Al-Rafidain Dental Journal, Vol. 23, Issue No.1, 2023 (37-52)

Al-Rafidain Dental Journal

rden.mosuljournals.com

Nanoparticles as Endodontic Irrigation: An Update Overview

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Article information

Received: April,20 2022
Accepted: December 20, 2022
Available online: March 5, 2023

Keywords
Nano dentistry
Nanoparticles
Root canal
Endodontic irrigation.

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Abstract

Aims: The purpose of this study is to provide a complete overview of the current scientific information on the use of nanoparticles in endodontic irrigation. The complicated structure of the root canals makes thorough cleaning and disinfection difficult. The removal of infection from the root canal system is the primary goal of root canal treatment. Irrigation is the only way to sterilize inaccessible anatomic irregularities. Because of the nanoparticles ultra-small sizes, big surface area/mass ratio, and enhanced chemical reactivity, applying them with irrigants improve disinfection efficiency .**Conclusion**: The use of nanoparticles in irrigation can improve the antibiofilm efficacy of endodontic treatment particularly against chronic endodontic infections like E. faecalis. Many more researches are required to identify the best nanoparticles for use in root canal irrigation, which is still in the works.

الخلاصة

الاهداف: تهدف الدراسة الى تقديم لمحة كاملة عن المعلومات العلمية الحالية حول استخدام الجسيمات النانوية في الري اللبي. الهيكل المعقد لقنوات الجذر يجعل التنظيف الشامل والتطهير صعبًا. الهدف الأساسي من علاج قناة الجذر هو إزالة العدوى من نظام قناة الجذر. الري اللبي هو الطريقة الوحيدة لتعقيم الأجزاء الدقيقة التي يتعذر الوصول إليها. نظرًا للأحجام الصغيرة جدًا للجسيمات النانوية، ومساحة السطح الكبيرة / نسبة الكتلة، والتفاعل الكيميائي المعزز، فإن استخدامها مع مواد الري يحسن كفاءة التطهير. **الاستنتاج**: يمكن أن يؤدي استخدام الجسيمات النانوية في الري إلى تحسين فعالية المضادات الحيوية في العلاجات اللبية خاصةً ضد التهابات اللبية المزمنة مثل .E. faecalis هناك حاجة إلى المزيد من الأبحاث لتحديد أفضل الجسيمات النانوية لاستخدامها في ري قناة الجذر، والتي لا تزال قيد العمل.

DOI: 10.33899/rdenj.2023.133586.1161,

INTRODUCTION

The oral cavity comprises many microorganisms [1]. The complexity of the root canal enhances biofilm formation. Endodontic infection is a complex and mixed infection, and the elimination of these biofilms from the endodontic canals is the primary goal of endodontic treatment[2].

Several pathways increase the pathogenicity and virulence of endodontic microorganisms in a biofilm state[3]. Kishen outlined the underlying pathways by which endodontic infections are able to resist routinely used root canal irrigants and medicaments in 2010[4]. These pathways are commonly linked to the extracellular polymeric matrix, bacterial growth rate, and nutritional state [4]. The extracellular polymeric matrix has the potential to improve endodontic biofilm resistance to root canal irrigants and medicaments [3].

Antimicrobial materials penetration rate was also found to be reduced by the extracellular polymeric matrix [5]. Another aspect contributing to endodontic infections' greater pathogenicity in a state of biofilm is the capacity of microorganism to display distinct gene patterns when contrasted to planktonic germs. As a result, microbial biofilms have been discovered to be more resistant [6].

To fight endodontic infections, a variety of root canal irrigants and medications are available. However, no confirmation of total pathogen clearance using these treatments has been found [7].

Sodium hypochlorite (NaOCl) is the most often used endodontic irrigant, with concentrations ranging from 0.5 percent to 5.25 percent [8]. Traditional research has frequently emphasized its tissue dissolving and antibacterial effects [9]. However, using (NaOCl) can result in making the dentine matrix weak and deteriorated, injury to the periapical area, and the growth of persistent microorganisms, all of which are undesirable results [10].

