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Review

An Overview of Nanotechnology in Dental Medicine

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Abstract: The dentistry industry has been modernized by nanotechnology, as this emerging field has opened up new doors for dental treatment, restoration, and tissue regeneration. The potential applications of nanomaterials in dentistry are reviewed in this paper, ranging from advanced restorative materials to targeted drug delivery systems. Due to their unique characteristics (e.g., high surface area-to-volume ratios and tunable physicochemical properties), nanomaterials allow for the precise control of material behavior at the nanoscale. The ability of nanostructured materials to promote tissue regeneration offers the prospect of developing new approaches in bone and periodontal regeneration. Therefore, this review thoroughly analyzes nanomaterials' characteristics and biomedical applications, highlighting how they can aid in overcoming challenges in dental care and create possibilities for more individualized and less-invasive dental treatments.

Keywords: nanomaterials; dental applications; drug delivery; nanoparticles; nanocomposites; nanocoatings

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1. Introduction

Over time, dental materials have undergone an impressive transformation caused by the need for more durable and effective solutions in dentistry. Dental materials have evolved from primitive substances to sophisticated nanotechnologies, reflecting a constant search for innovation and advancement in dental care [1]. Dental care involved basic elements like metals, stones, and plant-based compounds in earlier times. According to archaeological discoveries, the ancient Egyptians used materials such as gold, silver, and ivory for dental applications [2]. The use of metallic alloys, particularly gold and silver, for dental restorations started gaining popularity in the Middle Ages. These metals were preferred because they were biocompatible, durable, and malleable. Furthermore, the widespread use of dental amalgam, a mixture of metals including mercury, silver, tin, and copper, emerged in the 18th and 19th centuries. Throughout a significant portion of the 19th and 20th centuries, dental amalgam replaced precious metal fillings as the most common and accessible option [3,4].

Significant developments in synthetic materials in dentistry occurred in the 20th century, the most important being the introduction of composite resins. When composite resins were developed, they completely changed restorative dentistry since they were more robust and more aesthetically pleasing. Composite materials consist of a blend of resin and filler particles, allowing for customized colors and an improved appearance. Furthermore, composite resins are biocompatible and can be used in various dental restorations, such as veneers, fillings, and bonding processes [4,5]. Because porcelain can replicate the color and translucency of natural teeth so well, it became very popular in the late 20th century.

Compared to traditional materials, porcelain restorations, such as dental veneers and crowns, offer better durability and an improved appearance. Thanks to materials science and manufacturing developments, contemporary ceramics are now essential to restorative and aesthetic dentistry [4–6].

Modern dental materials with improved qualities and functionalities have been created due to the application of nanotechnology in dentistry in recent years. Nanomaterials with potential uses in dentistry include nano-hydroxyapatite, nanocomposites, and nanostructured surfaces. These materials represent a new approach to customized and regenerative dental treatments because of their unique properties [1,4].

Nanomaterials are compounds engineered at the nanoscale with sizes typically between 1 and 100 nanometers. When compared to their bulk counterparts, materials frequently display distinct qualities at the nanometric scale, such as increased surface area, improved conductivity, and enhanced optical, magnetic, or mechanical properties [7]. When nanotechnology is used in dentistry, the field is known as nanodentistry. It supposes the utilization of nanomaterials and nanorobots in dentistry to identify, treat, and prevent dental conditions. Dental care has been revolutionized by nanodentistry in areas such as cavity treatment, teeth whitening, and orthodontics. Nanoparticles (NPs) can help remove stains and promote remineralization, while nanocomposites increase the longevity of restorations. Nanotechnology enhances the strength and convenience of orthodontic materials. Furthermore, dental treatments made using nanomaterials are supposed to be biocompatible and long-lasting, requiring fewer replacements over time. Nanodentistry represents a major breakthrough in dental healthcare by providing precise, long-lasting, and patient-friendly therapies [8,9].

There are two approaches when creating nanomaterials for dental applications: top–down and bottom–up. For the top–down approach, larger structures or materials are progressively reduced to the nanoscale through a few steps. The surface area increases as the size of its particles decreases, leading to a noticeable improvement in its physical characteristics [10,11]. On the other hand, bottom–up fabrication involves combining smaller structures into larger ones via the gradual construction of nanostructures from atomic or molecular components. This process depends on molecular synthesis and self-assembly techniques, in which atoms or molecules spontaneously arrange themselves into appropriate patterns [10,11].

The technique can be chosen by considering the desired structure, properties, and application of nanomaterials in dentistry. Nanomaterials can be precisely engineered to possess specific properties [12], and they can be used in different areas of dentistry, as presented in Figure 1. For example, therapeutic or imaging substances can be functionalized into NPs to provide targeted drug delivery (TDD) and efficient diagnostics. There are many benefits of using nanomaterials in dental treatments. These materials allow for less invasive processes because they can accurately interact with biological tissues at the nanoscale, reducing tissue trauma and speeding up the healing process [12,13].

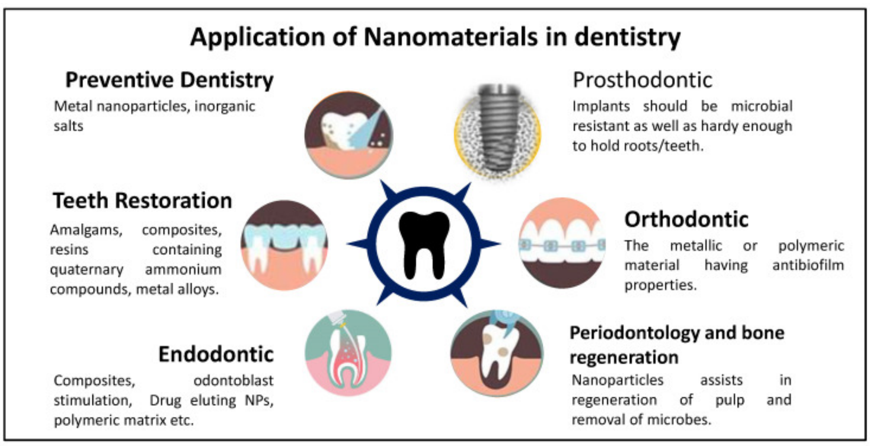

Figure 1. Nanomaterial applications in dentistry. Reprinted from an open-access source [11].

Examples of nanomaterials for different applications in dentistry, as well as their mechanisms of action and limitations, are illustrated in Table 1.

Table 1. Examples of nanomaterials, their applications, mechanisms of action, and limitations.

NPs	Applications	Mechanism of Action	Limitations	Refs.
Silver NPs (AgNPs)	Composites Antibacterial coatings Toothpaste additives Dental implants	Release silver ions that disrupt bacterial cell walls Bacterial growth inhibition Reduce biofilm formation	Potential toxicity to human cells	[14–18]
Titanium Dioxide (TiO_2) NPs	Implants Antibacterial coatings Composites	Photocatalytic activity under UV light breaks down organic stains Improves mechanical properties	Potential for UV-induced damage Can cause oxidative stress	[19–22]
Zinc Oxide NPs (ZnO NPs)	Toothpaste formulations Dental varnishes Antibacterial agents	Disrupts microbial cell membranes Provides a protective barrier	Potential cytotoxic effects	[23–26]
Hydroxyapatite NPs (HAp NPs)	Tooth enamel remineralization Dental fillers Bone regeneration	Similar to natural tooth mineral structure—it repairs and strengthens enamel Promotes bone growth in implants	Poor mechanical properties	[27–30]
Gold NPs (AuNPs)	Mouthwashes formulations Toothpaste additives Implants	Antibacterial properties Osteoinductive action	High cost Potential toxicity	[31–33]
Silica NPs	Dental fillers Coatings	Improves mechanical properties and durability of fillers	Potential toxicity	[34–36]
Copper NPs (CuNPs)	Toothpaste formulations Coatings	Prevents biofilm formation Release copper ions that disrupt microbial cell membranes and inhibit bacterial growth	Potential toxicity Risk of corrosion	[37–40]
Polymeric NPs	Drug delivery Adhesives	Controlled release of drugs Improves adhesiveness	Potential toxicity	[41–44]
Magnetic NPs	TDD Antibacterial agents	Uses magnetic fields to guide particles to targeted locations Antibacterial properties	Biocompatibility issues	[45–48]
Graphene oxide	Dental implants Coatings	Enhances mechanical strength and bioactivity in implants Antibacterial activity through oxidative stress and physical disruption	Potential toxicity	[49–52]

In this context, this review paper aims to provide a thorough overview of how nanomaterials improve dental care. This work attempts to provide insight into the prospective applications of nanomaterials in dentistry, including restorative materials, implantology, and drug delivery systems, by highlighting current research findings and technological advancements. This review also emphasizes the benefits, challenges, and potential directions of applying nanotechnology to dentistry.

2. Nanomaterials in Preventive Dentistry

2.1. Nanoparticles in Oral Hygiene Products

Using nanomaterials in dental care products improves the effectiveness of toothpaste and other oral hygiene products. TDD, remineralization, and antibacterial activity are just a few uses for NPs [53].

