results', *J. AOAC Int.*, 2017, **100**, (4), pp. 900–904
[29] Pang L., Dai C., Bi L., ET AL.: 'Biosafety and antibacterial ability of graphene and graphene oxide in vitro and in vivo', *Nanoscale Res. Lett.*, 2017, **12**, (1), pp. 564–564
[30] Ioannidis K., Niazi S., Mylonas P., ET AL.: 'The synthesis of nano silver-graphene oxide system and its efficacy against endodontic biofilms using a novel tooth model', *Dent. Mater.*, 2019, **35**, (11), pp. 1614–1629
[31] He J., Zhu X., Qi Z., ET AL.: 'Killing dental pathogens using antibacterial graphene oxide', *ACS Appl. Mater. Interfaces*, 2015, **7**, (9), pp. 5605–5611

[32] Lee J.H., Jo J.K., Kim D.A., ET AL.: 'Nano-graphene oxide incorporated into PMMA resin to prevent microbial adhesion', *Dent. Mater.*, 2018, **34**, (4), pp. e63–e72
[33] Lee D.K., Kim S.V., Limansubroto A.N., ET AL.: 'Nanodiamond-Gutta percha composite biomaterials for root canal therapy', *ACS Nano*, 2015, **9**, (11), pp. 11490–11501
[34] Slowing I., Vivero-Escoto J., Wu C.-W., ET AL.: 'Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers', *Adv. Drug Deliv. Rev.*, 2008, **60**, (11), pp. 1278–1288
[35] Tian L., Peng C., Shi Y., ET AL.: 'Effect of mesoporous silica nanoparticles on dentinal tubule occlusion: an in vitro study using SEM and image analysis', *Dent. Mater. J.*, 2014, **33**, (1), pp. 125–132
[36] Zhu J., Liang R., Sun C., ET AL.: 'Effects of nanosilver and nanozinc incorporated mesoporous calcium–silicate nanoparticles on the mechanical properties of dentin', *PLoS One*, 2017, **12**, (8), p. e0182583
[37] Kang M.S., Lee N.H., Singh R.K., ET AL.: 'Nanocements produced from mesoporous bioactive glass nanoparticles', *Biomaterials*, 2018, **162**, pp. 183–199
[38] Kishen A., Peters O.A., Zehnder M., ET AL.: 'Advances in endodontics: potential applications in clinical practice', *J. Conserv. Dent.*, 2016, **19**, (3), pp. 199–206
[39] Ibrahim A.I.O., Moodley D.S., Petrik L., ET AL.: 'Use of antibacterial nanoparticles in endodontics', *S. Afr. Dent. J.*, 2017, **72**, pp. 105–112
[40] Abbaszadegan A., Sahebi S., Gholami A., ET AL.: 'Time-dependent antibacterial effects of Aloe Vera and Zataria Multiflora plant essential oils compared to calcium hydroxide in teeth infected with *Enterococcus Faecalis*', *J. Investig. Clin. Dent.*, 2016, **7**, (1), pp. 93–101
[41] Abbaszadegan A., Dadolahi S., Gholami A., ET AL.: 'Antimicrobial and cytotoxic activity of Cinnamomum Zeylanicum, calcium hydroxide, and triple antibiotic paste as root canal dressing materials', *J. Contemp. Dent. Pract.*, 2016, **17**, (2), pp. 105–113
[42] Shrestha A., Kishen A.: 'Antibacterial nanoparticles in endodontics: a review', *J. Endod.*, 2016, **42**, (10), pp. 1417–1426
[43] Wang L., Hu C., Shao L.: 'The antimicrobial activity of nanoparticles: present situation and prospects for the future', *Int. J. Nanomedicine*, 2017, **12**, pp. 1227–1249
[44] Nabavizadeh M., Abbaszadegan A., Gholami A., ET AL.: 'Antibiofilm efficacy of positively charged imidazolium-based silver nanoparticles in *Enterococcus Faecalis* using quantitative real-time pcr', *Jundishapur J. Microbiol.*, 2017, **10**, (10), p. e55616
[45] Abbaszadegan A., Nabavizadeh M., Gholami A., ET AL.: 'Positively charged imidazolium-based ionic liquid-protected silver nanoparticles: a promising disinfectant in root canal treatment', *Int. Endod. J.*, 2015, **48**, (8), pp. 790–800
[46] Abbaszadegan A., Gholami A., Abbaszadegan S., ET AL.: 'The effects of different ionic liquid coatings and the length of alkyl chain on antimicrobial and cytotoxic properties of silver nanoparticles', *Iran. Endod. J.*, 2017, **12**, (4), pp. 481–487
[47] Toledano M., Munoz-Soto E., Aguilera F.S., ET AL.: 'A zinc oxide-modified hydroxyapatite-based cement favored sealing ability in endodontically treated teeth', *J. Dent.*, 2019, **88**, p. 103162
[48] Raie D.S., Mhatre E., El-Desouki D.S., ET AL.: 'Effect of novel quercetin Titanium dioxide-decorated multi-walled carbon nanotubes nanocomposite on Bacillus Subtilis biofilm development', *Materials. (Basel)*, 2018, **11**, (1), p. 157
[49] Rezvani M.B., Atai M., Hamze F., ET AL.: 'The effect of silica nanoparticles on the mechanical properties of fiber-reinforced composite resins', *J. Dent. Res. Dent. Clin. Dent. Prospects.*, 2016, **10**, (2), pp. 112–117
