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Nanoparticles in Endodontics: A Deep Dive into Their Antimicrobial and Regenerative Efficacy

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Endodontics stands for endo, meaning inside, and odont, meaning teeth and is the branch of dentistry that deals with the diagnosis and treatment of the pulp of a tooth and the surrounding area, which lies at the base of the roots of the tooth. With rather great significance in contemporary Dentistry, endodontics also has paramount roles in preventing, diagnosing, and treating diseases and injuries in the pulp and root canal system. Endodontic treatment is aimed at retaining teeth; however, their tissues are affected by diseases or injuries (Roy, 2019). Besides, endodontists can solve different complicated dental problems, including root canal therapy, pulp regeneration, and surgeries that can only permit tooth extraction in normal cases (Samiei, 2016).

1. Introduction

Endodontics stands for endo, meaning inside, and odont, meaning teeth and is the branch of dentistry that deals with the diagnosis and treatment of the pulp of a tooth and the surrounding area, which lies at the base of the roots of the tooth. With rather great significance in contemporary Dentistry, endodontics also has paramount roles in preventing, diagnosing, and treating diseases and injuries in the pulp and root canal system. Endodontic treatment is aimed at retaining teeth; however, their tissues are affected by diseases or injuries (Roy, 2019). Besides, endodontists can solve different complicated dental problems, including root canal therapy, pulp regeneration, and surgeries that can only permit tooth extraction in normal cases

(Samiei, 2016). The speciality of endodontics has seen many changes over the last three decades, and this is because of improved material and technology, as well as the understanding of biological processes in the tooth and its supporting tissues. This speciality also involves the treatment of pain and infection. Still, it also concerns itself with the function and aesthetics of natural teeth as they are instrumental in general well-being as well as quality of life (Shrestha, 2016).

1.1. Structure and Function of the Dental Pulp

The dental pulp, which is a soft tissue located in the central part of any specific tooth. Nerves, blood vessels, and connective tissue form the pulp, and they are vital during the growth of the tooth. The pulp has essentially three roles in the tooth: nutritional and sensory (thermal, painful, etc.) and as a signalling centre for the formation of dentin, the structure encasing the pulp. Although the dental pulp is involved in tooth formation and maturation, it is of paramount importance in the life of a mature tooth. However, there is a problem because the pulp is still exposed and susceptible to damage or infection in some way. Factors that can expose the pulp to injury include caries that have reached the pulp, cracks in the teeth, an injury to the tooth or harm from prior procedures. When the pulp is exposed or damaged, it can become inflamed or infected, causing pain, further swelling and sometimes even an abscess. If not treated, that infection can extend to the surrounding tissues and cause the loss of teeth (Raura, 2020).

1.2. The Scope of Endodontics

Root canal therapy is a broad umbrella of services for maintaining and restoring the integrity of the tooth through different modalities such as retreatment or apicoectomy, surgical endodontics, treatment of traumatic injuries, and innovative regenerative procedures (Wong, 2021).

Root Canal Therapy (RCT)

Endodontic treatment, particularly root canal therapy, is the primary method used to treat a tooth that has inflamed or infected pulp. During this procedure, the pulp is removed, and the chamber and root canals are disinfected. Later, they are filled with a material that does not deteriorate when in contact with the body fluids and tissues to avoid reinfection. This not only helps the patient avoid the negative consequences of tooth extraction, such as the loss of bone alveolar support and the shifting of neighbouring teeth but also allows for restoration by prosthodontic means (Sevagaperumal, 2024).

Endodontic Retreatment

The tooth which has undergone endodontic treatment may not heal or may end up getting infected months or years after the procedure. In such cases, endodontic retreatment may be done. This procedure involves reopening the affected tooth, removing the previous filling material from the canals, and thoroughly cleaning out the infection.

Endodontic Surgery

If the endodontic therapy or further treatment is not sufficient to treat an infection, then surgery may be called for. Apicoectomy is the most frequent type of endodontic surgery. It entails removal of the tip of the tooth's root (apex) and then sealing of the end of the root for treatment of the infected tissue and healing. Endodontic surgery is typically the final attempt to save the tooth if the infection does not respond to earlier treatments.

Trauma Management

Endodontists are also able to deal with dental emergencies, including injured teeth, which are teeth that are chipped, split, or have been knocked out of someone's mouth. These injuries may affect the dental pulp and, therefore, need specific treatment dealing either with the healing of the pulp or its removal, as well as maintenance of the structure of the tooth. Consequently, endodontic intervention is needed to prevent adverse long-term consequences such as infection, tooth colour change and permanent loss of the tooth.

Pulp Regeneration

An emerging field in endodontics is called pulp regeneration, which targets damaged pulp tissue through the application of stem cells and growth factors in the bioengineering of scaffolding materials. The aim is to renew the Pulp-Dentin complex in order to stimulate the healing process and recover the mechanical function of the tooth. Young permanent teeth can usually be treated with pulp capping, a developing step in this innovative technique, which will save teeth that otherwise would have been extracted due to pulp necrosis or infection.

1.3. The Importance of Endodontics in Modern Dentistry

Endodontics as a discipline has recently experienced an enhancement in visualization, the technology of what can be used in operating on teeth and material science. Apart from that, some of the significant changes include the integration of cone beam computed tomography or CBCT, which offers three-dimensional images of the tooth and its environment. This enables dentists to make the right diagnosis and perhaps the right intervention and planning, especially when it involves complicated teeth structures or if the teeth have been treated before (Shi, 2024). Also, improvements in the nickel-titanium (NiTi) rotary instruments have enhanced the process of canal cleaning and shaping, which has helped to improve the predictability of the technique. NiTi instruments are flexible, thus preserving the initial canal curvature and do not cause canal transportation or perforation in most cases. In addition, biocompatibility of materials like MTA obviously enhanced the survival rate of endodontic treatment, especially in root-end cavity filling and perforation repair (Khoroushi, 2016).

In addition, one of the most recent procedures involving endodontics is the application of regenerative procedures that aim to utilize the capabilities of the self-healing process. Stem cells, scaffold, and bioactive molecules can be used in tissue engineering to replace the non-viable pulp tissue or to induce the formation of reparative dentin and creative a suitable substrate for cell attachment, limiting the application of root canal treatment. This branch of research is still in its infancy. It has the prospect of changing the basic approach to endodontic treatment, not limiting itself to the treatment of infection but also reconstructing the biological activity of the tooth (Harris, 2019).

Endodontics is a very crucial branch in dentistry, whose goal is to maintain and restore the function of the tooth pulp and the related tissues. By the use of root canal treatment, surgical micro endodontic and regeneration techniques, endodontics are in a position to restore affected teeth that would have otherwise been extracted due to injuries or infections. Technological advancements and materials are also dynamic, and the future of endodontic treatment, as seen today, contains broader and enhanced prospects of better predictable, less invasive methods for the management of teeth. Regenerative techniques in endodontics offer significant potential for the future. They will likely enhance the treatment and patient quality of life in the pediatric and adult population (Nivedhitha, 2020).

2. Nanoparticles Used in Endodontics

Nanotechnology is highly recognized as a revolutionary method of treating endodontic problems due to improved antimicrobial activities and tissue-forming capabilities of nanoparticles during the past few years (Figure 1). These particles with a size of 1-100 nanometers are characterized by a large surface area to volume ratio and possess unique biological properties appropriate for dental purposes. In endodontics, nanoparticles are included in medicaments, sealers, and scaffolds to enhance root canal sterilization, periapical tissue repair, and regeneration. It should be noted that the types of nanoparticles which are used in this field are diverse, and the unique properties of their constituting material play crucial roles in determining their functional features in regard to antimicrobial activity and tissue regeneration (Zakrzewski, 2021).

In this review, we will focus on the major categories of nanoparticles employed in endodontics and the manner in which they work. A graphic design of the different types of nanoparticles included in this review is shown in Figure 2.