Bacteria are important in various dental problems, including tooth decay, gum disease, and oral infections. Many different types of bacteria in the oral cavity, such as *Streptococcus mutans*, *Porphyromonas gingivalis*, and *Streptococcus oralis*, are known to play a major role in developing periodontal and dental caries [54,55]. Because of their unique physio-chemical characteristics, metallic NPs seem to be promising substitutes to treat various illnesses caused by bacteria. Their properties and potential applications in oral hygiene products are presented in Table 2 [56].

Table 2. Properties and potential applications of NPs in oral hygiene products.

NPs	Properties	Application in Oral Hygiene	Refs.
AgNPs	Strong antimicrobial activity Bacterial growth inhibition	Toothpaste—to prevent dental caries Alcohol-free mouthwashes	[57–60]
AuNPs	Antimicrobial activity Effective against *S. oralis*	AuNP-based mouthwashes Toothpaste formulations	[61–63]
CuNPs	Anti-biofilm formation Antimicrobial activity	Toothpaste formulations	[63,64]
ZnO NPs	Anti-inflammatory and antibacterial activity	Toothpaste formulations	[26,65]

Several metallic NPs have demonstrated antimicrobial and anti-inflammatory activity. *S. mutans* has an impact on caries formation since it creates a biofilm on the surface of teeth, known as plaque. AgNPs have shown bactericidal effects against *S. mutans* through mechanisms such as disrupting bacterial cell membranes and inhibiting enzymatic processes [60,66]. AgNPs synthesized using lemon peel exhibited higher antibacterial activity in toothpaste formulations, as evidenced by a larger diameter of the inhibition zone compared to that of other brands of toothpaste existing on the market [67]. A few studies demonstrate that the use of AuNPs in toothpaste has antimicrobial effects, although the data are limited. A specific study tested the antibacterial effect of different toothpastes against Gram-positive and Gram-negative bacteria [68]. Although the antibacterial effect was not the most significant among them, AuNPs still showed an effect against Gram-positive bacteria, which could be further studied for creating novel oral hygiene products.

Another important class of NPs that can be used in oral hygiene is ceramic NPs, especially HAp NPs, since they are dental enamel's primary inorganic component [69]. HAp NPs have exceptional remineralization properties that support tooth structure and aid in restoring damaged enamel. HAp NPs could promote enamel remineralization in toothpaste formulations, which may lower the risk of tooth decay and sensitivity [29,69]. Additionally, studies have shown that HAp NPs can be used for teeth whitening when it is incorporated into toothpastes and mouthwashes in concentrations up to 10%. It demonstrated comparable results with other teeth whitening products available on the market [70,71]. Florea et al. [72] developed toothpaste with both enamel remineralization and antibacterial properties by using nano-HAps (nHAps) and birch extract. They tested eleven different formulations with variations in birch extract concentrations and types of nHAps. Toothpaste formulations containing nHAps demonstrated an excellent level of enamel repair and normalized the enamel nanostructure within 10 days of treatment. Toothpaste P5, containing both nHAps and birch extract, showed a good balance of antibacterial activity and remineralization potential, which makes it a good candidate for dual-purpose oral care. Another important observation was that nHAps in some formulations seemed to reduce the immediate antibacterial effect of the birch extract, possibly by delaying the release of active molecules. Ionescu et al. [73] investigated two commercially available toothpastes containing n-HAps substituted for metal ions in terms of early bacterial colonization (EC) and biofilm formation. The toothpastes tested were α (Zn-carbonate substituted n-HAp) and β (F, Mg, Sr-carbonate substituted n-HAp). The β toothpaste outperformed the α and control groups in reducing bacteria, likely due to its combination of fluoride and strontium.

Both kinds of toothpaste left residues on enamel- and resin-based composite surfaces, and β showed potential to prevent secondary caries. The results suggest that brushing twice daily with β toothpaste could improve oral health by reducing harmful biofilms. Amaechi et al. [74] compared the effectiveness of several n-HAp toothpastes with a commercial desensitizing toothpaste containing calcium sodium phosphosilicate (CSPS) in relieving dentin hypersensitivity (DHS). The results showed that 15% nano-HAp and 10% n-HAp with potassium nitrate were as effective as the CSPS toothpaste in reducing DHS. The 10% n-HAp alone was a bit less effective for thermal sensitivity over time.

Silica NPs have also been investigated in preventive dentistry. Barma et al. [75] studied the antibacterial properties of mouthwash infused with silica NPs against common oral pathogens like *Streptococcus mutans*, *Staphylococcus aureus*, and *Enterococcus faecalis*. The NPs inhibited bacterial growth, particularly at higher concentrations. The mouthwashes were effective against Gram-positive bacteria but were not tested against Gram-negative bacteria, suggesting a need for further research. Wang et al. [76] developed a novel type of NPs, nMS-nAg-Chx, containing mesoporous silica (nMS) with nanosilver (nAg) and chlorhexidine (Chx), which aimed to prevent and treat dental caries. The NP system inhibited the growth of cariogenic bacteria and promoted the growth of non-cariogenic (benign) bacteria, transforming the biofilm into a non-harmful one. These findings indicate that nMS-nAg-Chx could be used for various dental applications, such as mouthwashes or toothpaste, to prevent caries and biofilm formation. Silica NPs have also been investigated for retaining toothpaste on oral surfaces in a study by Aspinall et al. [77]. Silica NPs with different functional groups, including chitosan, acryloyl, phenylboronic acid, and others, are incorporated into toothpaste formulations. These toothpastes were tested on sheep tongue mucosa to see how well they adhered to the oral surfaces. The kinds of toothpaste containing functionalized silica, particularly those with chitosan, acryloyl, and phenylboronic acid, had better retention compared to those with unmodified silica. This happens because the functionalized silica has mucoadhesive properties, and it interacts more with the mucosal surface. This kind of formulation could improve oral care, since the active ingredients in the oral care products will be kept in the oral surfaces for longer.

2.2. Nanocoatings

Dental implant nanocoatings are a state-of-the-art method of extending the lifespan and performance of implants. Through nanotechnological approaches, dental implant surface modifications can be made more effective and long-lasting. For example, nanocoatings can reduce inflammation, accelerate healing, and improve tissue integration [78,79]. The antibacterial activity, corrosion resistance, and biocompatibility of TiO_2 NPs make them significant in nanocoatings. TiO_2 NPs can be added to dental implant surfaces to improve osseointegration, reduce inflammation, and decrease the chance of bacterial colonization [78]. A study conducted by Memarzadeh et al. [80] proved that TiO_2 nanocoatings on implants have an antimicrobial effect, which makes them beneficial, as it lowers the risk of infection. It also showed an increased proliferation of osteoblasts. Another study by Li et al. [81] revealed that dental implants coated with TiO_2 NPs facilitated cell adhesion and proliferation. These findings underscore the significant role of nanocoatings in enhancing the initial stages of implant healing, ultimately contributing to improved clinical outcomes. Hammad et al. [82] evaluated the effects of ZnO nanocoating on nickel-titanium (NiTi) orthodontic wires, focusing on antibacterial properties and frictional resistance. The ZnO nanocoating was successfully applied, and a uniform layer of NPs was formed. The coated wires showed better antibacterial activity against Gram-positive bacteria and reduced frictional resistance by 34% compared to uncoated wires. These findings suggest that ZnO nanocoating not only improves the antibacterial behavior of NiTi wires but also their mechanical performance.

The effects of HAp NP nanocoatings include promoting faster and more robust osseointegration, reducing the risk of implant failure, and enhancing implant stability [83]. A. Besinis et al. modified the surface of titanium alloy implants by using silver, TiO_2, and HAp nanocoatings [84]. The findings showed strong antibacterial properties against *S. sanguinis*. The nanocoatings restricted bacterial growth in the surrounding environment and stopped biofilm formation on the implant surface. Pang et al. [85] investigated a combination of bone morphogenetic protein-2 (BMP-2) and nHAp to improve the osseointegration of Ti dental implants. It was found that coating Ti implants with nHAp and BMP-2 promoted the differentiation of human mesenchymal stem cells (BM-MSCs) into osteoblasts, which are responsible for bone formation. The in vivo studies showed that there was a strong expression of early bone formation markers, but no visible bone formation was observed at 4 weeks post-implantation. They might have potential for long-term bone formation, but the short observation period may have been insufficient. De Oliviera et al. [86] tested the effectiveness of nHAp coatings on dental implants by comparing them to traditional implant surfaces. A gene expression analysis showed that nHAp-coated implants increased markers related to bone formation, especially in the early stages of healing. This suggests that nHAp coatings help in boosting bone cell activity. Micro-CT scans showed that nHAp-coated implants had better bone integration and formation compared to traditional implant surfaces since they provided higher percentages of bone volume and a higher bone quality around the implants. These findings highlight the properties of nHAp coatings, the most significant one being that they can improve bone formation around implants.

