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Nanoparticles in Irrigation and Disinfection of the Root Canal System – A Review

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Abstract
This article discusses use of nanoparticles in disinfection of the root canal system. the various nanoparticles discussed here are chitosan, silver, zinc oxide, bioactive glass and polylacticoglycolic acid nanoparticles. Further it describes the mechanisms of action in eradication of bacteria present in the dentinal tubules. This paper also describes the mechanism of nanoparticle delivery.

Introduction
An important objective in endodontic therapy is to eliminate residual organic and inorganic debris and bacteria as much as possible from the root canal system. To accomplish this goal effective root canal irrigation is required, as instrumentation alone is insufficient and inadequate.[1] The goals of irrigation mainly are to facilitate removal of micro-organism, tissue remnants and dentin chips from root canal during and after instrumentation

as also to prevent packing of hard and soft tissue in the apical root canal and to kill bacteria and yeast with its antimicrobial properties. [2]

Endodontic irrigants desirable properties are that they should have broad antimicrobial spectrum and high efficacy against anaerobic and facultative microorganisms organised in biofilms, dissolve necrotic pulp tissue, inactivate endotoxins, and prevent formation and removal of smear layer during instrumentation.[3]

For nanoparticles to be successful endodontic irrigants of the future they should have these desirable properties. So the basic question is what are nanoparticles and how are they use effective and helpful in endodontic therapy? *Nanoparticles* are small stable particles whose size is measured in nanometers. These particles are used in various biomedical application in which they can be utilized as drug carriers or imaging agents. (1nm= 10^{-9} m).[4] This nanoparticles are available in different forms as given in Table 1.

Table 1. Different forms of Nanoparticles

Nanoparticle	Average Diameter	Mechanism Of Action	Antibacterial efficacy
Chitosan	70nm	Alteration of cell wall permeability and leakage of intracellular components.[6]	Yes
Zinc oxide	60-100nm	ROS (reactive oxygen species) production Cell membrane and lysosomal damage.[7]	Yes
Silver	40-60nm	inhibit respiratory enzyme and ATP production ROS production Cell membrane damage. [7]	Yes
Bioactive glass	20-60 nm	alteration in cell wall permeability through constant release of silica.[7]	Yes
Polylacticogylcolic acid	150-250nm	production of singlet oxygen[8]	Yes

Mechanism of Action

Antibacterial activity of nanoparticles is based upon contact mediated lipid peroxidation via production of reactive oxygen species. Interfacial forces, especially electrostatic, will control contact between nanoparticles and bacterial membrane. Attractive forces are generated between positively charged nanoparticles and negatively charged bacterial cell. A repulsive force is generated between bacterial cells and negatively charged nanoparticles. Processes which alter the surface charge of nanoparticles may indirectly alter the interaction between affected nanoparticles and bacterial cell. Once in contact with bacterial membrane, nanoparticles cause lethal cell damage by producing ROS (reactive oxygen species), eventually allowing ingress of nanoparticles into the periplasm. Exopolymers –secreted carbohydrates and proteins may prevent nano-particles or ROS contacting the cell membrane thus preventing cell damage.[5]

Why Nanoparticles Should Be Preffered

The reasons for the nanoparticles to be given prime importance are discussed below;

1. Better Penetration into The Dentinal Tubules

The average diameter of dentinal tubules is 1 µm and the average diameter of nanoparticle is 100nm (100×10^{-3} µm) i.e 0.1 µm. Thereby suggesting that dentinal tubules are ten times greater than nanoparticles and allowing easier penetration of nanoparticles in the tubules.[9]

2. Antimicrobial Activity:

An inverse relationship between nanoparticle size and bactericidal activity has been seen, here expressed as percentage reduction in viability after 4 hours exposure, compared to unexposed cells. Data shown for gram negative bacteria E.coli and Staphylococcus aureus exposed to 1mg/ml of nanoparticles in a nutrient broth.[5]

3. Broad spectrum of activity:

Bacteria are far less likely to acquire resistance against metal nanoparticles as metals can act on a broad range of microbial targets and many mutations would have to occur for microrganisms to resist their antimicrobial activity.[7]

4. Alternative to $Ca(OH)_2$

The average size of $Ca(OH)_2$ particles was 1-2.5 µm.[11] Nanoparticles being a lot smaller in size i.e 40-250 nm. With such variability in size increases the surface area to 10 fold. Thus increasing in the active exchange surface as compared to $Ca(OH)_2$.[7]

5. Hinder bacterial adherence

Nanoparticles disinfect root canal system inhibiting bacterial adherence. Studies show reduction in adherence Zinc oxide nanoparticle is about 95% and Chitosan nanoparticle is about 83%.[6]

6. Biocompatibility

Shrestha A et al (2010) stated Zinc Oxide and chitosan nanoparticles showed a high biocompatibility.[10] It was also stated that silver nanoparticle dispersion is also biocompatible when compared to sodium hypochlorite solution.