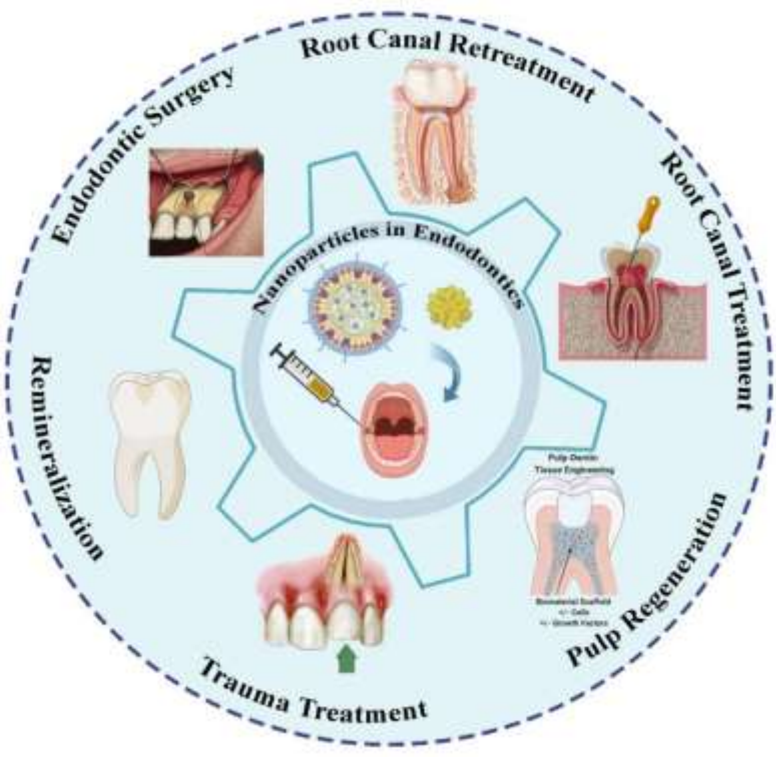

Figure 1. Applications of nanomaterials in endodontics.

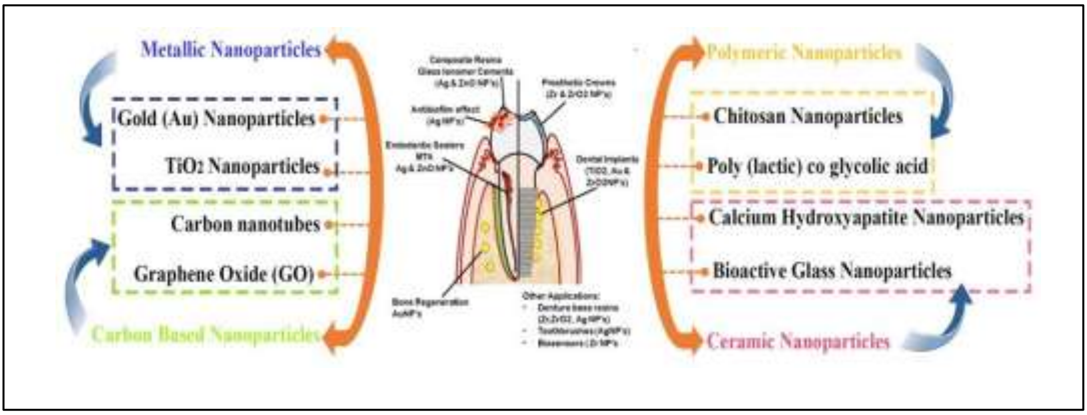

Figure 2. Types of nanoparticles including metallic and polymeric nanoparticles in endodontics.

2.1. Metallic Nanoparticles:

2.1.1. Silver (Ag), Nanoparticles

Silver nanoparticles (Ag NPs) are amongst the most frequently applied metallic nanoparticles in endodontics because of their high antimicrobial efficiency. The broad spectrum antimicrobial properties of silver nanoparticles have been reported against bacteria, fungi, and viruses. They hence can be used to combat Endodontic infection caused by Enterococcus faecalis (Oncu, 2021). Currently, the antimicrobial properties of AgNPs have been evidenced to act in various systems through the action of released silver ions (Ag^{+}), which affect bacteria cell wall synthesis and other metabolic activities and cause DNA damage. In the same way, gold nanoparticles (AgNPs) are being investigated for their toxicity and application of drug delivery to the site of infection. Silver nanoparticles (AgNPs) are metallic nanoparticles consisting of pure crystalline silver with a size of approximately 1–100 nm. They have recently been used in various biomedical applications because of their improved and distinct physicochemical characteristic such as smaller size, higher surface area, and quantum confinement effect apart from the bulk or powder materials. Currently, AgNPs account for 56 % of all used nanoparticles globally. In dentistry, AgNPs are used in endodontics, restorative, orthodontics, implantology, prosthodontics and periodontology (González-Luna, 2016).

Copper and zinc oxide nanoparticles also have efficacy in terms of bacterial adhesion reduction and through the generation of ROS and consequent cell oxidative stress. The TiO_2 nanoparticles are very effective in photocatalytic activity. The semiconductor property of TiO_2 increases under light exposure, which produces ROS, which in turn increases the antimicrobial conc. These metallic nanoparticles have other advantages, including the ability to penetrate deeper into biofilms, which is quite important given the complicated nature of the root canal space (Ertem, 2017).

The application of AgNPs in the dentistry field has previously started with microorganisms killing ability under the umbrella of its broad-spectrum bactericidal and fungicidal properties. To the best of our knowledge, Ibrahim et al. (2017) presented one of the first attempts to investigate the AM activity of AgNPs against oral microorganisms. It is reported that the

AgNPs displayed a high level of antibacterial activity against S mutants, which is known to cause dental caries and root canal infections. According to the findings, the DLS and TEM of silver nanoparticles showed that they could penetrate inside bacterial cells through cell wall damage and produce cell wall lysis and death. The preliminary findings on AgNPs have highlighted their potential as an alternative or adjunct to sodium hypochlorite in endodontics, offering lower cytotoxicity at comparable concentrations (Ibrahim, 2017). The antimicrobial actions of silver nanoparticles have been reported several times in the literature, and maybe for the following reasons. One of the primary working mechanisms is the release of the positively charged Ag+ ions that affect bacterial cell membranes of gram-positive species by inducing structural change. Ioannidis et al. (2019) also confirmed the potential of the AgNPs to fill the bacterial biofilms due to the high resistance of the biofilms to conventional disinfectants. Biofilms are complex microbial communities embedded in an extracellular matrix known as EPS and are arguably the biggest factor responsible for endodontic treatment failure. These particles affect the structure of the biofilm and increase the efficiency of Debridement of the antimicrobial agents in the protective matrix (Ioannidis, 2019).

Another important process is the production of reactive oxygen species (ROS), which creates oxidative stress in microbial cells. Tülü et al. (2021) proved that when AgNPs interact with bacterial cells, they generate ROS, which includes hydroxyl radical and superoxide anion, to cause cell damage to proteins, lipids, and DNA. These oxidative damages result in apoptosis and, consequently, microbial death (Figure 3). The generation of ROS from AgNPs has significant potential in removing biofilms in the root canal, which cannot ordinarily be eliminated by conventional disinfectants (Tülü, 2021).

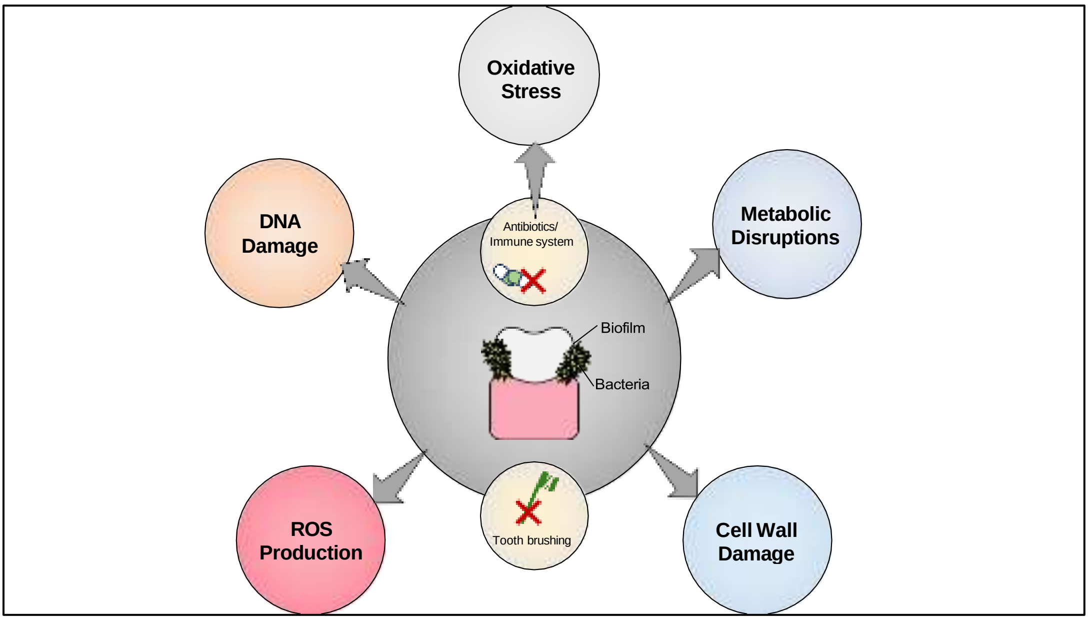

Figure 3. ROS-Induced Bacterial Damage and Biofilm Breakdown.