The utilization of nanocoatings in dental implants represents a novel approach to prolonging the life and efficacy of the implants. Through nanotechnology, surface modifications of dental implants can be optimized for enhanced effectiveness and durability. Findings demonstrated that coatings offer antibacterial properties, promote osseointegration, reduce inflammation, and prevent biofilm formation. Through continued research, nanocoatings can lead the way toward safer, more effective, and longer-lasting implants.

Nanocoatings also have applications in orthodontics. Orthodontic braces may be more prone to plaque formation during extended wear, which raises the risk of gum disease and dental damage. Moreover, it can result in more friction building up between the teeth and the braces. The patient may experience discomfort and irritation due to this increased friction, which could lengthen the adjustment period and impact treatment results [87,88]. An innovative way to improve orthodontic braces is with nanocoatings. This has advantages such as less friction, biocompatibility, and improved aesthetics by adding NPs to the brace surface. These coatings offer smoother surfaces, which lessen patient discomfort and may shorten treatment durations. They may also include antibacterial properties, which promote good dental hygiene [88].

The antibacterial properties and ion release of nanocoated nitinol archwires were investigated by Ilic et al. [89]. Copper-doped titanium nitride (TiN-Cu) coating was created to enhance corrosion resistance and achieve antibacterial properties to orthodontic nitinol (NiTi) archwires. Coatings with uniformly distributed CuNPs were discovered by a physicochemical examination. TiN-Cu nanocoated archwires exhibited substantially reduced Ni release. The antibacterial activity was demonstrated by the quantities of *Streptococcus mitis*, which were significantly lower on the TiN-Cu-coated archwires. According to the study, TiN-Cu-nanocoated archwires may be good candidates for more clinical research due to their potential for improved biocompatibility and antibacterial qualities.

In another recent study conducted by Selvaraj et al. [90], the researchers investigated the synthesis and characterization of clove- and cardamom-reinforced ZrO_2 NPs for coating orthodontic archwires. At a concentration of 50 µL, there was very little cytotoxicity shown. The NPs demonstrated strong antibacterial action against a range of oral infections. Furthermore, adding cardamom and clove improved the NPs' anti-inflammatory effects. A uniform surface coating was obtained when NiTi and SS archwires were coated with a digital magnetic stirrer. However, static and kinetic friction assessments revealed no significant differences between coated and non-coated NiTi and SS wires with ZrO_2 in a study by Golshah et al. [91]. Although ZrO_2 has been found in other domains to be effective in lowering friction, its treatment on TMA wires had no apparent impact on friction in their investigation. These studies highlight that while ZrO_2 NPs coatings may be biocompatible and hold an antibacterial effect, they may not have an impact on the static and kinetic friction.

Polydopamine-graphene oxide (PDA-GO) nanocoatings were added to NiTi archwires via self-assembly in another study conducted by Chen et al. [92]. The coated archwires demonstrated uniform characteristics, consequently minimizing Ni dissolution. Its antibacterial effectiveness against *Streptococcus mutans* was established, along with its biocompatibility. Additionally, it demonstrated enhanced corrosion resistance in the oral fluid media. Another study by Gracco et al. [93] examined the effects of coating orthodontic wires with Ni + MoS_2 and Ni + WS_2. It found that the coated wires consistently reduced friction when compared to uncoated and Ni-coated wires, especially in "dry" conditions, and that there was uniform adherence and effective lubricant incorporation. More research is necessary to understand their performance in settings that mimic the buccal environment.

Overall, research has shown the potential of different nanocoatings to improve biocompatibility corrosion resistance and exhibit antibacterial effects, although their impact on friction and other properties may vary. Further research is necessary to fully understand their performance in clinical settings and optimize their benefits for orthodontic patients.

3. Nanomaterials in Restorative Dentistry

3.1. Nanocomposites for Dental Fillings

Dental fillings are essential for repairing tooth structure and preventing further decay. They have traditionally been made of amalgam, composite resins, or glass ionomer cement-based materials. Nonetheless, developments in nanotechnology have resulted in nanocomposites made particularly for dental fillings [94,95]. A few examples and their properties are described in Table 3.

Table 3. Nanocomposites and their properties for dental fillings.

Nanocomposite	Properties	Refs.
Silica NPs	Improved mechanical properties Reduced polymerization shrinkage Enhanced wear resistance	[36,96,97]
TiO_2 NPs	Increased tensile strength Improved stiffness and toughness	[98,99]
Calcium phosphate (CaP) NPs	Increased wear resistance Stress-bearing capacities	[100]
Zirconium Oxide (ZrO_2) NPs	Enhanced wear resistance and hardness	[101]
Graphene Oxide NPs	Improved mechanical strength Crack propagation resistance	[102,103]
AgNPs	Improved flexural strength Increased surface microhardness	[104,105]
ZnO NPs	Improved microhardness High flexural strength and modulus	[106,107]
Carbon nanotubes	Increased elastic modulus Increased compressive strength Improved flexural strength	[108,109]

One of the key advantages of nanocomposites is their improved mechanical strength. The inclusion of NPs, such as silica or zirconia, improves the hardness and wear resistance of the filling material. Furthermore, nanocomposites have superior bonding to tooth structures. The NPs can penetrate the micro-structures of dentin and enamel, which makes a more effective seal and reduces the risk of secondary caries [110,111].

A study by Azmy et al. [112] investigated how the mechanical properties of light-cured dental composite resins (DRCs) were affected by adding nanoparticles (ZrO_2, TiO_2, and SiO_2). The concentration of NPs was found to possess a substantial impact on the flexural strength (FS). Although the FS of the control DRCs was below ISO requirements, the FS of the ZrO_2 and 3 wt.% of TiO_2 and SiO_2 increased and were above the ISO's 80 MPa threshold. In another study by Nikolaidis et al. [36] to alter silica NPs, the researchers created novel methacrylated quaternary ammonium silanes, which were then added to a Bis-GMA/TEGDMA-based matrix for dental nanocomposite resins. The mechanical properties and dispersion of the altered NPs were improved. All composites experienced less polymerization shrinkage when silica NPs were added, reducing the amount of stress applied to the tooth structure. Saridou et al. [113] synthesized dental nanocomposite resins using organically modified silica and Quaternary ammonium-clay NPs. An increased clay content lowered the solubility and shrinkage strain without compromising the final strength or flexural modulus. These results provide significant insights for the development of novel dental fillings using nanomaterials. Toledano et al. [114] created polymeric Zn-doped NPs to improve the mechanical properties of dentin. The NPs increased hardness and elasticity by promoting mineral deposition, which helped prevent cracks and fractures. In root dentin, Zn-NPs improved the strength and reduced microleakage. The dentin was more durable, especially in endodontic treatments. Moreover, the Zn-NPs helped preserve collagen. Alshamrani et al. [115] investigated how adding zirconia and glass Si NPs to 3D-printed dental resin impacts its properties. Adding 10–20% zirconia and 5% glass silica NPs significantly improved the resin's flexural strength, and it made it more resistant to mechanical stress, which is very important for dental restorations. The NPs likely reinforced the resin by distributing stress more effectively and preventing crack propagation. Aati et al. [103] studied the effects of ZrO_2 NPs on the properties of an acrylate ester-based resin for dental restoration. Adding ZrO_2 NPs improved the resin's hardness, flexural strength, and toughness. Optimal properties were observed with 3 wt.% ZrO_2, because the resin had the highest fracture toughness and modulus. Higher filler concentrations (5 wt.%) led to lower toughness and flexural modulus values due to the agglomeration of NPs. After 3 months of aging in artificial saliva, the resin showed improved properties such as the degree of conversion and microhardness. Rudolf et al. [116] created a poly(methyl methacrylate) PMMA and ZnO composite and studied its properties. The PMMA-ZnO composite showed an improved compressive strength compared to that of pure PMMA and had an improved durability. Moreover, the nanocomposite was found to be non-cytotoxic.

From their improved mechanical strength to their superior aesthetic qualities, nanocomposites offer a great solution for addressing the challenges associated with traditional dental materials. Nanocomposites promise to improve dental fillings' durability, longevity, and overall performance.

3.2. Nanoadhesives

When it comes to tooth fillings, the adhesive layer plays an important role because it helps stop microleakage between the filling and the tooth that results from the filling material shrinking. This layer prolongs the filling's longevity by sealing off potentially harmful substances. An ideal adhesive should repel bacteria and prevent biofilm formation. It also should improve the filling's adhesive properties. To achieve these characteristics, nanomaterials can be incorporated into the adhesive [117,118]. Nanoadhesives provide a better bonding strength. The small size of these NPs allows for the better wetting and infiltration of the adhesive into the tooth substrate, reduces gaps, and increases bond strength. They also offer improved resistance to degradation [119,120].