Delivery Of Nano- Particles In The Tubules:

Research To Generate High Intensity Focused Ultrasound [HIFU]

In this experiment conducted by Shrestha A et al high-speed jetting of collapsing cavitation bubbles produced by HIFU has been tested for the delivery of antibacterial nanoparticles into the dentinal tubules.

The basic principle behind the application of ultrasound is the formation of cavitation bubbles. These bubbles are in a non-equilibrium state and will oscillate and collapse. The bubble dynamics involved is often complex due to the proximity of the nearby tissues. The violent bubble collapse with high-speed jetting could be used beneficially (for example, for the removal of biofilm), or could cause undesirable collateral damage (for instance, vascular damage or hard and soft tissue damage in ultrasonic therapy. One way of generating an oscillating bubble is via the ultrasonic system used in root canal treatment known as endosonics (coined by Martin and Cunningham). In an endosonic system, a frequency of between 25 and 40 kHz is employed. The activated endosonic file is expected to produce cavitation, acoustic streaming, and heat within the irrigating solution. The rapid movement of fluid in a circular or vortex-like motion around a vibrating instrument such as the endosonic file is described as acoustic micro-streaming. The acoustic micro-streaming leads to energy dispersal which causes radiating pressure and subsequently leads to shear stresses imposed along the root canal wall, thereby dislodging the debris and adherent bacterial cells. HIFU may act as a supplementary method to reach the bacteria persisting within the anatomical complexities and dentinal tubules, thus to improve the success of root canal disinfection. The nanoparticles used in the study possessed antimicrobial properties and biocompatibility which have also been investigated in drug delivery and cancer therapies, and for the treatment of bacterial infections. These chitosan nanoparticles are small enough (<100 nm) to be delivered into the root canal complexities and dentinal tubules.

This study was conducted in order to understand the basic mechanism of HIFU. The experiments were conducted in two stages. Characterization experiments were carried out using a spark bubble experiment to test the bubble's efficiency to propel particles through channels. These experim-ents were designed to help in the understanding of the mechanism involved in the delivery of nanoparticles into dentinal tubules. High speed photography is used to capture the transient bubble dynamics. Experiments were conducted to further reconfirm the bubble dynamics observed in the characterization experiments using human dentine specimens to deliver antibacterial nanoparticles into the dentinal tubules by using the HIFU system.[9]

Clinical Use In The Delivery Of Nanoparticles

High Intensity Focused Ultrasound

To apply HIFU in endodontics, focused ultrasound should be generated intracanally. This can be achieved by using piezo ceramic crystal on the tip of a nonvibrating file or extracorporeal use of HIFU with HIFU device touching only the tooth surface.[9]

Photodynamic Therapy

Methylene blue loaded polylactico glycolic acid nanoparticles. The irradiation source was a diode laser (BWTEK Inc, Newark, DE) with an output of 1 W and a wavelength of 665 nm. Due to the production of singlet oxygen when the sensitizer is activated with the laser there is photodestruction of root canal bioflims.[8]

Shortcomings

Field emission scanning electron microscopic (FESEM) showing nanoparticles as clumps (arrow) which formed a coating along the tubule walls. Antibacterial nanoparticles are found to be non uniform along the lumen of dentinal tubules and nanoparticles showed tendency to form aggregates.

To help prevent aggregation of nanoparticles, stabilizing agents that bind to the entire nanoparticles surface can be used; these include oligo and polysaccharides, sodium dodecyl sulphate, polyethylene gycol and glycolipids.[7]

Conclusion

Although research has shown that nanoparticles by themselves are effective in tackling endodontic microflora, more research is required for efficient delivery of nanoparticles in the complexities of root canal system. Considering that chitosan particles are freely available in the Indian market, they would make an interesting endodontic research topic for us.

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