However, there are more mechanisms that the silver ions possess their function; they inhibit important enzymes for microbes necessary for metabolic processes and DNA synthesis (Figure

4). Due to these multiple antimicrobial modes of action, AgNPs should be considered an effective tool for the treatment of resistant pathogens often associated with root canal infections, including Enterococcus faecalis. Madla-Cruz et al. (2020) have carried out a particular study which focused on the effectiveness of the AgNPs against E. faecalis; it has been determined as the bacterium with high resistance to basic endodontic procedures. The research findings of this study corroborated the effectiveness of AgNPs against E. faecalis biofilms and their application in the decontamination procedure during root canal treatment.

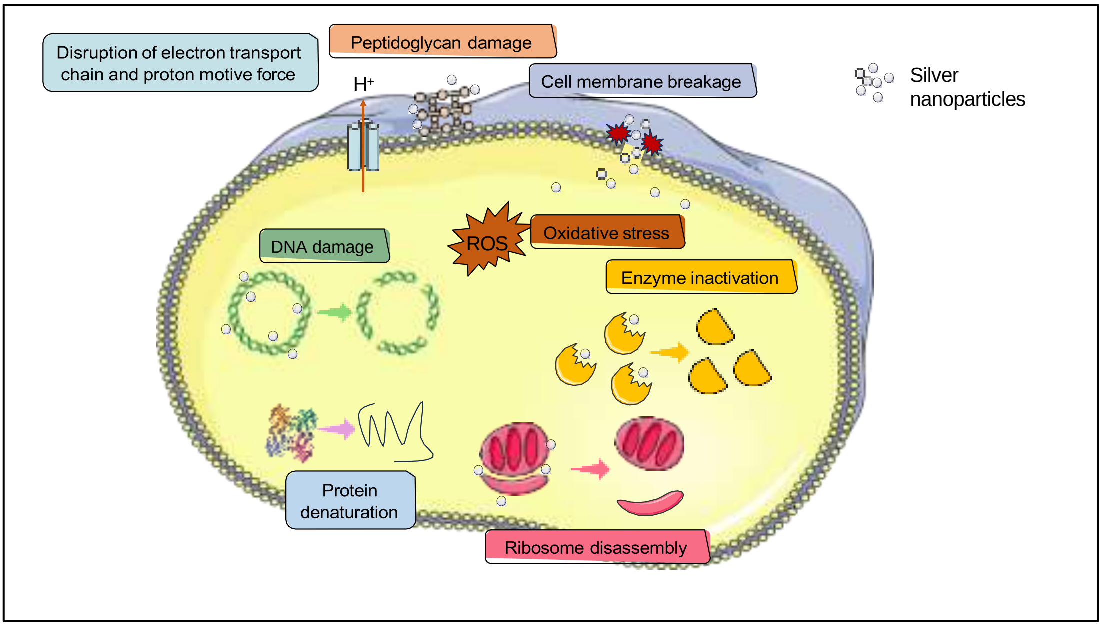

Figure 4. The mechanism of antimicrobial activity of AgNPs.

Silver nanoparticles have been included in numerous endodontic materials to enhance their antimicrobial efficacies. The primary use of AgNPs in endodontics is to enhance the root canal disinfectants. The past decade has shown that sodium hypochlorite (NaOCl) is the most commonly used irrigating solution for root canal disinfection. Still, the toxicity to periapical tissues at high concentrations reduces the efficiency of the treatment. Research has been conducted to look for possibly safer and equally effective nanocarriers such as AgNPs. Bhandi et al. (2021) explained that silver nanoparticle solutions provided similar antimicrobial performance as NaOCl without excessive harm to the nearby tissues. This makes AgNP-based disinfectants to be a better option to embrace in making root canal disinfection safer and more effective.

Another vital use of AgNPs is in root canal sealers. Cement sealers are employed in the space between the root canal walls and the gutta-percha core material. However, the majority of traditional sealers exhibit short-term antimicrobial properties. To overcome this weakness, Nam et al. (2017) used AgNPs and included them in endodontic sealers, then investigated their antibacterial efficacy against E. faecalis. This research showed that sealers with AgNPs possessed noticeable antibacterial properties, and this proved to enhance extended releases of antimicrobial attributes despite the set material. Furthermore, the addition of AgNPs did not have any negative impact on the physical or mechanical properties of the tested sealers, thus for clinical applicability (Nam, 2017). Silver nitrate intracanal medicaments containing AgNPs have also been evaluated. Medicaments are intracanal dressing materials used on a temporary basis to minimize microbial count before the root canal is sealed. Vazquez-Garcia et al. (2016) assessed the antibacterial activity of AgNPs as an intracanal medicament against calcium hydroxide. This study demonstrated that AgNPs had a better efficacy in decreasing bacterial load in the root canal system than calcium hydroxide, particularly against E. faecalis. The study also revealed that exposure to AgNPs had no impact on the healing of the periapical tissues and, thus, showed that they are biocompatible when they are used as intracanal medicament (Vazquez-Garcia, 2016).

AgNPs have shown good antimicrobial properties, but cytotoxicity is the major concern associated with AgNPs. Any material to be used in this area of application must not be toxic to the surrounding living tissues of the tooth. Initial works also posed that silver ions could be lethal to human cells given sufficient concentration. However, today's studies are aimed at fine-tuning the concentration of AgNPs in order to potentiate the antimicrobial activity and reduce toxicity simultaneously. In a systematized review by Akter et al. (2017) to investigate the biocompatibilities of AgNP-entangled sealers, the researchers saw that AgNPs still had low cytotoxicities in the human cells when the concentrations were accurate. In the present experiment, the cytotoxicity of AgNP-modified sealers on human PDLFs was tested using in vitro cell culture models. The authors concluded that the sealers were non-cytotoxic and could be used safely and clinically (Akter, 2017).

Endodontic flare-ups are significant issues in the overall management of endodontic treatment because of microbes such as E. faecalis. These infections are the main reason why many root canal situations are deemed non-successful and hence called for retreatment or apicoectomy. Some literature has pointed out some chances of using AgNPs to this end. Algazlan et al. (2022) have also found that because of the size of AgNPs and their capacity to penetrate biofilms, AgNPs were more effective in breaking down the biofilms of E. faecalis, irrigation and medicament and conventional. The present research was able to show that growing bacterial biofilms can be impaired even at low concentrations of AgNPs, and bacterial count decreased significantly, suggesting that these may be useful in infections that are difficult to treat (Algazlan, 2022).

2.1.2. Gold (Au) Nanoparticles

AuNPs, in particular, have attracted a lot of interest in the field of endodontology owing to the unique characteristics and improved performance characteristics that can be used to improve dental therapies. While a liberal amount of literature is present on the use of silver nanoparticles for antimicrobial activity, AuNPs provide better stability, biocompatibility, and variable functionalization. These properties make AuNPs especially desirable for diverse applications in endodontics, such as antimicrobial therapy, regenerative care, or diagnostic tools. The following discussion focuses on dental applications of AuNPs through consideration of their synthesis and characteristics, antimicrobial action, biocompatibility, and applicability to regenerative medicine (Xia, 2018). Gold nanoparticles refer to nano-structures made from pure gold that measure up to one hundred nanometers. These particles are usually between 1 and 100 nanometers in size, which gives them several useful properties, including optical, electrical and catalytic properties that are, in some cases, very different from those of macroscopic gold. AuNPs have a large surface area to volume ratio and are very small; hence, their interaction with biological systems is quite ideal for medical and dental uses. Moreover, the size, geometry and surface chemistry of AuNPs can be adjusted by the researchers to suit biomedical needs. The AuNPs are relatively biocompatible, and few reactions occur, making them unique in comparison to other metallic nanoparticles in the sensitive root canal environment, thus having minimal chances of inducing immune reactions in patients (Bapat, 2020).

One of the main interests of using AuNPs in endodontics is their antibacterial properties. In cases of endodontic infections, polymicrobial biofilms are difficult to eradicate and contain bacteria such as Enterococcus faecalis that are resistant to conventional decontamination techniques. The structure of these bacterial biofilms may also hinder efforts to remove them since they may be resilient to antimicrobial agents. Bacteria contained in the biofilms, due to their large number and the virtual barrier that is posed by the biofilm matrix to the microbicidal agents, pose a major problem in the treatment of infections, but this can be overcome by using nanoparticles because of their nano-size and high surface reactivity.