Recent studies have explored the incorporation of various NPs into dental adhesives to enhance their properties. Abdul et al. [120] synthesized zirconia/silver phosphate NPs to create experimental dental adhesives. The adhesive demonstrated antibacterial activity against Gram-positive and Gram-negative bacteria. Additionally, it had an improved bond strength and long-term color stability. Melo et al. [121] studied the effects of incorporating AgNPs and amorphous calcium phosphate (ACaP) into novel adhesives on dentin bond strength and plaque. ACaP delivers calcium and phosphate ions for remineralization, whereas AgNPs add antimicrobial properties. As a result, there was significant antibacterial activity without any decrease in dentin bond strength. Rao et al. [122] aimed to improve the bond strength of caries-affected dentin (CAD) by remineralizing it using PAMAM-loaded bioactive glass NPs. The experimental groups had a stronger micro-tensile bond strength (MTBS) than the control group, indicating better bonding to the teeth. The remineralization process aided by MBG NPs improved the binding strength of the CAD. Furthermore, altering the adhesive with PMBG helped distribute PAMAM polymer to collagen fibrils, facilitating remineralization. Another study by Kreutz et al. [123] investigated how several NPs, such as BAG-Bi, CAP/MA-POSS, SiO2@Ag, and MA-POSS, affected dental adhesives. It was discovered that BAG-Bi enhanced water adsorption and the sol fraction, whereas MA-POSS reduced water adsorption. CAP/MA-POSS enhanced the shear viscosity, but SiO_2@Ag did not affect the material characteristics. All of the NPs caused mineral precipitation, but none had an antimicrobial effect. Additional study is required to investigate their long-term antibacterial effects and optimize NP doses for therapeutic usage.

Another study by Mirhashemi et al. [124] investigated how adding ZnO NPs and chitosan NPs to orthodontic composite resins affects their shear bond strength (SBS), which measures how well the composite sticks to teeth and also compared it to the commercially available Transbond XT. Adding ZnO and chitosan NPs up to 5% did not change the SBS of the composite resins compared to the standard Transbond XT composite. However, adding 10% NPs decreased the SBS. This might be due to the disruption of the composite's consistency and possible toxicity of the high NP concentration. This study indicates that adding lower concentrations of NPs is safe and maintains a good bond strength, while higher concentrations can be harmful. Binhansan et al. [125] studied how adding two different concentrations of carbon NPs (CNPs) of 2.5% and 5% to a control adhesive (CA) impacts its properties. The 2.5% CNP adhesive achieved the highest SBS (25.15 MPa), followed by the 5% CNP adhesive (24.25 MPa), both showing an improved bond strength compared to the CA. The 5% CNP adhesive displayed thicker resin tags and a more uniform hybrid layer compared to the 2.5% CNP and CA. The addition of CNPs improved the bond strength of the adhesive, with the 2.5% sample showing the best performance. However, both CNP concentrations resulted in a reduced viscosity and degree of conversion. These findings indicate the need for further research.

The effects of adding NPs to adhesives were also investigated in an ex vivo clinical trial by Allende et al. [126]. This study involved fifteen participants and a total of 30 third molars. The researchers investigated how adding 0.2% CuNPs and 5% ZnONPs to a commercial adhesive affects its performance and the hybrid layer in teeth. When observing its effects on the microtensile bond strength and degree of conversion, no significant differences were found between the experimental and control groups (standard adhesive), indicating that adding NPs did not negatively impact the adhesive's bonding strength or polymerization. Moreover, the experimental group showed lower nano leakage and gelatinolytic activity at the hybrid layer than the control group. This modification could improve dental restorations' long-term performance by reducing the adhesive–dentin interface's breakdown.

Nanoadhesives show potential for improving antibacterial characteristics and mechanical strength. While recent studies have revealed promising outcomes, additional research is required to fully understand the long-term consequences and improve NP formulations for therapeutic usage. With continuing advances in nanotechnology, NP-based dental adhesives may provide novel options for increasing the longevity and performance of dental restorations, thereby boosting patient oral health.

4. Nanomaterials in Endodontics

4.1. Nanoparticles in Root Canal Disinfection

Endodontic disorders are the fourth most costly illnesses in industrialized countries. Endodontics is an area of dentistry that studies, diagnoses, and treats dental pulp and the tissues surrounding the roots of teeth [127]. Treating these disorders includes cleaning the canal and using antimicrobial substances. NPs have a promising role in endodontic disinfection. Their size enables them to penetrate the challenging root canal architecture, reaching regions that standard disinfectants may miss. NPs can also be included in root canal filling materials or utilized as irrigants to increase antibacterial effectiveness [128,129].

Calcium hydroxide, potassium iodine, and chlorhexidine (CHX) are some of the most often used root canal disinfectants. In a study by Haseeb et al. [130], the researchers produced CHX-loaded PEG–b–PLA NPs using a biodegradable polymer to promote drug delivery to dentin tubules. The CHX release lasted up to three weeks, with a brief peak followed by a controlled release, indicating the benefits of using NPs in root canal treatment. Parolia et al. [131] examined the effect of propolis NPs (PNPs) against *Enterococcus faecalis* when used as a canal irrigant. The study found that PNPs demonstrated significant antimicrobial effectiveness against *E. faecalis,* comparable to conventional irrigants like sodium hypochlorite (NaOCl) and CHX. Elmsmari et al. [132] also explored the use of calcium hydroxide; more exactly, it was loaded into poly(lactic-co-glycolic acid) (PLGA) NPs for improving endodontic disinfection procedures. Calcium hydroxide PLGA NPs showed a minimum inhibitory concentration (MIC) of 10 μg/mL against *Porphyromonas gingivalis* and *Enterococcus faecalis* and 5 μg/mL against *Fusobacterium nucleatum*, which demonstrates effective antibacterial activity. Moreover, a significant reduction (40%) in bacterial metabolic activity was observed with a single dose of calcium hydroxide PLGA NPs after 28 days of infection. Their ability to reach and act in complex root canal systems could address the limitations that are present in traditional methods. Further studies are needed to test their effectiveness against more resistant bacterial biofilms before their clinical use.

Since silver has antibacterial properties, it is a promising agent in root canal disinfection. Marín-Correa et al. [133] compared the effectiveness of a nanosilver gel with the traditional calcium hydroxide treatment in root canal treatment. The nanosilver gel had effective antibacterial properties against *E. faecalis*, comparable to the traditional calcium hydroxide treatment. Due to their small size, AgNPs can access areas in the root canal that other treatments might miss. They are also less likely to lead to microbial resistance, offering a good alternative for root canal treatments. Gholami et al. [134] were also interested in investigating the potential of silver in root canal treatments. More exactly, they created and tested a positively charged silver nanocomplex loaded with CHX (CHX@AgNPs+) for improved antibacterial activity against *E. faecalis* in endodontic treatments. CHX@AgNPs+ demonstrated a consistent release of CHX. CHX@AgNPs+ showed superior antibacterial activity against *E. faecalis*, with MIC and minimum bactericidal concentration (MBC) values of 50 μg/mL, compared to CHX (100 μg/mL) and AgNPs+ (no MIC determined). This nanocomplex offers a promising treatment for root canal disinfection. Razumova et al. [135] studied the effectiveness of a 1% nanosilver solution (Argitos) as a final irrigation agent in root canal treatment. Seventy single-rooted extracted teeth were divided into two groups: one where the smear layer was removed and one where it was not. Nanosilver adhered to the dentinal surface and formed a film in the teeth with the smear layer preserved. In the teeth with the smear layer removed, nanosilver was present in 73.5% of cases but did not form as consistent a film. The nanosilver solution shows promise as a final irrigation agent by forming a protective film on the dentinal surface, which may help manage pulpitis and apical periodontitis.

Tonini et al. [136] evaluated the bactericidal effect of silver-citrate root canal irrigants and their ability to remove residues created during root canal treatment. Citric acid and a new silver-citrate-based irrigant (BioAKT) showed potential for eliminating the smear layer and increasing sealer penetration. BioAKT had high antibacterial action against *E. faecalis* biofilms, similar to NaOCl. However, the use of silver ions and NPs may cause tooth discoloration and cytotoxicity. More research is needed to investigate their synergistic antibacterial activities and identify possible downsides in endodontic applications. Ravi et al. [137] examined the efficacy of NaOCl, AgNPs, and zinc oxide NPs (ZnO-NPs) against Candida biofilms in root canals. Ag-NPs and ZnO-NPs showed promise in decreasing the fungal load. However, total eradication was not accomplished, probably due to biofilm resistance. These NPs interact with microbial cell targets, breaking cell walls and altering permeability, resulting in cell death.

From their antimicrobial activity to their ability to penetrate and eradicate biofilms, NPs offer a promising solution for overcoming the challenges associated with conventional root canal disinfection methods. However, further research is needed to fully understand their long-term effects.

4.2. Nano-Based Sealers

In root canal therapy, an endodontic sealer is a substance that fills the gap between the root canal's interior walls and the filling material [138]. Conventional endodontic sealers might not properly cover the root canal, creating tiny gaps where bacteria may enter and lead to infections. Furthermore, in general, they do not have antimicrobial properties and have long setting times [139]. Adding NPs to existing endodontic materials can improve their performance in several ways. Initially, they can aid in improving the root canal's sealing, which lowers the possibility that germs will enter and lead to problems. Secondly, bacteria can also be prevented by NPs since NPs have the ability to enter small gaps and release antibacterial agents [140].