Chlorhexidine (CH) has been advocated as a less traumatic endodontic irrigant and is commonly used at 2 percent concentration; nevertheless, its primary disadvantages consist of the incapacity to breakdown dead tissue and its lower efficiency against microorganisms of Gram-negative type [11].

EDTA (EthyleneDiamineTetraAcetic acid) is a chemical chelating agent that is frequently used to remove the smear layer. The biofilm of E. faecalis was showing higher sensitivity to (NaOCl) at 2.5 percent together with EDTA at 17 percent [12]. Heavy use of EDTA, however, might cause demineralization of dentine, particularly when paired with (NaOCl) irrigant [13].

Despite improvements in treatment procedures, data-based information suggests that the rate of treatment failure has not decreased beyond 18-26 percent over the last 4-5 decades[14]. This could be owing to present technologies' inability or inefficiency to handle the disease's consequences completely[15].

Because of the limits of conventional irrigation procedures, the use of nanoparticle-based irrigant has grown in popularity [16]. Nano dentistry refers to the use of nanomaterials in the detection and treatment of oral diseases, with the goal of improving overall oral health[17].

The term "nano" comes from a Greek word that means "dwarf." [18]. Nanoparticles are available in a variety of shapes and sizes. The size of nanoparticles ranges from 1-100nm. They have a variety of characteristics, including extremely small sizes, and higher chemical activity[7]. Nanoparticles have a wide range of uses in infection control strategies because to their biocidal, anti-adhesive, and transport properties, particularly in the complex oral cavity environment [19].

The greater surface areas of nanoparticles, and the higher concentrations at the target site, are the most effective factors in antibacterial behavior as compared to their conventional counterparts [20].

Classification of Nanoparticles in General

A. According to their Origin

1. Naturally occurred: are those nanoparticles which are created by biological species or by human activity in the environment. Regardless of human activity, naturally occurring nanoparticles exist in all of the Earth's spheres (including the hydrosphere, atmosphere, lithosphere, and even the biosphere) [21][22].
2. Synthetic: are those nanoparticles which are made by physical, chemical, biological, or hybrid means of synthesis, as well as mechanical grinding, engine exhaust, and smoke[21] [22].

B. According to their dimension

1. Zero- dimension or nano structure: are the most prevalent kind of nanopaterials, which have dimensions that are on the nanoscale (larger than 100nm). These nanoparticles are tiny particles that resemble points. Quantum dots (uniform particle arrays), hollow spheres, nanolenses, and hollow spheres are the most prevalent types of these particles Fig (1)[21] [23].
2. One- dimension or nano rods: These nanoparticles have at least one dimension that exceeds nanoscales, and they have additional dimensions that fall within the nano range. The most frequently seen one-dimensional nanoparticles are nanofibers, nanotubes, and nanorods Fig (1)[21] [23].
3. Two- dimensional or thin films: These nanoparticles are larger than nanoscale (100nm) by two dimensions. Nanofilms, nanolayers, and nanocoatings are some of this class's most prevalent instances. This class of nanoparticles presented in plate-like structures Fig (1) [21] [23].
4. Three-dimensional or nano cones: These nanoparticles have three dimensions larger than 100nm, but their elements are smaller than 100nm. Nano range particles combine to form three-dimensional nanomaterials. These materials are usually nonporous in nature and have a wide range of applications. Nanocomposites, nanofiber bundles, and multinanolayer-type structures are the most popular examples of three-dimensional nanomaterials Fig (1) [21] [23].