Many researchers have confirmed that AuNPs have inherent antibacterial characteristics. Bapat et al. (2020) also profiled the antimicrobial activity of gold nanoparticles to the pathogenic bacterial species Enterococcus faecalis, often responsible for persistent root canal infections. The research showed that the use of AuNPs reduced bacterial viability within biofilms. This study has identified the main approach by which AuNPs inhibit bacterial growth by damaging bacterial cell membranes in a manner that causes the release of contents of cells. Furthermore, gold nanoparticles can cause chemiluminescence and release reactive oxygen species ROS, which also contributes to the oxidative stress killing of bacterial cells (Bapat, 2020). Apart from the inherent broad-spectrum antimicrobial properties, these AuNPs can be coated with other antimicrobial molecules. For example, Feng et al. (2024) synthesized AuNPs functionalized with ampicillin and evaluated their ability to inhibit S. mutans. The obtained antimicrobial activity of both ampicillin and AuNPs was improved five-fold when both were used together; this suggests AuNPs could act as carriers of antimicrobial drugs or agents. Such a discovery points to the fact that the possibility of using AuNPs in enhancing the delivery of antagonistic agents in the root canal chamber cannot be overemphasized, particularly where fresh, hardy biofilms are present (Feng, 2024).

In addition to their antimicrobial characteristics, AuNPs offer the potential for use as diagnostic aids in endodontics. The two most important aspects of AuNPs that make them so suitable for a variety of imaging procedures are their capacity for absorbing and scattering light. Gold nanoparticles have a feature that is called surface plasmon resonance, where gold particles vibrate with light at certain frequencies, causing high optical responses. This property has been investigated in a number of studies to progress diagnostic use in endodontics to enable infections to be detected and the results of treatment to be evaluated. In another work, Trišić et al. (2019) wanted to investigate the use of AuNPs as diagnostic markers through Raman spectroscopy to reveal the presence of bacterial cells in infected root canals. It was established that AuNPs could amplify the Raman signal of bacterial cells and thereby provide a highly sensitive means of detecting microbial contamination within the root canal system. These diagnostic devices may be extremely useful in evaluating the efficacy of the procedures for root canal disinfection and in determining the presence of residual bacteriological threats before the canal is sealed (Trišić, 2019).

Periodontitis has been treated by composite nanoplatforms of E-Au@H activated by NIR light to exhibit the properties of angiogenesis, cell migration enhancement, osteogenesis, and antimicrobial properties. Based on these results, E-Au@H possessed the potential to enhance bone renovation of periodontal infection models in the in vitro experiment. More importantly, the trials validated the biosafety of the composite. The work of the Investigator indicates the potential benefits of E-Au@H on periodontitis models and opens up a new method in the treatment of periodontitis.

Capuano et al. (2023) applied gold nanoparticles in fluorescence imaging, with bacterial biofilms being the target of gold nanoparticles used. By conjugating fluorescent dyes to the AuNPs, the researchers wanted and were able to visualize biofilms within the root canal, thus providing a noninvasive approach to evaluate the severity of infection. The presented method seems to be especially useful in the identification of possible biofilm remnants that might be present after conventional irrigation procedures, thus making the endodontic treatments even more efficacious (Capuano, 2023).

The second aspect of higher concern is the biocompatibility of AuNPs, particularly for long-term use in endodontic treatments. As a matter of fact, gold nanoparticles have clearly been acknowledged to be friendly with human tissues. When in contact with tissues, they do not cause any toxic or inflammatory reactions. This characteristic is especially critical since the tissues in the root canal area can be rather sensitive, and any materials should not cause negative responses. Russo et al. (2017) investigated the cytotoxicity of AuNPs in human dental pulp cells and observed that when used in a concentration relevant to endodontic treatment, low cytotoxicity prevailed. Finally, the authors stated that AuNPs, if employed in optimal concentration, are not toxic for dental use (Russo, 2017).

Feng et al. (2024) moved a step further to investigate the synergistic effect of gold nanoparticles with scaffold on pulp tissue engineering. The presented work of AuNPs in improving the proliferation and differentiation of stem cells for the formation of vascular tissue that is crucial for the proper functioning of regenerated pulp manifested the successful integration of AuNPs into a hydrogel scaffold. This work emphasizes the ability of AuNPs to boost the efficiency of regenerative therapies in endodontics, thereby improving expectations for patients (Feng, 2024). Although gold nanoparticles have significant potential in the field of endodontics, some limitations are observed that need to be addressed before the gold nanoparticles can be implemented in the clinical setting. However, one major drawback of AuNPs is their prompt aggregation in biological environments. It is reported that there is a tendency for nanoparticles to aggregate, which causes a reduction in their efficacy and has potential complications. The researchers are still seeking ways of fixing the AuNPs, such as modifying their surface and adding stabilizing agents in order to enhance their efficiency in endodontic procedures for the longest time.

2.1.3. Zinc Oxide (ZnO) Nanoparticles

The nanomaterial that has recently gained considerable interest in the field of endodontics is ZnO NPs, owing to their strong antibacterial activity, stability, and stem cell differentiation ability. ZnO has long been established in dental science for several uses in different products, such as in dental cement, owing to some desirable properties in the physical, chemical and biological attributes (Figure 6). The development of nanotechnology has brought ZnO into broader usage because nanoscale ZnO has a higher surface area, reactivity and mechanical properties than bulk-type ZnO (Pushpalatha, 2022). In this section, we will discuss the practical uses of ZnO nanoparticles in endodontics, including antibacterial activity, mode of action on bacterial biofilms, biocompatibility features and possible prospects in tissue engineering.

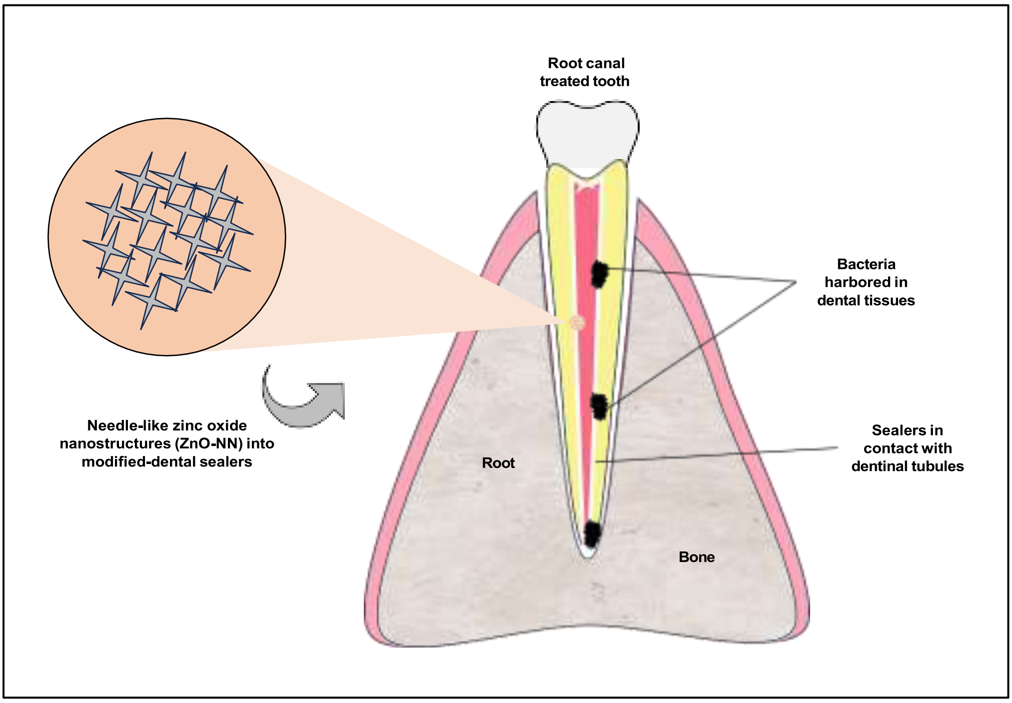

Figure 6. Graphic depiction of the envisaged strategy of needle-like zinc oxide nanostructures (ZnO-NN) for enhancing dental resin sealers.