ZnO NPs can help prevent bacterial growth and increase a sealer's physical strength and durability [141,142]. This was demonstrated through a study conducted by Choi et al. [143]. The researchers investigated how incorporating different weight percentages of ZnO NPs into a commercially available pit and fissure sealant impacts its properties. Various concentrations of ZnO NPs (0.5%, 1%, 2%, and 4% by weight) were tested to assess their impact on the sealant's antibacterial properties, ion release, and physicochemical and mechanical properties. Sealants with ZnO NPs showed significant antibacterial effects against *Streptococcus mutans*. The 4% ZnO NP sealant showed the strongest antibacterial activity. Sealants with ZnO NPs had increased water sorption and solubility compared to the control, potentially affecting long-term durability. However, these properties did not impact the sealant's overall performance. The addition of ZnO NPs did not alter the flexural strength of the sealants, meaning that the mechanical integrity of the sealants was maintained. Collares et al. [144] also studied the effects of ZnO nanostructures, more specifically, needle-like ZnO nanostructures (ZnO-NN), on methacrylate-based dental sealers. ZnO-NN with a needle diameter of 40 nm was added to dental sealers at concentrations of 20%, 30%, and 40% by weight. All sealers with ZnO-NN demonstrated antibacterial effects against *Enterococcus faecalis*. The antibacterial activity was linked to the generation of ROS by ZnO-NN, which disrupts bacterial cell membranes and reduces viability. Moreover, the addition of ZnO-NN increased the film thickness of the sealers and improved their radiopacity. The authors suggest that there is a need for more research on this subject to also understand the long-term effects. Zubizarreta-Macho et al. [145] compared two types of inorganic bactericidal additives, G3T glass-ceramic and ZnO-enriched glass, when incorporated into a root canal sealer (AH Plus) in a Beagle dog model. Both G3T glass-ceramic and ZnO-enriched glass showed good biocompatibility and did not negatively impact tissue health. They also showed some antimicrobial characteristics. Both maintained the physical properties of the sealer, but further research is needed to ensure effective contact and sustained antimicrobial activity in clinical applications.

Other types of nanomaterials have been investigated for their potential in nano-based sealers. The aim of a recent study was to enhance their handling and sealing ability by investigating the usage of endodontic sealers based on nano-apatite. Two formulations using nano-apatite, PEG 1000, and propanediol in one and nano-apatite, glycerin, and PEG 200 in the other were found to be promising. Both formulations successfully sealed dentinal tubules, while the first exhibited superior acid resistance [146]. In a study by Al-Sabawi et al. [147], the researchers developed a calcium silicate-based root canal sealer by using phosphate-buffered saline (PBS) as a liquid precursor and nano-tricalcium silicate-58s bioactive glass as a precursor. The results showed that adding ZrO2 lowered the level of solubility and setting time while adhering to ADA regulations. The resulting formula showed promising physicochemical characteristics, but further research is needed to learn more about its potential use in clinical applications.

Raheem et al. [148] created a sealer using propolis-loaded NPs. The nano-sealer they created showed a sealing performance that was similar to the industry's "gold standard" sealer. It demonstrated hydrophobicity and slow deterioration, which contribute to improved sealing, while its nanosized particles enable effective entry into dentinal tubules. Ibrahim et al. [149] studied the addition of CaP NPs to endodontic sealers. The findings showed that the sealer held antibacterial capabilities without compromising the biocompatibility. The modified sealer strengthens and remineralizes dentin by releasing calcium and phosphate ions, increasing the pH level, and successfully neutralizing acidity. Addressing bacterial development and strengthening tooth root structure can potentially improve endodontic treatment.

Overall, nano-based sealers represent a promising avenue in endodontic therapy, offering an enhanced sealing ability and level of biocompatibility. These advancements hold great promise for improving clinical outcomes in root canal treatment. Further research is necessary to fully explore the efficacy and safety of nano-based sealers in practical applications.

5. Nanomaterials in Periodontology

5.1. Nanoformulations for Targeted Drug Delivery in Periodontal Therapy

Periodontitis is a chronic inflammatory condition affecting the gums and supporting structures of the teeth, which can further lead to tooth loss [150]. Surgical interventions, systemic antibiotics, scaling and root planing, and other conventional treatments for periodontitis frequently have drawbacks, including a limited ability to reach deep periodontal compartments, systemic side effects from the drug distribution, and invasiveness [151,152]. Several methods for the application of drug delivery systems to teeth are illustrated in Figure 2.

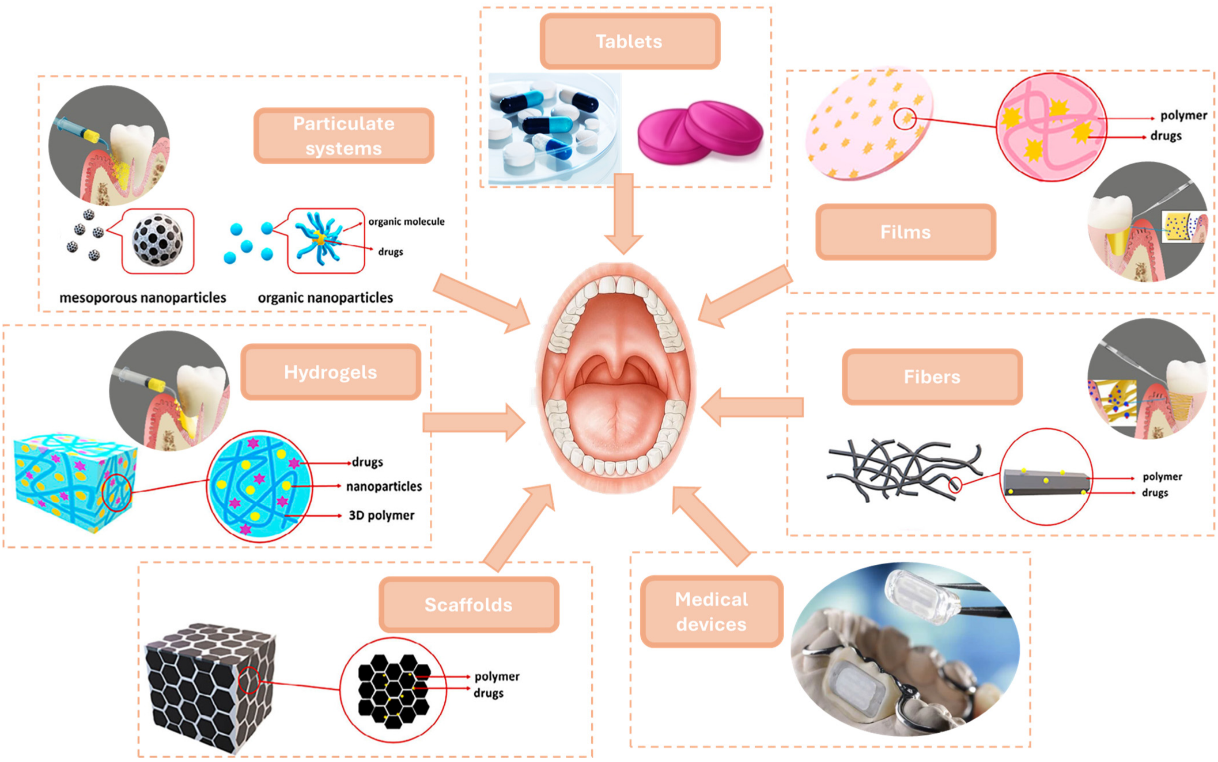

Figure 2. Methods of the application of drug delivery systems to teeth. Created based on information from [151,153–156].

Films provide a convenient and discreet option, adhering to the gingival tissue for the sustained release of therapeutic agents. Strips offer an ease of application, allowing for precise placement into periodontal pockets and targeting specific areas of concern. Gels provide versatility, enabling thorough coverage of the affected area while offering the flexibility to adjust the dosage as needed. Tablets offer an ease of application and patient compliance [153,157,158]. Using NPs in periodontal therapy can precisely administer therapeutic drugs to the diseased periodontal tissues, allowing for TDD. When it comes to periodontal therapy, NPs have several benefits. First, because of their small size, they can easily enter periodontal pockets and reach regions that are difficult for traditional therapies. By increasing the concentration of therapeutic medicines at the infection site, this TDD maximizes their efficacy while reducing systemic exposure and possible negative effects. Furthermore, medications can be designed into NPs to be released over a longer period and in a controlled manner, resulting in sustained therapeutic activity and an overall decrease in treatment frequency [152,157].

Many studies have investigated different types of NPs for TDD in periodontal therapy.

Steckiewicz et al. [159] evaluated the efficacy of AgNPs as drug delivery vehicles for metronidazole (MET) and CHX in periodontal treatment. AgNPs showed anti-inflammatory characteristics, were non-toxic to mammalian cells at low concentrations, and had synergistic antibacterial actions with the medications. Furthermore, when internalized in eukaryotic cells, they did not cause any structural alterations. Constantin et al. [160] created biocomposite PVA/chitosan films with ibuprofen and AgNPs for periodontal therapy. The system exhibited superior antibacterial action against pathogens, particularly *S. aureus*, and demonstrated biocompatibility with human dermal fibroblast cells, making it a promising alternative for periodontal therapy.