[50] Gerasymchuk Y., Lukowiak A., Wedzynska A., ET AL.: 'New photosensitive nanometric graphite oxide composites as antimicrobial material with prolonged action', *J. Inorg. Biochem*, 2016, **159**, pp. 142–148
[51] Saghiri M.A., Orangi J., Tanideh N., ET AL.: 'Effect of endodontic cement on bone mineral density using serial dual-energy X-ray absorptiometry', *J. Endod.*, 2014, **40**, (5), pp. 648–651
[52] Fan W., Wu D., Tay F.R., ET AL.: 'Effects of adsorbed and templated nanosilver in mesoporous calcium-silicate nanoparticles on inhibition of Bacteria colonization of dentin', *Int. J. Nanomedicine*, 2014, **9**, pp. 5217–5230
[53] Zand V., Mokhtari H., Hasani A., ET AL.: 'Comparison of the penetration depth of conventional and nano-particle calcium hydroxide into dentinal tubules', *Iran. Endod. J.*, 2017, **12**, (3), pp. 366–370
[54] Han Y., Kiat-amnuay S., Powers J.M., ET AL.: 'Effect of nano-oxide concentration on the mechanical properties of a maxillofacial silicone elastomer', *J. Prosthet. Dent.*, 2008, **100**, (6), pp. 465–473
[55] Xia Y., Chen H., Zhang F., ET AL.: 'Injectable calcium phosphate scaffold with iron oxide nanoparticles to enhance osteogenesis via dental pulp stem cells', *Artif. Cells Nanomed. Biotechnol.*, 2018, **46**, (sup1), pp. 423–433
[56] Xia Y., Chen H., Zhang F., ET AL.: 'Gold nanoparticles in injectable calcium phosphate cement enhance osteogenic differentiation of human dental pulp stem cells', *Nanomedicine*, 2018, **14**, (1), pp. 35–45
[57] Gupta J.: 'Nanotechnology applications in medicine and dentistry', *J. Investig. Clin. Dent.*, 2011, **2**, (2), pp. 81–88
[58] Cecilia S., Divyarani S., Lakshya K., ET AL.: 'Preparation of silver nano particles using aqueous solution of Ocimum Sanctum and Piper Betle and evaluation of its antimicrobial activity against *Enterococcus Faecalis*', *Int. J. Pharmaceutical and Clinical Res.*, 2016, **8**, (7), pp. 1118–1120
[59] Ebrahimi N., Rasoul-Amini S., Ebrahiminezhad A., ET AL.: 'Comparative study on characteristics and cytotoxicity of bifunctional magnetic-silver nanostructures: synthesized using three different reducing agents', *Acta Metallurgica Sinica (English Letters)*, 2016, **29**, (4), pp. 326–334
[60] Samiei M., Shahi S., Ghasemi N., ET AL.: 'Effect of different additives on genotoxicity of mineral trioxide Aggregate', *Iran. Endod. J.*, 2018, **13**, (1), pp. 37–41
[61] Rosario F., Hoet P., Santos C., ET AL.: 'Death and cell cycle progression are differently conditioned by the AgNP size in osteoblast-like cells', *Toxicology*, 2016, **368-369**, pp. 103–115
[62] Shameli K., Ahmad M.B., Jazayeri S.D., ET AL.: 'Investigation of antibacterial properties silver nanoparticles prepared via green method', *Chem. Cent. J.*, 2012, **6**, pp. 73–73
[63] Gholami A., Rasoul-amini S., Ebrahiminezhad A., ET AL.: 'Lipoamino acid coated superparamagnetic iron oxide nanoparticles concentration and time dependently enhanced growth of human hepatocarcinoma cell line (Hep-G2)', *J. Nanomater.*, 2015, **2015**, p. 451405
[64] Acosta-Torres L.S., Mendieta I., Nunez-Anita R.E., ET AL.: 'Cytocompatible antifungal acrylic resin containing silver nanoparticles for dentures', *Int. J. Nanomedicine*, 2012, **7**, pp. 4777–4786
[65] Memarzadeh K., Sharili A.S., Huang J., ET AL.: 'Nanoparticulate zinc oxide as a coating material for orthopedic and dental implants', *J. Biomed. Mater. Res., Part A*, 2015, **103**, (3), pp. 981–989
[66] Opacic-Galic V., Petrovic V., Zivkovic S., ET AL.: 'New nanostructural biomaterials based on active silicate systems and hydroxyapatite: characterization and genotoxicity in human peripheral blood lymphocytes', *Int. Endod. J.*, 2013, **46**, (6), pp. 506–516
[67] Lee J.K., Kim S., Lee S., ET AL.: 'In vitro comparison of biocompatibility of calcium silicate-based root canal sealers', *Materials (Basel)*, 2019, **12**, (15), p. 2411
[68] Abramovitz I., Beyth N., Weinberg G., ET AL.: 'In vitro biocompatibility of endodontic sealers incorporating antibacterial nanoparticles', *J. Nanomaterials*, 2012, **2012**, p. 858073
[69] Connolly M., Fernandez-Cruz M.L., Quesada-Garcia A., ET AL.: 'Comparative cytotoxicity study of silver nanoparticles (AgNPs) in a variety of rainbow trout cell lines (Rtl-W1, Rth-149, Rtg-2) and primary hepatocytes', *Int. J. Environ. Res. Public Health*, 2015, **12**, (5), pp. 5386–5405





doi: 10.1049/mnl.2019.0747