Among the key properties of ZnO nanoparticles, the antibacterial activity has been proven to be wide-spectrum, enabling the author to tackle one of the major concerns in endodontic pathology – polymicrobial biofilms. Invasively resistant endodontic infections include Enterococcus faecalis and Streptococcus mutans as predominant microorganisms characterized by antibiotic biofilms with the root canal. Often, these microorganisms form biofilms that provide a shield for the organisms from eradication during regular root canal procedures. These biofilms offer a scalable architectural organization that ensures these pathogenic microorganisms are harder to treat due to the failure of traditional antimicrobial agents; ZnO NPs, however, have better chances of success in eliminating these biofilms (Tiwari, 2022). The present literature reveals that there is strong evidence available about the use of ZnO nanoparticles as an antimicrobial agent in dental healthcare. For example, Tiwari et al. (2022) studied ZnO nanoparticles eradication of Enterococcus faecalis in infected root canals and discovered that ZnO NPs reduced the bacterial viability in biofilm. The nanoparticles were, as mentioned earlier, more efficient in breaking down the biofilm structure to make the bacteria more vulnerable. Further, Hadi et al. (2019) also affirmed their findings that ZnO NPs possessed very high antimicrobial activities against S. mutans and other microorganisms involved in apical pathoses. The authors were able to hypothesize that this could be because ZnO NPs were very reactive, and the size of the nanoparticles could enter the bacterial cell and cause oxidative stress.

Tsuru et al. have postulated that there are several mechanisms for the antimicrobial properties of ZnO nanoparticles. The first mecahnism includes the generation of Reactive Oxygen Species (ROS), which includes hydrogen peroxide, hydroxyl radicals and superoxide anions. These ROS produce oxidative attacks at bacterial cells through the cell membrane, proteins, lipids and DNA that lead to cell death. Besides the generation of ROS, ZnO NPs affect bacterial cell membranes and cause cell membrane rupture followed by leakage of bacterial intracellular components. This membrane disruption mechanism is beneficial in the species that are often identified in endodontic infections, such as the Gram-positive Enterococcus faecalis, as identified by Nair (2018). Also, ZnO nanoparticles can cause the liberation of zinc ions (Zn^{2+}), which also plays a role in the antimicrobial activity of the particle. It has also been established that zinc ions affect the enzymatic activities, protein synthesis, and metabolism of bacteria. Due to the ability of ZnO-NPs to generate ROS, disrupt bacterial membranes, and release zinc ions, ZnO nanoparticles are potent antimicrobial agents effective against many bacterial agents elicited in chronic root canal infection. Further, ZnO nanoparticles possess great antimicrobial activity besides biocompatibility, thus making good candidates for use in endodontic therapy. Another important characteristic of endodontic regenerative materials is biocompatibility because the materials used come into direct contact with living tissues without eliciting inflammation or cytotoxicity reactions. Recent work has described cytocompatibility with ZnO NPs in human dental pulp cells and in other tissues which are relevant to endodontic treatment. Ravi et al. (2024) investigated the cytotoxicity of ZnO nanoparticles using human dental pulp stem cells and concluded that ZnO NPs at the concentration usual for dental application are nontoxic. The following study pointed out that ZnO nanoparticles did not elicit significant adverse reactions when used in endodontic materials and applied to human tissues.

The biocompatibility of ZnO nanoparticles is mainly due to their biosorption mechanism, through which the nanoparticles disintegrate into harmless compounds, such as zinc ions, which are vital for the human system. Zinc is an active participant in the body’s activity, sustaining enzymatic activity, immune system, and cell division. This makes ZnO nanoparticles unique for application in regenerative endodontics, where the aim is not just to eradicate pathogens but also to stimulate tissue repair. ZnO nanoparticles have demonstrated the emergent capacity to stimulate the bio-dental regeneration treatment that is designed to rejuvenate the dental vitality of pulp cells and encourage new complex dentin-pulp formation. Another issue within the field of regenerative endodontics is the ability to keep conditions conducive for the survival, proliferation and differentiation of dental pulp stem cells (DPSC) and other progenitor cells. In the recent past, the observed property was newly seen in ZnO nanoparticles that could help transform the stem cells and put them into the osteogenic lineage, and this may be of high value in dentin regeneration.

Cierech et al. (2019) experimented in order to test the effect of ZnO nanoparticles on the osteogenic differentiation of DPSCs. Researchers also found that the ZnO NPs enhanced DPSC mineralization and dentin-like architecture formation (Cierech, 2019). There is the possibility of using ZnO nanoparticles to introduce them into some scaffolding or other regeneration structures to hasten tissue repair after pulpal damage. In another study by Kumar et al. (2021), authors explored the characteristics of enhancing pulp tissue engineering using calcium phosphate scaffold combined with ZnO nanoparticles. The authors also discovered that the approaches used to integrate ZnO NPs into the scaffold of the tissues supported the growth and differentiation of stem cells to complement tissue repair (Hojati, 2013). Moreover, the study hasn't mentioned that ZnO nanoparticles also possess anti-inflammatory characteristics that can also contribute to the healing process in regenerative endodontics. Also, it was revealed that ZnO NPs could decrease the secretion level of pro-inflammatory cytokines and create conditions that can support tissue repair. Inflammation is still a problem in pulpal healing, Rao and colleagues showed that ZnO nanoparticles help decrease it in an in vitro binary culture experimental model of pulpitis, indicating that the nanoparticles may be helpful to encourage an improved healing response in regenerative endodontic procedures (Manobharathi, 2024).

2.1.4. Titanium Dioxide Nanoparticles (TiO_2)

Titania or titanium dioxide (TiO_2) nanoparticles have attracted considerable attention in diverse biomedical areas as well as in endodontic applications because of their distinctive physicochemical and biological characteristics. In particular, it is known that TiO_2 has biocompatibility, photo reactivity, and antimicrobial effects and, therefore, is promising for applications in dentistry. When treatment is concerned with the treatment of infected root canal tissue and stimulation of tissue reparative processes, TiO_2 nanoparticles (TiO_2 NPs) may be advantageous in the process of endodontics (Mustafa, 2024). In this section, we will discuss the characteristics, antibacterial action, biocompatibility and the ability for tissue regeneration of TiO_2 NPs in endodontics.

Endodontic applications of TiO_2 nanoparticles involve the use of the nanoparticles as antimicrobial agents. Some forms of proliferation in the root canal system are, therefore, hard to be eliminated by the use of antibiotics because these bacteria possess a biofilm structure that is hard to eliminate. These biofilms form a resilient structure through which penetration by conventional disinfection agents and antibiotics is limited. This is due to properties of the TiO_2 NPs, such as the high surface area and the photo-reactive nature that is reported to possess antimicrobial activity that can be used to prevent biofilm formation or enhance disinfection of infected root canals (Jowkar, 2020).

The real bactericidal effect of TiO_2 nanoparticles is mostly due to the photocatalytic procedure in which the nanoparticles produce ROS when cumulating with UV or visible light energy. ROS such as hydroxyl radicals and superoxide anions played a critical role in supressing bacterial cells by stressing them; cell membrane rupture, protein denaturation and DNA strand breakage result from this stress. Al-Sa'ady et al. (2020) showed that TiO_2 nanoparticles had a high killing efficiency of bacteria of the root canal infection under UV light illumination. The present study also revealed that TiO_2 NPs could substantially eliminate biofilms of Enterococcus faecalis, which is one of the most resistant and potentially pathogenic bacterial species known to participate in endodontic infections when combined with UV irradiation (Al-

Sa'ady, 2020). In addition to the photocatalytic effect, morphological analysis revealed that TiO_2 nanoparticles altered the shape of bacterial cells, and there is evidence that the nanoparticles had a mechanical disruption effect on the cell membrane as it was damaged. This membrane-disrupting action is especially beneficial in removing biofilms since TiO_2 NPs can chelate the bacterial cells themselves through the protective biofilm matrix. In the study conducted by Mahendra et al., 2022, the authors learned that TiO_2 nanoparticles have an efficient bactericidal action even in the absence of a light stimulus. These data suggest that the inhibitory actions of TiO_2 NPs are intrinsic and not affected by light, which might be useful for the elimination of root canal pathogens (Mahendra, 2022).

The functionalization of TiO_2 nanoparticles with other antimicrobial agents can also be applied to endodontic therapy. For instance, TiO_2 NPs can be added to AgNPs to obtain improved antimicrobial activity of NPs. Omer et al. (2013) established that TiO_2-Ag composite nanoparticles showed higher antibacterial efficiency than using either TiO_2 or AgNPs alone because the antibacterial activity depended on photocatalysis as well as the discharge of Ag^+. This two-in-one method appears to have the potential to enhance the disinfection of root canals and lower the rates of reinfection (Omer, 2013).