Tong et al. [161] studied the effect of ferromagnetic NPs loaded with minocycline for eliminating periodontal biofilm in rats. The system effectively delivered antibacterial drugs to target periodontal biofilms. When paired with a magnetic field, the minocycline-loaded NPs showed a decrease in inflammatory cell infiltration in the gingival tissue of treated rats, confirming the efficacy of treatment in a rat periodontitis model. Furthermore, pro-inflammatory markers showed a significant decrease in mRNA and protein levels, suggesting that this treatment effectively relieves periodontal inflammation.

Propolis NPs administered subgingivally were assessed in a recent study by Sahu et al. [162] to treat periodontal pockets. Comparing the results to those from areas treated with saline, the propolis system had a better outcome when addressing specific parameters, such as the plaque index, gingival index, or relative attachment loss. The study also showed that the propolis NP group had substantially better gingival indices at one and three months. Further research is needed to explore higher concentrations, increased administration, and mechanisms of action for addressing its safety in human subjects.

A clinical trial study evaluated the effectiveness of AgNP gel periodontitis treatment. It was compared to commercially available tetracycline gel and scaling and root planing alone. Three different groups received one of the treatments. Group A (treated with AgNP gel) showed a considerable decrease from baseline in the probing pocket depth, clinical attachment level, and plaque and gingival indices. Colony forming units (CFUs) significantly decreased after microbiological evaluation, indicating the antibacterial activity of AgNPs. Compared to Group C (root planing), Group A and Group B (tetracycline gel) showed notable improvements in several clinical indicators. However, it is difficult to conclude which treatment was better in this trial without data from a direct comparison between Group A and Group B [163].

Other examples of studies for TDD are summarized in Table 4.

In summary, nanoformulations show great promise for TDD in periodontal therapy. We can enhance treatment outcomes by using different NPs with significant therapeutic effects, such as silver and propolis NPs while minimizing side effects. More research in this area is needed to optimize these innovative approaches and improve periodontal care.

Table 4. Summary of studies on NPs for TDD in periodontal therapy and their findings.

Nanomaterial	Effect	Refs.
Chitosan NPs loaded with atorvastatin (AS) and doxycycline (DOX)	AS showed a sustained release over 9 days, while DS had a quicker release, stabilizing around 5 days AS/DS chitosan NPs were more effective against *Staphylococcus aureus* compared to *Escherichia coli* The system was non-cytotoxic	[164]
Ce-doped mesoporous calcium silicate nanopowders loaded with artemisinin (ART)	Hemocompatible and promoted cell proliferation of human periodontal ligament fibroblasts (hPDLFs) Protected cells from oxidative damage by neutralizing ROS	[165]
Polydopamine (PDA)-functionalized MS NPs loaded with minocycline hydrochloride (MH)	PDA and MH shifted macrophages from a pro-inflammatory (M1) to an anti-inflammatory (M2) state Reduced bone loss Prevented inflammation	[166]
Nanocomposite hydrogel (NCHG) loaded with CHX and metronidazole	The NCHG released metronidazole within 12 h and CHX over more than 7 days, with the release strongly dependent on pH Biocompatible Targeted bacteria in acidic, inflamed environments	[167]
Protease-loaded CuS NPs	Eliminated bacterial biofilms, particularly *Fusobacterium nucleatum* Biocompatible Reduced bone resorption and inflammation	[168]
Metformin hydrochloride-loaded PLGA NPs	Controlled drug release, sustained metformin's plasma concentration for over 72 h, and required a lower dosage Slower elimination rate, resulting in a more efficient and long-lasting treatment option	[169]
Cefixime-loaded NPs within chitosan films	Sustained drug release Better antimicrobial activity against periodontal bacteria than conventional mouthwash Maintained their drug release profile and structural integrity over six months	[170]
Human serum albumin (HSA)-crosslinked manganese-doped Prussian blue NPs (HSA-MDSPB NPs)	Antioxidant, anti-inflammatory, and osteogenic properties Reduced inflammation, oxidative stress, and bone loss in periodontal tissues Promoted macrophage polarization toward an anti-inflammatory state	[171]

5.2. Nanoparticles in Regenerative Periodontal Treatment

When considering regenerative periodontal treatment, most conventional treatments rely on allogenic transplants from cadavers or living donors. Yet, they hold various disadvantages, such as the potential for disease transmission, the risk of immunological rejection, the scarcity of donor tissue, and invasive procedures. Furthermore, there is a chance that these methods will not always produce the best tissue integration and long-term stability [172,173]. Nanotechnology can improve regenerative periodontal treatment since biomaterials can be used as an alternative. The mechanical strength, biocompatibility, and bioactivity of biomaterials used in tissue engineering can be improved by adding

NPs to them. Additionally, growth factors, medicines, and other bioactive substances can be transported by NPs, allowing for controlled release and encouraging tissue regeneration [172,174].

Many studies assessed the benefits of using NPs in periodontal regeneration. Takallu et al. [175] synthesized antibacterial collagen membranes for periodontal regeneration with different concentrations of AgNP, ranging from 0.5% to 3%. Collagen/Ag 2% and 3% membranes outperformed other formulations in the evaluated samples' antibacterial efficacy against Gram-positive and Gram-negative microorganisms. Compared to collagen/Ag 3%, collagen/Ag 2% showed greater cytocompatibility with mammalian cells, suggesting a lower risk of toxicity. This emphasizes AgNP's potential as a periodontitis therapy option that shows promise and has strong antibacterial properties without causing considerable damage to healthy cells. Ren et al. [176] have investigated the effect of CeO_2 NPs on human periodontal ligament stem cells (hPDLSCs). CeO_2 NPs exhibited excellent levels of biocompatibility and stimulated cell proliferation. They also improved the development of hPDLSCs into osteogenesis. Electrospun fibrous membranes containing CeO_2 NPs demonstrated the controlled release of CeO_2 NPs. These composite membranes stimulated the development of new bone in rat models with cranial defects, indicating their potential for periodontal bone regeneration.

Other studies have demonstrated the potential of nano-hydroxyapatite (nHA) in regenerative periodontal therapy since it promotes mineralized tissue development by increasing osteogenic differentiation. Osteoblasts and periodontal ligament cells are able to adhere to and proliferate more easily because of the large surface area that their nanostructure offers them. Additionally, the distribution and effectiveness of bioactive compounds like growth factors and antibiotics in periodontal therapy can be improved by using nano-hydroxyapatite particles as carriers. Better treatment outcomes can be achieved by using this power to release therapeutic substances in a targeted, controlled manner [177–180]. Research has also demonstrated the antibacterial characteristics of nano-hydroxyapatite, which encourage tissue regeneration and prevent infection by decreasing microbial colonization in periodontal defects [87,181].

Through their unique properties, NPs offer enhanced bone regeneration, controlled drug delivery, and antibacterial effects, making them valuable assets in periodontal therapy.

6. Safety and Toxicity Considerations

Nanomaterials' unique characteristics make them extremely promising for use in dental applications. Nonetheless, concerns about their toxicity continue to exist, which raises significant questions about their safety in dentistry procedures [182]. The possibility of NP release and subsequent systemic distribution within the body is one of the main causes of concern. Although a number of nanomaterials have demonstrated encouraging outcomes in vitro, very little is known about how they behave in a complex oral environment. Research indicates that some NPs may produce cytotoxic effects, which can further affect human health over time [183]. A few examples of NPs and their toxicity are presented in Table 5. Studies have shown that NPs (such as AgNPs) can induce cytotoxic effects on various cell types, including oral epithelial cells and fibroblasts [184,185]. AgNPs' elevated reactivity is further attributed to their small size and high surface-area-to-volume ratio, which may cause oxidative stress, DNA damage, and inflammatory responses in oral tissues [186].

Table 5. Potential toxicity of various NPs.