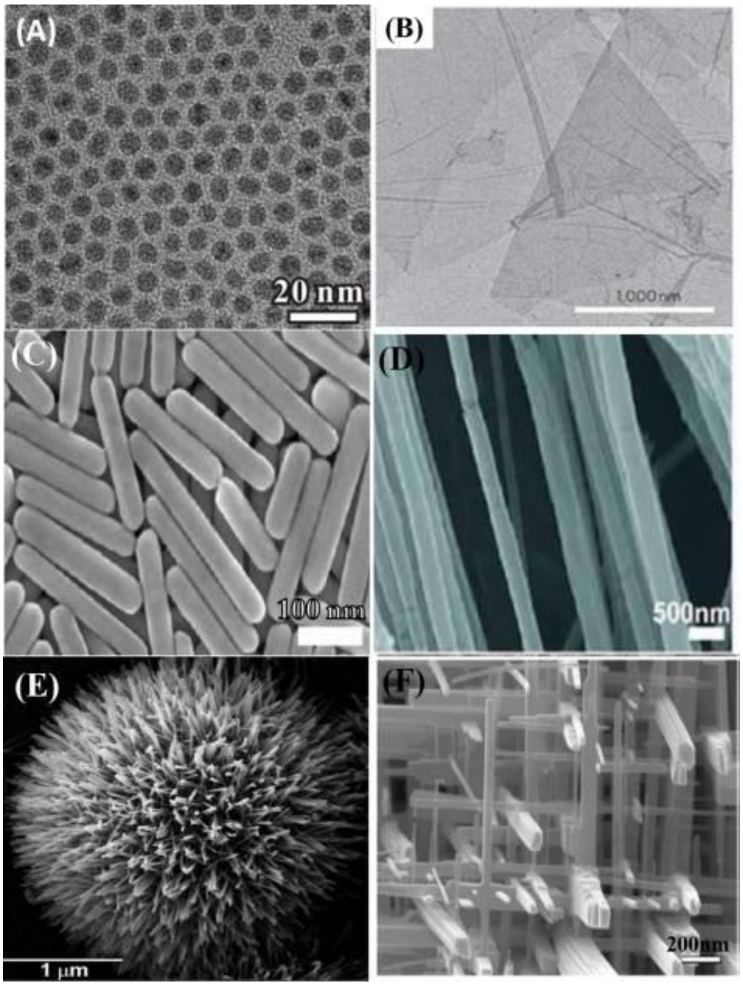

Figure (1): classification of nano particles according to their dimension (A) nonporous Pd NPs (0D) (B) Graphene nanosheets (2D), (C) Ag nanorods (1D), (D) polyethylene oxide nanofibers (1D), (E) urchin-like ZnO nanowires (3D), (F) WO3 nanowire network (3D). [22]

C. According to their composition [24]

1. Metallic, which includes silver, magnesium, gold, iron, and copper.
2. Inorganic, which include iron oxide, Zinc oxide, cerium oxide titanium dioxide, aluminum oxide, and bioactive glass.
3. Polymeric, which includes chitosan and alginate,
4. Functionalised with drugs like photosensitizers, antibodies, and proteins.
5. Quantum dots which include cadmium, cadmium sulfide, and selenide.

D. According to their shape [24]

1. stars
2. rods
3. Spheres
4. triangles and many other shapes Fig (2.

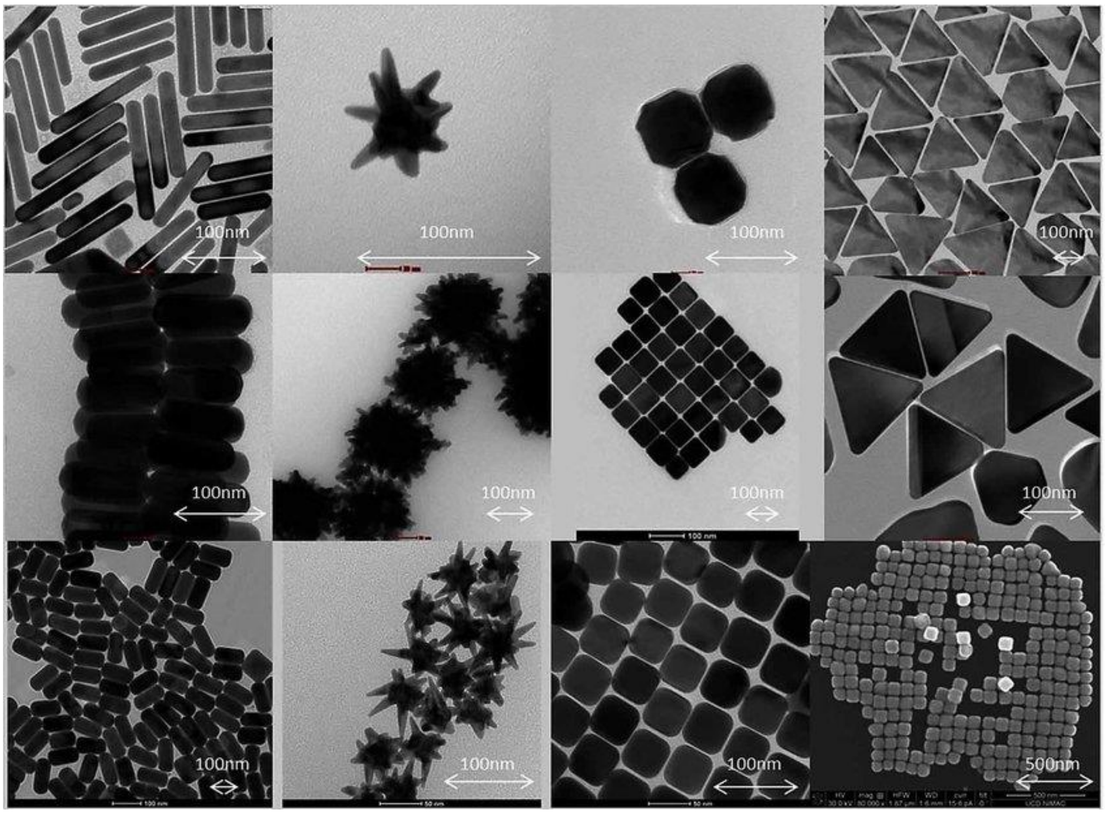

Figure (2): SEM of different shapes of nano particles. [25]

Mechanism of Action of Nanoparticles

The following are a few of the known mechanisms via which NPs work:

1. Disruption of Cell Wall as a result of Interaction of Electrostatic Forces

Because the different charges are attracted to one another, these NPs which are positively charged successfully attach to the bacteria and disrupt the bacterial cell wall structure and increase membrane permeability, allowing more NPs to enter bacteria and cause cellular content to escape [2]. By adhering to mesosomes, these NPs influence respiration, division, and DNA replication [26].

2.Homeostasis of Metal Ions

Metal ion homeostasis is a main regulator of metabolic processes in microorganisms. Excess NPs of metal origin disrupt the process, which is essential to the survival of cells, causing irreversible damage as well as delaying or killing bacteria [27].

3. Reactive Oxygen Species (ROS) Production

When NPs gain access to a microorganism's cell membrane and cause the formation of Reactive Oxygen Species (ROS), the cell experiences oxidative stress, which leads to an attack on the microbe. Respiration and ATP synthesis are reduced as a result of this attack, resulting in cell membrane rupture. The ATP is an enzyme that directly produces adenosine triphosphate (ATP) during the process of cellular respiration and it is the primary energy molecule found in cells.[2][28].

4.Dysfunction of Proteins and Enzymes

By catalyzing the process of oxidation of amino acid chains, NPs produce a naturally protein bound known as carbonyls, leading to protein degradation, and deactivation of multiple enzymes [29].

5.Genotoxicity and Signal Transduction Inhibition

Because of electrical characteristics of NPs, they are going to react with nucleic acid molecules, which has deleterious impact on DNA replication, leading to suppression of signal transmission [30].

Nanoparticles Used in Endodontic Irrigation

A. Metallic and Inorganic Nanoparticles

1 .Silver Nanoparticles

In dentistry, AgNPs have been extensively studied. AgNPs have antibacterial and antifungal effects due to their multi-level mechanism of action [31,32] . Silver nanoparticles can bind to the negative charge region of the bacterial cell wall, resulting in cytoplasmic content leakage and eventual bacterial cell rupture [7]. As a consequence, the nanoparticles will enter the cytoplasm and react with proteins containing sulfur and phosphorus, such as RNA and DNA, inflicting more harm to the bacteria [33]. Furthermore, when AgNPs come into contact with aqueous media, they produce silver ions, disrupting bacterial activities even more [34].

AgNPs have been demonstrated to have antibacterial and antibiofilm activity against E. faecalis in endodontic diseases [35]. Afkhami et al. observed that 100 ppm silver nanoparticles had a superior antibacterial action as irrigant in a comparison with 2.5 percent of sodium hypochlorite. When compared to sodium hypochlorite, poly vinyl coated Silver nanoparticles were found to have lower cytotoxicity [36].

However, the physical and structural features of root dentine may be influenced by irrigation with AgNPs solutions. When compared to NaOCl, using a final irrigant containing silver nanoparticles will increase the resistance to fracture of the teeth that are treated endodontically to the double [37].

In a recent study disinfecting for surfaces based on a unique mixture of electrolytically produced silver ions (0.003 percent) in citric acid (4.846 percent) has been tested as an innovative material for cleaning and disinfecting of root canals [38]. This novel root canal disinfectant has intriguing antibacterial capabilities, but it also has some serious drawbacks, such as low pH-related toxicity that could limit their safe clinical application [39].

It can be presumed silver citrate solution was poisonous when utilized at concentrations more than 0.5 percent. Further studies are required with this class of irrigants to ascertain the best dilution capable of assuring biocompatibility and a successful root canal cleaning [38].

Another new colloidal solution of silver nanoparticles, odorless and colorless (ARGITOS) was developed using enhanced nanobiotechnologies and “green chemistry” techniques and consists of silver, bidistillate and sodium peroxide (stabilizer). The solution was formed with concentrations of particles 1-2 nm in size (1000–10,000 ppm). The nanosilver Argitos solution, has a strong capacity to impregnate the smear layer (size 1-2 nm). This solution has a potent antibacterial action against E. faecalis [40].

Silver nanoparticles have shown promise as an antibacterial agent against endodontic infections. However, more research is needed to determine whether there is any influence on tooth structure color stability, or potential cytotoxic impact on cells of human being [7].

2 .Zinc Oxide Nanoparticles (ZnONPs)

Zinc oxide NPs having a method of action comparable to silver NPs, they have been promoted for their bactericidal characteristics. After 90 days of age, a Zinc oxide NPs containing irrigant solution was appeared to remove planktonic E. faecalis and destroy the biofilm matrix while their bactericidal efficacy will remain. However, when compared to planktonic bacteria, its bactericidal effects were lower prominent against bacteria in biofilm status [41].

When zinc oxide NPs come into contact with aqueous media, their bactericidal activity is proportional to their size; when the size is smaller, the bactericidal activity will be stronger and also the generation of oxygen species such as "hydrogen peroxide" [42].

In addition, ZnONPs can create zinc ions within the bacteria, affecting the bacterial cell's enzymatic system and the metabolism of amino acid, leading to significant destruction[43]. Zinc oxide nanoparticles have an antibacterial effect that is proportional to their concentration, with higher concentrations having a great antibacterial effect [44].

When both silver NPs and zinc oxide NPs were combined in solution in polymeric state, they had better antibacterial action against E. faecalis than when they were employed separately, however using NaOCl in a percent of 2.5 more successful in terms of minimizing colony forming units (CFU) [16].

According to a research, a zinc oxide NPs containing irrigant had lower antibacterial activity against bacteria of E. faecalis type than 2 percent chlorhexidine and 5 percent NaOCl, although the difference was negligible statistically [45] .When compared to NaOCl, the ZnONPs usage as a last irrigant produced an increase in a fracture resistance mean about 400N of root canal that is endodontically treated [37] .Another study found that polymeric suspension usage as irrigation comprising silver NPs and zinc oxide NPs negatively affected the endodontic sealers push-out bond force, probably due to nanoparticle deposition on the surface of dentine, reducing the adhesion of sealer [46].

3 .Magnesium Nanoparticles (Mg-NPs)

Magnesium containing NPs have bactericidal activities against both gram positive and negative bacteria, viruses, and spores. They have been proposed for use as bactericidal materials against root canal infections [47]. Magnesium containing NPs can be "magnesium oxide" NPs or "magnesium halogen" NPs like fluorine, chlorine and bromine [48] .Multiple mechanisms were proposed to explain the antibacterial activities of magnesium containing nanoparticles[7].

"Magnesium halogen" containing NPs inter inside the bacteria, causing a disruption in the activity of bacterial cell membrane, which is similar to the conventional antibacterial actions of nanoparticles[17].

The "magnesium oxide" nanoparticles' DNA binding and lipid peroxidation activities were enhanced by the penetration, resulting in increased bacterial cell death [49]. Because of the effect of superoxide anions generated on the surface of bacterial cell, "magnesium oxide" NPs were reported to have antibacterial activity when administered in aqueous state [50].

Monzavi et al. investigated the bactericidal activity of different percentage of magnesium oxide NPs (5 mg/L and 10 mg/L), as well as 5.25 % and 2% of sodium hypochlorite and chlorhexidine respectively, against different types of endodontic pathogens. The antibacterial potency of different irrigating solutions used to fight different endodontic microorganisms exhibited no significant differences, according to the findings. However, when compared to sodium hypochlorite, adding Mg-NPs to root canal irrigation solution resulted in increased antimicrobial efficacy [17,51].

4 .Gold Nanoparticles

Gold nanoparticles are a promising nanomaterial with significant biomedical implications, according to reports [52]. However, due to concerns about their antibacterial activity, they haven't been studied as thoroughly for use in endodontics [16,47,53].

Kushwaha et al. investigated the effects of silver and gold nanoparticles containing irrigant solutions on removal of microbial infection of E. faecalis type in teeth, with and without using of Nd: YAG laser stimulation. While the antibacterial activity of gold nanoparticles was improved by using the Nd:YAG laser, the usage of silver containing nanoparticles caused reduction of CFU mean[53] .

Besides that, using gold containing nanoparticles demonstrated to have antimicrobial activities in different conditions, such as infections of wound burn, which could be related to changes in composition of microbial pathogens and resulted in production of more sensitive types of microorganisms than in root canal infections [31, 54].

5 .Titanium Dioxide Nanoparticles

Titanium dioxide nanoparticles (TiO2) are extremely stable particles with excellent photocatalytic capabilities. The production of reactive oxygen species produces oxidative stress. Because of its lipid peroxidation property, it has better membrane fluidity and cell membrane disruption. It's also utilized to treat fluconazole-resistant fungal strains[55].

6 .Iron Oxide Nanoparticles (IO-NPs)

IO-NPs (Fe3O4) have been found to have powerful antibiofilm activities without causing harm to oral tissues. These NPs have peroxidase-like activity, allowing them to catalyze hydrogen peroxide (H2O2) to create free radicals in a pH-dependent manner [56].

Iron oxide nanocatalysts can improve H2O2's antibiofilm efficacy. After topical application, the IO-NPs maintained inside the biofilm can quickly catalyze H2O2 at an acidic pH, creating free radicals and killing the bedding bacteria within minutes, leading in an effective and biocompatible treatment [56].

B. Non-Organic Nanoparticles

Bioactive Glass Nanoparticles

Bioactive glass based NPs are made up of SiO2, Na2O, and P2O5 in various concentrations. Their dimensions range from 20 to 60 nanometers[2].

The following are some of the benefits:

1 .Alkaline ph: In an aqueous environment, the release of ions causes the pH to rise.

2 .Effects of osmosis: Many bacteria die when they are exposed to high osmotic pressures of more than 1%.

3 .Demineralized enamel surface was mineralized as a result of calcium-phosphate precipitation.

4. In nature is highly amorphous.

Waltimo et al. concluded that if we combined pH with high value together with alkaline materials that have continues flow appeared to be more efficient in an in vitro research employing the optimal Bioactive Glass solutions preparation for root canal treatment[57].

Furthermore, Because of the disparity in findings obtained by different research, using bioactive glass nanoparticles antibacterial agent as a substitute for routinely used endodontic antibacterial agents remains a matter of discussion. Following advancements in the production of bioactive glass NPs, more study is necessary [7].

C. Polymeric Nanoparticles

Chitosan Nanoparticles

Chitosan is a multifunctional biopolymer that may be manufactured into a different form: (powder, capsules, scaffolds, films, beads) among other things. Chitosan nanoparticles (average particle size of 70 nm) have mostly been created for drug/gene delivery applications[58].

Antibacterial abilities of chitosan nanoparticle solutions against E. faecalis were discovered, as well as the ability to suppress biofilm development. However, according to another study, its antibacterial efficiency may be dependent on the bacteria's condition, since planktonic bacteria were completely destroyed whereas biofilm bacteria remained after 72 hours[59,60].

After 90 days of aging, chitosan nanoparticles maintained their antibacterial capabilities. Its bactericidal actions are also duration, concentration, and contact dependent. The presence of inhibitors such as pulpal fragments and bovine serum albumin inhibited antibacterial activity, whereas the lipopolysaccharides (LPS) and dentine matrix had no effect [24]. To improve the diffusion of chitosan nanoparticles NPs inside the root canal, diode laser application, electrophoresis, ultrasound of high-intensity, and manual dynamic activation, have all been proposed [61].

Kishen et al. were the first in the realm of NPs to examine the efficacy of Chitosan nanoparticles in root canal disinfection. Chitosan may penetrate root canal and dentinal tubules complexities because it depends on time and concentration, removing microorganisms even after 3 months. In an in-vitro investigation, Barreras US et al. employed Chitosan Nanoparticles in combination with CHX to eliminate Enterococcus faecalis from the canals. Membrane barriers formed at the peri-radicular area as a result of this combination [62].

Several investigations have shown that chitosan can serve as a chelator and perhaps increase wetting of dentine. Simultaneously, chitosan NPs demonstrated the ability to preserve the collagen of dentine tissue by preventing breakdown of collage by the action of bacteria [63].

According to a recent study, treating dentine using "chitosan hydroxyapatite precursor nanocomplex" before applying a sealer of tricalcium silicate type enhanced mean sealer penetration into tubules substantially [63]. Even though it has been proposed that treatment for a long time and contact dependent character of chitosan NPs containing irrigants are drawbacks that require to be discussed in further research, chitosan NPs containing irrigants offers a potential contender for new and more effective irrigant when combined with its antimicrobial properties [64].

CONCLUSION

The huge number of NP materials accessible today allows for a variety of applications in medicine. The antibacterial capabilities of certain nanoparticles as novel agents against endodontic infections are now being investigated in endodontic research .Studies demonstrate that the use of several types of NPs as antimicrobial agents has promise, particularly against chronic endodontic infections like E. faecalis .

The use of nanoparticles in irrigation can improve the antibiofilm efficacy of endodontics. When considering the therapeutic efficacy of nanoparticles, it is necessary to optimize their physical, chemical, and biological properties, with special attention paid to tissue-specific parameters at the site of infection and the strategy for successfully delivering nanoparticles in the target tissue .

Furthermore, the antibacterial activity of the nanoparticles must be explored against a wide range of endodontic microorganisms that are resistant. Further study is required to asses these innovative materials.

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