Besides biocompatibility, any material utilized for endodontic therapy must have compatible interaction with living tissues or, in this case, teeth and their pulp. TiO_2 nanoparticles are known to have biocompatibility, which makes then popular in applications such as use in dental implants and other biomedical applications. Some prior works have shown that TiO_2 NPs are safe when used in dental and endodontic procedures. Sodagar et al. (2017) employed the MTT assay to evaluate the cytotoxicity of TiO_2 nanoparticles in human dental pulp cells in relation to TiO_2 incorporated into endodontic materials: The results revealed that TiO_2 nanoparticles were cytocompatible at the concentration used in endodontic-mediated endodontic materials. The study also showed that the phosphotungstic TiO_2 nanoparticles that were utilized in this study are harmless when used in root canal therapy and did not trigger substantial inflammatory reactions (Sodagar, 2017).

The biocompatibility of TiO_2 nanoparticles can also be increased depending on the surface characteristic changes of TiO_2 nanoparticles or the fabrication of biocompatible matrices containing TiO_2 nanoparticles. For instance, chitosan-coated TiO_2 nanoparticles can be created; not only does chitosan improve the stability of the core material, but also the antimicrobial properties are improved. Abdulridha et al. (2022) noted that the antibacterial efficiency of TiO_2 nanoparticles coated with chitosan was higher against Enterococcus faecalis than uncoated and additive and biocompatibility with human dental pulp cells. Such alteration makes TiO_2 NPs more appropriate for endodontic treatment performed with the possibility of remaining in periapical tissues for an extended period (Abdulridha, 2022).

For this purpose, Jowkar et al. (2020) designed a study to determine the osteoinductive effects of TiO_2 nanoparticles in cultured DPSCs. In their case, the researchers supplied well-documented facts proving that TiO_2 NPs enhanced the osteoid proliferative differentiation of DPSCs along with the regeneration of mineralized tissue that copied with dentine. This finding suggests that the incorporation of TiO_2 nanoparticles into scaffolds or another regenerative endodontic biomaterial assists in the healing and regeneration of the dentin-pulp complex during endodontic therapy (Jowkar, 2020). Other related studies explored the immobilization of TiO_2 nanoparticles into the calcium phosphate scaffold for pulp tissue engineering. The studies also showed that increasing values of TiO_2 NPs in the scaffold enhanced cell adhesion and differentiation within the scaffold and consequently held significant promise for tissue engineering (Ameli, 2022).

Furthermore, the study also shows that TiO_2 nanoparticles have inflammatory properties on their own and could thus also serve as an anti-inflammatory in endodontics when used in the regenerative process. Inflammation is a natural reaction to microbial invasion or tissue damage in root canal and can lead to inhibition of tissue regeneration if it was not well controlled. It has also been demonstrated that TiO_2 nanoparticles can shift the ratio of cytotoxic factors towards a less inflammatory state and promote conditions conducive to tissue repair. Hoveizi et al. (2019) proved that the obtained TiO_2 nanoparticles kept comparably significant anti-inflammatory activity like indomethacin in an experimental model of pulpitis, which points to the possibility of applying them for the treatment of severe pulp inflammation and the stimulation of tissue repair (Hoveizi, 2023).

2.2. Polymeric Nanoparticles:

Among all the polymeric nanoparticles under research in the biomedical field, PLGA nanoparticles take on an important position because they are biocompatible, disintegrate under controlled conditions, and can encapsulate various types of therapeutic agents. PLGA is a biodegradable copolymer which has been approved for use in the USA by the FDA and is a breakdown product of lactic and glycolic acids, which, in themselves, result in nontoxic products of CO_2 and H_2O, which are normal metabolites of the body. Endodontics are considered for their ability to deliver antimicrobial agents, growth factors, and other bioactive molecules that prevent and treat infection and facilitate dental tissue healing (Toledano, 2020).

However, one of the major benefits of utilizing PLGA nanoparticles in endodontics is to release or perhaps deposit antimicrobial agents in a controlled manner. The conventional antimicrobial procedures used in endodontic therapy include disinfectants and medicaments that are less effective in reaching deep into the dental tubules or may remain effective for the prolonged time required for infection control. PLGA nanoparticles can incorporate drugs such as chlorhexidine, calcium hydroxide, or antibiotics again and deliver them over a long period, thereby enhancing the efficacy of the treatment. Marques et al. (2024) also demonstrated that the synthesized PLGA nanoparticles containing chlorhexidine can be used for endodontic disinfection. The goals of the study presented here aimed to find that such particles could penetrate the biofilm structures of Enterococcus faecalis and gradually release chlorhexidine, leading to the death of bacterial cells.

Of special interest is that PLGA nanoparticles are not only applied to antimicrobial medications in endodontics. These nanoparticles can also be used to incorporate anti-inflammatories, growth factors or other substances that can help heal the tissue in question. For example, Quiram et al. (2018) assessed whether the loading of TGF-β into PLGA nanoparticles would be effective in promoting pulp-dentin regeneration. Based on the results of this work, it could be concluded that the release of TGF-β from the surface of PLGA nanoparticles would facilitate the differentiation of DPSCs into odontoblast-like cells and the subsequent formation of new dentin –like matrix. This suggests that PLGA nanoparticles could largely supplement the regenerative endodontic procedure, which considers treating the pulp of the tooth and the healing of tissues (Quiram, 2018).

Chitosan nanoparticles are prepared from natural polysaccharide chitin; these nanoparticles are extensively used in endodontics because of their inherent antibacterial properties and unlimited capacity to be used as drug delivery systems. First, chitosan is known to be a cationic biopolymer, and that puts chitosan in a privileged position to make contact with negatively charged bacterial cell walls, break bacterial cell membranes, and thus kill bacteria. This makes chitosan nanoparticles most appropriate in the fight against bacterial biofilms, which are prevalent in inflammation of the root canal. The main advantage of Chitosan nanoparticles in endodontic applications is their properties; they are not only an antimicrobial agent but also a drug delivery system. Elshinawy et al. (2018) identified that chitosan nanoparticles eliminated Enterococcus faecalis biofilms in the root canal. From this study, it would be possible to demonstrate that chitosan nanoparticles can penetrate the biofilm structure, adhere to the bacterial cell membrane and drastically decrease bacterial survival. In addition, the study revealed an idea indicating that chitosan nanoparticles can combine with other antimicrobial agents for the disinfection of the root canal (Elshinawy, 2018).

Chitosan nanoparticles also have unique uses in regenerative tissues that are central to regenerative endodontics. Regarding the biocompatibility and bioadhesive characteristics of chitosan, it is worth establishing chitosan as the best material for supporting stem cell growth and differentiation in the root canal system. It also has to be pointed out that chitosan nanoparticles can form hydrogels, which can be applied as scaffolds for tissue engineering. Chitosan nanoparticles are biodegradable materials, and their hydrogels can be used to encapsulate stem cells and growth factors to create an environment that allows cell proliferation and differentiation. Based on this background, Ibrahim et al. (2021) designed a chitosan nanoparticle hydrogel for regenerative endodontics, which the authors showed sustained the viability of DPSCs and promoted mineralized tissue formation in vitro. This study suggests that further work on chitosan-based scaffold structures would be relevant for regenerative endodontic applications, given the aim of such procedures is to re-establish the functionality of injured pulp tissue (Ibrahim, 2021).

Compared to PLGA, chitosan nanoparticles have better-controlled release characteristics, biocompatibility, and functional flexibility for modification with different active agents. However, PLGA nanoparticles are more effective for sustained drug delivery than chitosan nanoparticles. However, chitosan nanoparticles are more effective because of their inherent antimicrobial and bioadhesive properties. Furthermore, both types of nanoparticles can encapsulate growth factors and other factors that facilitate tissue regeneration, which makes them significant materials for the newly developing area of regenerative endodontics (Ibrahim, 2021).

However, there are limitations to using polymeric nanoparticles in endodontics. A major challenge is to prove that these nanoparticles could be delivered through the anatomy of the root canal system and reach areas of infection. However, the toxicity of the polymeric nanoparticles, especially when the nanoparticles are used in large concentrations and for longer periods, should also be assessed. Future studies involving the PLGA and chitosan nanoparticles should be conducted to determine the best formulations for endodontic treatments. More research should be done to evaluate the safety and effectiveness of nanoparticles in endodontic treatments over the long term in clinical practice.

Thus, polymeric nanoparticles such as PLGA and chitosan hold great potential to enhance the treatment of endodontic infections and the regeneration of the tissue. Because of their performance to release antimicrobial agents and growth factors in a controlled fashion, biocompatibility and regenerative properties, they have been used in standard and regenerative endodontic treatment modalities. Future advancements in research and development of such nanoparticles are expected to provide wider uses of these nanoparticles in the endodontic field and improved and more predictable prognosis of the procedure (Arafa, 2020).