Nanomaterial	Potential Toxic Effect	Refs.
AgNPs	DNA damage, oxidative stress, inflammatory response	[186,187]
ZnO	DNA damage, triggers inflammatory response, oxidative stress, ROS generation	[188,189]

Table 5. *Cont.*

Nanomaterial	Potential Toxic Effect	Refs.
ZrO_2	Tissue accumulation, gene alterations, oxidative stress	[190]
TiO_2	Tissue accumulation, ROS generation, oxidative stress, environmental damage	[190–192]
SiO_2	Genotoxicity, tissue accumulation, ROS generation, aggregation, oxidative stress	[193–195]

The NP's cytotoxicity may be concentration and time-dependent, with lower concentrations being considered safe. Research has demonstrated that higher NP concentrations can induce oxidative stress and apoptosis in immune system cells, potentially triggering inflammatory responses [196–198]. A study by Wang et al. [197] demonstrated that high NP concentrations can cause blood–brain barrier penetration, disrupting the balance and allowing pathogens or other harmful substances to enter the brain. This can lead to inflammation, neurotoxicity, and the development of serious neurological disorders. Chen et al. [199] demonstrated that ZnO NPs could have toxic effects on human gingival cells at higher concentrations. It was observed that the ZnO NPs inhibited cell proliferation, destroyed the integrity of cell membranes, and induced oxidative stress and apoptosis. Youssef et al. [200] also demonstrated that the cytotoxicity of NPs in dental applications (in this case, AgNPs) is dose and size-dependent. Higher doses and smaller NP sizes (<20 nm diameter) led to cytotoxicity and apoptosis. The authors suggest that these properties need to be carefully considered before using AgNPs in dental restorative materials. Ullah et al. [201] investigated the potentially harmful effects of calcium NPs on different tissues, including teeth. It was conducted on albino rats, and the researchers discovered that the NPs caused severe alterations to the dental pulp, root, and periodontal ligaments. It also caused inflammation. These findings were mostly found at higher concentrations, while the toxic effects were mild at lower concentrations. Solanki et al. [202] evaluated the cytotoxicity of AuNP mouthwash in vitro on brine shrimps. At low concentrations, no toxic effects were observed. However, at higher concentrations, the toxic effects were from mild to severe, even resulting in death. This indicates the importance of finding the appropriate concentrations of NPs when used in dental or other biomedical applications. Khanna et al.'s [203] study also supports this fact. During this study, the researchers investigated the effects of rosemary- and ginger-mediated titanium NP dental varnish. They found that the cytotoxicity of titanium NPs increased as the NPs' concentration increased. Another factor to consider is the exposure time since it has been found that longer times of exposure can cause the bioaccumulation of the NPs in the tissues, which can cause tissue damage and inflammation [196,204]. This was demonstrated through a study conducted by Kakakhel et al. [204] in vivo on fish. It was discovered that long-term exposure to AgNPs led to NPs' accumulation in certain tissues and caused harmful effects. The highest concentrations caused necrosis and even mortality, highlighting again the importance of choosing the appropriate concentration when using NPs in biomedical applications. Mohammadpour et al. [205] also observed that NPs could accumulate in certain organs (such as the liver and spleen), when a longer time of exposure was used and higher concentrations were administered.

A study by Bengalli et al. [206] on CuO and ZnO NP-coated textiles sheds light on the potential toxicity of NPs in dental applications. If these NPs cause harmful skin reactions, dental products containing them may also be toxic to oral tissues. For example, the high metal ion release from dental NPs, particularly in acidic oral environments, may substantially influence the viability of oral epithelial cells, comparable to the effects seen on keratinocytes. Moreover, the study's epidermal tissue's altered cytoskeleton and elevated inflammatory response may be similar to how NPs affect oral tissues, resulting in tissue damage and oral inflammation.

Nanomaterials offer immense potential for dental applications, yet concerns about their safety persist. There are serious worries over the systemic consequences of NPs due to their possible release and distribution within the body. Further research is necessary to completely understand the safety of various nanomaterials since their behavior in the oral environment is still not understood.

7. Conclusions

In conclusion, applying nanomaterials in dentistry indicates an evolution in dental regeneration, restoration, and care. These cutting-edge materials have the potential to completely transform many dental practice areas, including preventative dentistry and enhanced methods of treatment, due to nanoscale engineering.

The potential of NPs to improve the characteristics of conventional dental materials is one of their most important contributions. When NPs are added to dental restorative materials, the resulting nanocomposites have enhanced wear resistance, mechanical strength, and antibacterial qualities. This results in long-term dental restorations that have a lower chance of failing or developing secondary caries, eventually improving patient outcomes and satisfaction. Moreover, TDD systems created specifically for the challenges associated with oral healthcare were made possible by nanotechnology. Therapeutic substances can be precisely and continuously released by encapsulating them in NPs, which maximizes their therapeutic effects while reducing negative effects. This approach may be used to treat diseases like periodontal disease, dental caries, and oral infections.

Nanomaterials also offer opportunities for tissue engineering and regeneration. These can help the growth and differentiation of dental tissues, including periodontal ligaments, pulp, and bone. However, there are obstacles to the broad use of NPs in dentistry, just like there are with any new technology. The main concerns in NPs' interactions with oral tissues and systemic consequences include biocompatibility and safety. Further research on the nanomaterials used in dentistry should focus on long-term biocompatibility, fabrication optimization, and environmental impact.

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References

1. Kandavalli, S.R.; Wang, Q.; Ebrahimi, M.; Gode, C.; Djavanroodi, F.; Attarilar, S.; Liu, S. A brief review on the evolution of metallic dental implants: History, design, and application. *Front. Mater.* **2021**, *8*, 646383. [CrossRef]
2. Leek, F.F. The Practice of Dentistry in Ancient Egypt. *J. Egypt. Archaeol.* **1967**, *53*, 51–58. [CrossRef] [PubMed]
3. Hyson, J.M., Jr. Amalgam: Its history and perils. *J. Calif. Dent. Assoc.* **2006**, *34*, 215–229. [CrossRef] [PubMed]
4. Marin, E. History of dental biomaterials: Biocompatibility, durability and still open challenges. *Heritage Sci.* **2023**, *11*, 207. [CrossRef]
5. Rezaie, H.R.; Rizi, H.B.; Khamseh, M.M.R.; Öchsner, A. *A Review on Dental Materials*; Springer: New York, NY, USA, 2020.
6. Burke, F.T.; Mackenzie, L.; Sands, P. Dental materials—What goes where? class I and II cavities. *Dent. Updat.* **2013**, *40*, 260–274. [CrossRef]
7. Gajanan, K.; Tijare, S. Applications of nanomaterials. *Mater. Today Proc.* **2018**, *5*, 1093–1096. [CrossRef]
8. Malik, S.; Waheed, Y. Emerging Applications of Nanotechnology in Dentistry. *Dent. J.* **2023**, *11*, 266. [CrossRef]
9. Glowacka-Sobotta, A.; Ziental, D.; Czarczynska-Goslinska, B.; Michalak, M.; Wysocki, M.; Güzel, E.; Sobotta, L. Nanotechnology for Dentistry: Prospects and Applications. *Nanomaterials* **2023**, *13*, 2130. [CrossRef] [PubMed]
10. Sharma, H.; Verma, S.; Chevvuri, R. Nanotechnology in dentistry: Unleashing the hidden gems. *J. Indian Soc. Periodontol.* **2018**, *22*, 196–200. [CrossRef]
11. Sreenivasalu, P.K.P.; Dora, C.P.; Swami, R.; Jasthi, V.C.; Shiroorkar, P.N.; Nagaraja, S.; Asdaq, S.M.B.; Anwer, K. Nanomaterials in Dentistry: Current Applications and Future Scope. *Nanomaterials* **2022**, *12*, 1676. [CrossRef]

12. Besinis, A.; De Peralta, T.; Tredwin, C.J.; Handy, R.D. Review of nanomaterials in dentistry: Interactions with the oral microenvironment, clinical applications, hazards, and benefits. *ACS Nano* **2015**, *9*, 2255–2289. [CrossRef] [PubMed]
13. Zafar, M.S.; Alnazzawi, A.A.; Alrahabi, M.; Fareed, M.A.; Najeeb, S.; Khurshid, Z. Nanotechnology and nanomaterials in dentistry. In *Advanced Dental Biomaterials*; Elsevier: Amsterdam, The Netherlands, 2019; pp. 477–505.
14. Mallineni, S.K.; Sakhamuri, S.; Kotha, S.L.; AlAsmari, A.R.G.M.; AlJefri, G.H.; Almotawah, F.N.; Mallineni, S.; Sajja, R. Silver Nanoparticles in Dental Applications: A Descriptive Review. *Bioengineering* **2023**, *10*, 327. [CrossRef]
15. Bolenwar, A.; Reche, A.; Dhamdhere, N.; Rathi, S. Applications of Silver Nanoparticles in Dentistry. *Cureus* **2023**, *15*, e44090. [CrossRef] [PubMed]
16. Agusnar, H.; Yunita, F.; Yuandani, Y.; Utami, N.M. Synthesis and characterization of silver nanoparticle chitosan as toothpaste with antimicrobial activity. In *AIP Conference Proceedings*; AIP Publishing: Medan, Indonesia, 2023; Volume 2626, p. 030018.
17. Nie, P.; Zhao, Y.; Xu, H. Synthesis, applications, toxicity and toxicity mechanisms of silver nanoparticles: A review. *Ecotoxicol. Environ. Saf.* **2023**, *253*, 114636. [CrossRef]
18. Kaushik, A.; Gola, D.; Raghav, J.; Gupta, D.; Kumar, A.; Agarwal, M.; Chauhan, N.; Srivastava, S.K.; Tyagi, P.K. Synthesis of silver nanoparticles using egg white: Dye degradation and antimicrobial potential. *Biointerface Res. Appl. Chem.* **2022**, *12*, 2361–2372. [CrossRef]
19. Hsu, C.-Y.; Mahmoud, Z.H.; Abdullaev, S.; Ali, F.K.; Naeem, Y.A.; Mizher, R.M.; Karim, M.M.; Abdulwahid, A.S.; Ahmadi, Z.; Habibzadeh, S.; et al. Nano titanium oxide (nano-TiO_2): A review of synthesis methods, properties, and applications. *Case Stud. Chem. Environ. Eng.* **2024**, *9*, 100626. [CrossRef]
20. Leynen, N.; Tytgat, J.; Bijnens, K.; Jaenen, V.; Verleysen, E.; Artois, T.; Van Belleghem, F.; Saenen, N.; Smeets, K. Assessing the in vivo toxicity of titanium dioxide nanoparticles in Schmidtea mediterranea: Uptake pathways and (neuro)developmental outcomes. *Aquat. Toxicol.* **2024**, *270*, 106895. [CrossRef]
21. Abdulhameed, E.A.; Al-Rawi, N.H.; Omar, M.; Khalifa, N.; Samsudin, A.R. Titanium dioxide dental implants surfaces related oxidative stress in bone remodeling: A systematic review. *PeerJ* **2022**, *10*, e12951. [CrossRef]
22. El-Khatib, E.M.; Ali, N.F.; Nassar, S.H.; El-Shemy, N.S. Functionalization of natural fibers properties by using TiO_2 nanoparticles to improve its antimicrobial activity. *Biointerface Res. Appl. Chem.* **2022**, *12*, 4177–4191. [CrossRef]
23. Pushpalatha, C.; Suresh, J.; Gayathri, V.; Sowmya, S.; Augustine, D.; Alamoudi, A.; Zidane, B.; Albar, N.H.M.; Patil, S. Zinc Oxide Nanoparticles: A Review on Its Applications in Dentistry. *Front. Bioeng. Biotechnol.* **2022**, *10*, 917990. [CrossRef]
24. Barma, M.D.; Muthupandiyan, I.; Samuel, S.R.; Amaechi, B.T. Inhibition of Streptococcus mutans, antioxidant property and cytotoxicity of novel nano-zinc oxide varnish. *Arch. Oral Biol.* **2021**, *126*, 105132. [CrossRef] [PubMed]
25. Tiwari, A.K.; Jha, S.; Singh, A.K.; Mishra, S.K.; Pathak, A.K.; Ojha, R.P.; Yadav, R.S.; Dikshit, A. Innovative Investigation of Zinc Oxide Nanoparticles Used in Dentistry. *Crystals* **2022**, *12*, 1063. [CrossRef]
26. El Shahawi, A.M. Incorporation of zinc oxide nanoparticles and it's antibacterial effect on toothpaste. *Bull. Natl. Res. Cent.* **2023**, *47*, 2. [CrossRef]
27. Florea, D.A.; Mocanu, A.; Pop, L.C.; Tomoaia, G.; Dobrota, C.-T.; Varhelyi, C., Jr.; Tomoaia-Cotisel, M. Remineralization of Tooth Enamel With Hydroxyapatite Nanoparticles: An In Vitro Study. *Stud. Univ. Babes-Bolyai* **2023**, *68*, 99–113. [CrossRef]
28. Akhtar, K.; Pervez, C.; Zubair, N.; Khalid, H. Calcium hydroxyapatite nanoparticles as a reinforcement filler in dental resin nanocomposite. *J. Mater. Sci. Mater. Med.* **2021**, *32*, 129. [CrossRef] [PubMed]
29. Balhuc, S.; Campian, R.; Labunet, A.; Negucioiu, M.; Buduru, S.; Kui, A. Dental applications of systems based on hydroxyapatite nanoparticles—An evidence-based update. *Crystals* **2021**, *11*, 674. [CrossRef]
30. Abifarin, F.B.; Musa, Z.; Abifarin, J.K. mechanical processing of hydroxyapatite through sintering and multi-objective optimization technique for biomedical application. *MRS Adv.* **2023**, *8*, 532–537. [CrossRef]
31. Yazdanian, M.; Rostamzadeh, P.; Rahbar, M.; Alam, M.; Abbasi, K.; Tahmasebi, E.; Tebyaniyan, H.; Ranjbar, R.; Seifalian, A.; Yazdanian, A. The potential application of green-synthesized metal nanoparticles in dentistry: A comprehensive review. *Bioinorg. Chem. Appl.* **2022**, *2022*, 2311910. [CrossRef]
32. Jadhav, K.; Hr, R.; Deshpande, S.; Jagwani, S.; Dhamecha, D.; Jalalpure, S.; Subburayan, K.; Baheti, D. Phytosynthesis of gold nanoparticles: Characterization, biocompatibility, and evaluation of its osteoinductive potential for application in implant dentistry. *Mater. Sci. Eng. C* **2018**, *93*, 664–670. [CrossRef] [PubMed]
33. Sani, A.; Cao, C.; Cui, D. Toxicity of gold nanoparticles (AuNPs): A review. *Biochem. Biophys. Rep.* **2021**, *26*, 100991. [CrossRef] [PubMed]
34. Huang, Y.; Li, P.; Zhao, R.; Zhao, L.; Liu, J.; Peng, S.; Fu, X.; Wang, X.; Luo, R.; Wang, R.; et al. Silica nanoparticles: Biomedical applications and toxicity. *Biomed. Pharmacother.* **2022**, *151*, 113053. [CrossRef]
35. Pavanello, L.; Cortês, I.T.; de Carvalho, R.D.P.; Picolo, M.Z.D.; Cavalli, V.; Silva, L.T.S.; Boaro, L.C.C.; Prokopovich, P.; Cogo-Müller, K. Physicochemical and biological properties of dental materials and formulations with silica nanoparticles: A narrative review. *Dent. Mater.* **2024**. [CrossRef] [PubMed]
36. Nikolaidis, A.K.; Koulaouzidou, E.A.; Gogos, C.; Achilias, D.S. Synthesis of Novel Dental Nanocomposite Resins by Incorporating Polymerizable, Quaternary Ammonium Silane-Modified Silica Nanoparticles. *Polymers* **2021**, *13*, 1682. [CrossRef] [PubMed]
37. Rojas, B.; Soto, N.; Villalba, M.; Bello-Toledo, H.; Meléndrez-Castro, M.; Sánchez-Sanhueza, G. Antibacterial Activity of Copper Nanoparticles (CuNPs) against a Resistant Calcium Hydroxide Multispecies Endodontic Biofilm. *Nanomaterials* **2021**, *11*, 2254. [CrossRef]

38. Maawadh, A.; AlDeeb, L.; Almohareb, T.; Alahdal, K.; Alshamrani, A.S.; Alrahlah, A. Copper Oxide Nanoparticles Loaded in Adhesive to Carious Dentin. An In Vitro Study Assessing μTBS, Degree of Conversion, EDX, and SEM. *Sci. Adv. Mater.* **2024**, *16*, 1109–1115. [CrossRef]
39. Xu, V.W.; Nizami, M.Z.I.; Yin, I.X.; Yu, O.Y.; Lung, C.Y.K.; Chu, C.H. Application of Copper Nanoparticles in Dentistry. *Nanomaterials* **2022**, *12*, 805. [CrossRef] [PubMed]
40. Hedberg, J.; Karlsson, H.L.; Hedberg, Y.; Blomberg, E.; Wallinder, I.O. The importance of extracellular speciation and corrosion of copper nanoparticles on lung cell membrane integrity. *Colloids Surfaces B Biointerfaces* **2016**, *141*, 291–300. [CrossRef]
41. Higino, T.; França, R. Drug-delivery nanoparticles for bone-tissue and dental applications. *Biomed. Phys. Eng. Express* **2022**, *8*, 042001. [CrossRef]
42. Yudaev, P.; Chuev, V.; Klyukin, B.; Kuskov, A.; Mezhuev, Y.; Chistyakov, E. Polymeric Dental Nanomaterials: Antimicrobial Action. *Polymers* **2022**, *14*, 864. [CrossRef] [PubMed]
43. Toledano-Osorio, M.; Osorio, R.; Aguilera, F.S.; Medina-Castillo, A.L.; Toledano, M.; Osorio, E.; Acosta, S.; Chen, R.; Aparicio, C. Polymeric nanoparticles protect the resin-dentin bonded interface from cariogenic biofilm degradation. *Acta Biomater.* **2020**, *111*, 316–326. [CrossRef]
44. Prabha, A.S.; Dorothy, R.; Jancirani, S.; Rajendran, S.; Singh, G.; Kumaran, S.S. Recent advances in the study of toxicity of polymer-based nanomaterials. *Nanotoxicity* **2020**, 143–165.
45. Montoya, C.; Roldan, L.; Yu, M.; Valliani, S.; Ta, C.; Yang, M.; Orrego, S. Smart dental materials for antimicrobial applications. *Bioact. Mater.* **2023**, *24*, 1–19. [CrossRef] [PubMed]
46. Yu, Y.; Li, X. Current Application of Magnetic Materials in the Dental Field. *Magnetochemistry* **2024**, *10*, 46. [CrossRef]
47. Vakili-Ghartavol, R.; Momtazi-Borojeni, A.A.; Vakili-Ghartavol, Z.; Aiyelabegan, H.T.; