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Perspective

The antibacterial role of photodynamic activation of nanoencapsulated photosensitizing agents in root canals.

El rol antibacteriano de la activación fotodinámica de agentes fotosensibilizantes nanoencapsulados en los canales radiculares.

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The bacterial biofilm is considered the main virulence factor of primary and secondary infections of the root canal system. Therefore, the success of endodontic therapy strongly depends upon the effective eradication of bacteria, and this is more difficult due to the presence of biofilms, which are a complex and coordinated organization.[1] It has been reported that bacteria within biofilms can be at least 1000 times more resistant to antimicrobial therapies than their planktonic counterparts.

Current endodontic treatment strategies have proven to be insufficient to reduce endodontic pathogens to below detection limits, achieving around 77% of success in resolving persistent infections.[2] The most likely reason for this, apart from the general emergence of resistant pathogens, is the complex morphology of the root canal system, which makes it difficult to reach bacteria in regions inaccessible to antimicrobial agents. Furthermore, the efficacy of antibacterial agents can be limited by factors such as concentration, time, and volume within the root canals. Therefore, it is clear that new advanced disinfection approaches are required for the effective eradication of endodontic biofilms.

Nanotechnology is a strategy that has been in the spotlight in recent decades, due to its innovative and functional properties. Nanoparticles (NPs) are defined as submicroscopic particles between 1 and 100 nm in size. It has been observed that NPs can potentially improve the therapeutic efficacy of pharmaceutical products by promoting better bioavailability, serum stability, and drug pharmacokinetics. According to the literature, nano-formulations provide better penetration and allow the slow and controlled release of active ingredients at the target sites.[3] The most important characteristic of NPs is their large external surface area, as well as their high surface to volume ratio, factors that determine their physicochemical properties.[4]

In recent years, metallic NPs have attracted considerable interest due to their physicochemical properties, small size, and high monodispersity parameters.

Specifically, silver nanoparticles (AgNPs) have received special attention in the field of medicine due to their properties, their high antimicrobial activity at low concentrations and low bacterial resistance.[5] AgNPs have been synthesized through various physical and chemical processes, which are costly and of low efficiency; in addition hazardous wastes are generated

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that could present a significant environmental risk. An alternative method is based on the use of plant extracts, with several advantages.[6] The flavonoids, polyphenols, sugars, aromatic compounds and other functional compounds present in plant extracts have been assayed to produce AgNPs.

On the other hand, antimicrobial photodynamic therapy (aPDT) is an alternative therapy proposed to combat a wide spectrum of infectious diseases mediated by biofilms. Its application in endodontics is of particular interest since it is a simple approach, where a visible light source of a suitable wavelength, generally a diode or light-emitting diode (LED) light, is absorbed by a photosensitive non-toxic agent (PS).[7] After activation in the presence of molecular oxygen ($^3O_2$), it produces reactive oxygen species (ROS) such as singlet oxygen ($^1O_2$), which kills microorganisms without inducing resistance or while inflicting minimal damage to the host.[8]

The most studied and used PS in aPDT are phenothiazines (non-porphyrinic synthetic compounds), such as methylene blue and toluidine blue, at different concentrations. Studies have shown that when activated with specific wavelengths, they exhibited bactericidal effects and are capable of eliminating both Gram- negative and Gram-positive bacteria, including *E. faecalis*.[9] Indocyanine green (ICG) is one of the non-toxic photosensitizers approved by the U.S. Food and Drug Administration (FDA) that has been widely used in different medical applications.

Lately it has gained more attention in endodontics due to its valuable properties, including the wide absorption band in the near infrared region and the ability to produce ROS, allowing for the eradication of a wide range of microbial species.[10] The main disadvantage of conventional PS agents is that they are hydrophobic, thus poorly soluble in water. Therefore, a promising approach to improve PS performance within the root canal system is to encapsulate them in nanostructured materials. Recently,

PS-nanoparticle complexes have been studied that are based on reduced graphene oxide, poly (lactic-co-glycolic acid) (PLGA), poly (ethylene-glycol) -poly (ℭ-caprolactone) copolymers (PEG-PCL) and metal organic frameworks (MOF).

The use of aPDT associated with photosensitizing agents encapsulated in nanoparticles of different origins opens a new way to combat bacterial infections within the root canal system. So far, the reported results are promising and point to the activation of nanoencapsulated photosensitizing agents as a promising antimicrobial alternative in the endodontic field.

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REFERENCES.

1. Nair PNR. On the causes of persistent apical periodontitis: a review. Int Endod J. 2006; 39: 249-81.
2. Ng YL, Mann V, Gulabivala K. Outcome of Secondary Root Canal Treatment: A Systematic Review of the Literature. Int Endod J. 2008;41:1026-46.
3. Sans-Serramitjana E, Fusté E, Martínez-Garriga B, Merlos A, Pastor M, Pedraz JL, Esquisabel A, Bachiller D, Vinuesa T, Viñas M. Killing effect of nanoencapsulated colistin sulfate on Pseudomonas aeruginosa from cystic fibrosis patients. J Cyst Fibros. 2016;15:611-8.
4. Jaramillo AF, Riquelme SA, Sánchez-Sanhueza G, Medina C, Solís-Pomar F, Rojas D, Montalba C, Melendrez MF, Pérez-Tijerina E. Comparative study of the antimicrobial effect of nanocomposites and composite based on poly (butylene adipate- co-terephthalate) using Cu and Cu/Cu2O nanoparticles and CuSO4. Nanoscale Res Lett. 2019;14:158.
5. Durán N, Durán M, de Jesus MB, Seabra AB, Fávaro WJ, Nakazato G. Silver nanoparticles: a new view on mechanistic aspects on antimicrobial activity. Nanomed Nanotechnol Biol Med.2016;12:789-9.
6. Manosalva N, Tortella G, Diez MC, Schalchli H, Seabrea AB, Durán N, Rubilar O. Green synthesis of silver nanoparticles: effect of synthesis reaction parameters on antimicrobial activity. World J Microb Biot. 2019;35:88.
7. Plotino G, Grande NM, Mercadé M. Photodynamic therapy in endodontics. Int Endo J. 2019;52:760-774.
8. Diogo P, Fernandes C, Caramelo F, Mota M, Miranda IM, Faustino MAF, Neves MGPMS, Uliana MP, de Oliveira KT, Santos JM, Gonçalves T. Antimicrobial Photodynamic Therapy against Endodontic Enterococcus faecalis and Candida albicans Mono and Mixed Biofilms in the Presence of Photosensitizers: A Comparative Study with Classical Endodontic Irrigants. Front Microbiol. 2017;8:498.
9. López-Jimenez L, Fusté E, Martínez-Garriga B, Arnabat-Domínguez J, Vinuesa T, Viñas M. Effects of Photodynamic therapy on Enterococcus faecalis biofilms. Lasers Med Sci. 2015;30:1519-26.
10. Akbari T, Pourhajibagher M, Hosseini F, Chiniforush N, Gholibegloo E, Khoobi M, Shahabi S, Bahador A. The effect of indocyanine green loaded on a novel nano- graphene oxide for high performance of photodynamic therapy against Enterococcus faecalis. Photodiagnosis Photodyn Ther. 2017;20:148-153.

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