2.3. Ceramic Nanoparticles

The use of ceramic nanoparticles such as hydroxyapatite (HA) and bioactive glass (BG) has been reported in endodontic treatment because of their bioactive nature, evidence of tissue regeneration, and inherent antibacterial activity. These nanoparticles, prepared from bioceramic materials, have been discussed in terms of their contribution toward improved outcomes in both traditional and revascularization endodontic therapies. These bioceramics are used in dentistry due to their ability to adapt themselves to the surrounding biological environment, similar to the hardness of dental tissues (Antonijević, 2021). This section aims to discuss the characteristics and use of hydroxyapatite and bioactive glass nanoparticles in endodontics, Especially its antimicrobial, biocompatibility, and regenerative properties.

2.3.1. Calcium Hydroxyapatite Nanoparticles in Endodontics

HA is a calcium apatite mineral that is biocompatible, bioactive, bioresorbable, and a major constituent of human bones and teeth. HA nanoparticles (HANPs) have a structure close to the structure of dentin and enamel, so they are ideal for use in dentistry. Because of their bio-compatibility and bio-activity, osteoconductivity and the ability to form an interface with dental tissues, HANPs have emerged as a major interest in Endodontics with application in pulp capping, root canal obturation and regenerative endodontic procedures (Cai, 2008). One of the key uses of hydroxyapatite nanoparticles in endodontic procedures is to stimulate hard tissue formation. In another study to confirm this fact, Ribeiro et al. (2011) reported that dentin regeneration could be improved when HANPs are applied as the pulp capping material. In this study, HANPs were applied to the exposed dental pulp, and HANPs helped in the formation of reparative dentin. This was the reason attributed to the fact that HA is biologically active and chemically closest inorganic to dentine and enamel. The findings demonstrate that the composite of HANPs and dental pulp cells encourages the formation of calcium and phosphate to contribute to the formation of dentin-like tissue (Balhuc, 2021). In addition, hydroxyapatite nanoparticles have been found to have applications in sealing the root canal. One of the primary difficulties of root canal treatment is to seal the canals as tightly as possible to exclude the penetration of bacteria and fluids. HA nanoparticles have been incorporated into root canal sealers to enhance their performance during sealing. In a related study, Lee et al. (2016) also studied the effect of HANP–enhanced sealers, where the authors proved that HA provided superior sealing capability of the sealer, subsequent decrease in microleakage and also increased biocompatibility of the material. The study findings showed that HA-based sealers gave better seals and were more biocompatible with the hard tissue than the conventional sealers, which plays an important role in minimizing the chances of reinfection of the root canal system (Lee, 2016). Another crucial role of HANPs in endodontic therapy is their antimicrobial properties. Despite the fact that HA per se is not antimicrobial, due to the nanoscale of nanoparticles, it is possible to create new composite materials that incorporate HANPs in combination with antimicrobial substances. Lee et al. (2016) examined the application of the HA nanoparticles with antimicrobial agents such as AgNPs for treating biofilm-producing bacteria, including E. faecalis, of endodontic infections' persistence. In this study, the biocompatibility and the improved antimicrobial activity of the HANP-Ag composites were revealed, which may make them suitable for root canal disinfection (Lee, 2016). Additionally, hydroxyapatite nanoparticles are considered potential materials in the application of regenerative endodontics. Thus, the goal of RE is to restore the health of the dental pulp tissue and stimulate the formation of coronal dentin. HA nanoparticles have been multiplexed with scaffolds employed in regenerative bent because they provide favourable support to cell attachment, growth, and differentiation. A study by Yassen et al. (2015) assessed the osteogenic ability of HANPs within the context of cultured DPSCs. They noted that they supported the differentiation of DPSCs into odontoblast-like cells and promoted mineralized tissue formation. This indicates that HANPs could serve a central function in regenerative endodontic treatments through the development of a bioactive substrate that would foster dentin-pulp complex regeneration.

In summary, it can be concluded that hydroxyapatite nanoparticles have great prospects in endodontics. However, there is one major problem, particle aggregation, in the case of the HANP application. In addition, there is a great need to study the stability of HANPs in the biological environment so as to determine the longevity of these materials in real clinical applications. However, the existing challenges are still matters of ongoing research, and the future suggests possibilities of the use of a HANP in endodontic treatments (Erdem, 2020).

2.3.2. Bioactive Glass Nanoparticles in Endodontics

Another category of bioceramic materials that have been investigated for dental use, including endodontic use, is bioactive glass (BG). Bioactive glass is a glass in which the principal components are silica (SiO_2), calcium oxide (CaO), and phosphate (P_2O_5). The activity of the glass is due to its capacity to create an HCA layer when exposed to body fluid. When comparing this HCA layer with the mineral phase of bone and teeth, it is clear that BG is perfect for tissue regeneration and better interaction of used dental materials with hard tissues (Correia, 2022).

The bioactivity of bioactive glass nanoparticles (BGNs) determines their application in endodontics, mainly in root canal treatment and regenerative endodontics. Among the benefits of using BGNs, one should name the technology's capacity to stimulate hard tissue regeneration and the formation of new mineralized tissue. According to Farouk et al. (2021), the use of bioactive glass nanoparticles as pulp capping material prompted the formation of reparative dentin in teeth with exposed pulps. In this study, it was established that BGNs played a positive role in the differentiation of dental pulp stem cells into odontoblast-like cells that formed new dentin-like deposits at the site of injury. There was an indication that BGNs could be applicable in endodontically-related regenerative treatment procedures with the aim of enhancing tissue replacement and function in the pulp (Farouk, 2021).

Besides their ability to promote bone regeneration, the bioactive glass nanoparticles can eliminate bacteria, a factor that makes them useful in root canal disinfection. Obeid et al.

(2021) studied the BGNs' antimicrobial potential in root canal treatment and identified them as potent agents against Enterococcus faecalis, one of the most resistant bacteria causing endodontic infection. In the present study, it was found that BGNs interfered with the bacterial biofilm and decreased bacterial viability, which is an effective method to prevent the reinfection of the root canal. However, the exact way through which BGNs exert their antimicrobial effects is thought to involve the dissolution of calcium and phosphate ions, which neutralizes the bacterial process of countering acids and alters biomolecular structures to prevent biofilm development (Obeid, 2021). Furthermore, the addition of bioactive glass nanoparticles in root canal sealers results in improved bioactivity and sealing effectiveness of these materials. Root canal sealers are necessary for sealing off the root canal system to be impenetrable to bacteria and fluids. In another study by Chaudhari et al. (2021), the authors tried to incorporate BGNs into a root canal sealer, and the results showed that the bioactivity and the sealing property of the sealer were enhanced with the enhancement of BGNs. This study demonstrated that the application of the BGN-enhanced sealer made it possible to obtain a dense, thermostable layer of the sealer around the apex of the tooth root and induce the formation of new mineralized tissue at the root apex that is necessary for ensuring the long-term success of root canal therapy (Chaudhari, 2021).

Another possible application of bioactive glass nanoparticles in endodontics can be in the designing of the regenerative scaffold. When combined into scaffolds that maybe used in pulp tissue engineering, BGNs provide cell signalling for stem cell proliferation. Corral et al. (2017) fabricated an apatite bioactive glass nanoparticles scaffold for use in regenerative endodontics and noted that the scaffold impacts positively on DPSCs, which leads to the formation of new dentinal-like tissue. Based on this evidence, BGNs might play a very important part in regenerative medicine to re-establish the functionality of the dentin-pulp connection (Corral, 2017). However, there are a few constraints to the application of bioactive glass nanoparticles in endodontics, even when there are numerous advantages associated with it.

The first and obvious problem of the field is the inability to control the size, chemical composition, and surface characteristics of BGNs, which would suit them to the biological environment. Thirdly, the chronic impact of BGNs on the internal environment of a living organism, as well as the possibility of provoking inflammatory reactions, should have been taken into serious consideration. Further studies are also required in order to overcome these challenges and to make the best use of BGNs in clinical endodontic cases (Corral, 2017). Therefore, both hydroxyapatite and bioactive glass nanoparticles have the potential to increase the effectiveness of endodontic procedures. The biostimulation effects, affinity for hard tissue regeneration and microbial control give them a considerable value for normal operative as well as for regenerative endodontics. Thus, hydroxyapatite nanoparticles, due to their structure similarities with dentin and enamel, are more suitable for applications as root canal sealers, and in regenerative materials. Similar to root canal disinfection, sealing and tissue engineering, bioactive glass nanoparticles have the well-established ability to form a bioactive HCA layer and stimulate tissue regeneration. There are still some issues which need to be resolved. Still, the constant work towards the enhancement of these ceramic nanoparticles is expected to provide even more opportunities for use in endodontic treatment, and later on, the quality of the therapy and the health of the patients will be boosted (Huang, 2022).

2.4. Carbon-Based Nanoparticles

Carbon-based nanostructures such as carbon nanotubes (CNTs) and graphene oxide (GO) are now new-era materials with enormous potential in endodontics due to their structure, size, electrical conductivity, high surface area, and bioactivity. These nanoparticles reveal great antimicrobial efficiency, biocompatibility, and tissue regeneration ability; therefore, they have wide potential for application in dentistry and endodontics. In this section, emphasis will be placed on the carbon nanotubes and graphene oxide characteristics in endodontics, with special reference to the antimicrobial properties, biocompatibility, and regenerative properties (Mousavi, 2021).

2.4.1. arbon nanotubes in Endodontics

Carbon nanotubes refer to cylindrical nanostructures made from graphite sheets wrapped around in the form of a tube. CNTs have exceptional mechanical, thermal and electrical characteristics, and due to the nanoscale diameter, they can move through the tissues and interfere with cells. These re-existencies are most helpful in endodontic therapy, where CNTs serve the purpose of drug delivery, cell reinforcement, and antimicrobial properties. The roles of carbon nanotubes in endodontics therapy embrace it as an antimicrobial agent. The external morphology of CNTs enables the structures to freely engage with the bacterial cell membranes and, thus, kill the bacteria. Nahorny et al. (2017) also investigated the antibacterial activity of multi-walled carbon nanotubes (MWCNTs) against Enterococcus faecalis, the specific pathogen prevailing in chronic endodontic infection. The outcomes of the work evidence that MWCNTs had high antibacterial activity by the bacterial cell membrane and lower bacterial survival rate. Therefore, the present antimicrobial study supports the possible incorporation of CNTs into endodontic materials such as root canal sealers or root canal disinfectants so as to enhance their antimicrobial efficacy and, therefore, the efficiency of root canal treatments (Nahorny, 2017).

Apart from their antimicrobial properties, CNTs have been explored for various purposes, such as drug delivery. Because of their massive surface area and ability to cross biological barriers, CNTs can be functionalized with therapeutic agents that can incorporate antibiotic or anti-inflammatory agents and be delivered directly to the site of infection or injury. Similarly, in another study, Ghahramani et al. (2023) supported the use of CNTs as carriers of antibiotics in endodontic therapy. The work done by this study showed that CNTs could incorporate antibiotics and release them slowly in a sustained fashion to increase the microbial killing rate. This controlled release characteristic is quite beneficial during endodontic procedures because bacteria in the root canal system need constant exposure to antimicrobial agents (Ghahramani, 2023). Additionally, carbon nanotubes have displayed the ability to enhance tissue regeneration, which is important to the revitalization of the dental pulp and the regeneration of new dentin for regenerative endodontic treatments. CNTs have been employed to reinforce tissue engineering scaffolds with better mechanical and biomedical conductive characteristics for cell culturing. Zhang et al. (2015) investigated CNT-incorporated scaffolds for stimulating dental pulp tissue regeneration. They reported that CNTs improve cell attachment, proliferation, and differentiation of dental pulp stem cells into odontoblast-like cells. The formation of mineralized tissue was also confirmed in the study, and it can be postulated that CNTs can have a significant role in regenerative endodontic therapies (Marica,2021).

The applications of carbon nanotubes are very promising in endodontic treatment, but their use has a few problems that need to be surmounted. Safety is a major issue, especially with regard to the ability of CNTs to be toxic to the cells, depending on the concentration used. CNTs have the potential to provoke oxidative stress and inflammation in neighbouring tissues. In order to overcome this kind of problem, researchers are now looking for ways to functionalize the surface of CNTs so as to lessen their toxicity and enhance their compatibility. Kouklin et al. (2016) examined the biocompatible coatings on the surface of CNTs. They supported the claim that the CNTs with surface modifications had low cytotoxicity compared to the control, but they preserved their antibacterial and healing characteristics. This implies that an improved study on CNTs' alteration can improve their suitability for endodontic purposes without raising toxic concerns (Zhang, 2014).

2.4.2. The Role of Graphene Oxide (GO) in Endodontics

Graphene oxide (GO) is actually derived from graphene, which is a two-dimensional layer of carbon atoms in a hexagonal lattice. It is recognized that GO has oxygen-containing functional groups, and it has demonstrated distinct chemical and biological properties such as high surface areas, mechanical strength, and good dispersibility properties in an aqueous medium. Such properties make GO particularly useful for dental and endodontic applications, where antimicrobial, drug delivery and regenerative healing properties have been reported (Guazzo, 2018). Perhaps the major value of graphene oxide in endodontics is its bactericidal property action. Studies have been done to prove, without doubt, that the use of GO in endodontic medicine has beneficial results as it has been seen to possess significant antibacterial activity against most oral pathogens, including Enterococcus faecalis and Streptococcus mutans. Hu et al. (2017) conducted a study aimed at determining the antibiotic properties of graphene oxide on Enterococcus faecalis biofilm formed on a root canal. According to the present study, the GO matrix impacted the biofilm organization and notably decreased bacterial survival; thus, GO may be effective in the treatment of root canal infection. It is assumed that the antimicrobial activity of GO results from the effects of modifying the oxidative balance of bacterial cells and the impact on the bacterial cell membranes (Martini, 2020).

Besides the antimicrobial activity, the application of graphene oxide has been tested in drug delivery. Due to the high surface area and functional groups in GO, it is easy to attach multiple therapeutic agents, such as antibiotics, growth factors, or anti-inflammatory drugs. GO was used by Dan et al. (2021) to develop a drug delivery system for antibiotics in endodontic treatment. The work also revealed that the antibiotic incorporating GO could protect and release the antibiotic in a controlled manner, providing desirable antimicrobial energy in the root canal systems. This controlled release property is of great significance during endodontic therapy when patients require local delivery of antimicrobial agents to the infected root canal because biofilm-forming bacteria are involved in chronic infections (Dan, 2021).

Graphene oxide has also been used in regenerative endodontics because it enhances the ability of cells to attach to the surface and multiply while also providing the necessary stimuli for differentiation. GO may be well applied to the scaffold materials for tissue engineering applications to improve the mechanical strength of the scaffold and construct a biomimetic extracellular matrix for cell attachment. Tang et al. (2022) synthesized a GO-based scaffold for application in regenerative endodontics and evidenced that GO increases the proliferation of DPSCs and facilitates their osteodifferentiation. However, it should be noted that this work demonstrated that GO-based scaffold promotes the formation of mineralized tissue, which explains the important potential of GO in regenerative approaches designed for rebuilding the function of the dentin-pulp complex (Tang, 2022).

3. Conclusion

The incorporation of nanoparticles is a hallmark of modern endodontic therapy and provides solutions to conventional and regenerative problems. Different categories of nanoparticles, such as metallic, polymeric, ceramic, and carbon-based species, exhibit inherent physicochemical behaviours that have enhanced antibacterial action, biocompatibility and regenerative ability. Silver (Ag), gold (Au), zinc oxide (ZnO), and titanium dioxide (TiO_2), among other metals, have been noted for their strong biocidal properties and their ability to enhance the chemical and mechanical characteristics of endodontic materials. Chitosan, PLGA, etc., polymeric nanoparticles are capable of releasing the drug in a controlled manner and being biocompatible for the purposive improvement of tissue repair or regeneration processes. Hydroxyapatite (HA) and bioactive glass (BG) ceramic nanoparticles are much like teeth structure; they elicit bone-like tissue formation and have acceptable integration with dental tissues. Carbon-based nanoparticles such as CNT and GO present many attributes, such as high mechanical strength, antimicrobial properties, and tissue repair ability. All these materials have revealed the potential to degrade biofilms, locate delivery of effective therapeutic agencies in the infected sites, and enhance the regenerative dentin pulp technique.

Through the use of nanoparticles of various types, the following important concerns that often arise while performing endodontic therapy have been, to a large extent, addressed. Nevertheless, some issues are still evident and worth addressing, including enhancement of biocompatibility, stability, and long-term safety issues related to nanoparticle-based material. More studies are needed to improve the existing properties of these nanoparticles while trying to reduce cytotoxicity as much as possible so as to make the nanoparticles suitable for use in clinical practice. In this respect, the molecular interventions in antimicrobial activity, tissue healing, and better material characteristics of nanoparticles dominated the future of endodontics as a science and clinical practice that offers a new, more efficient and biocompatible paradigm. Thus, with increased research, clinical trials, and improving properties of nanoparticles that can be used in endodontics, endodontic treatments could substantially improve their predictability, success and long-term prognosis.

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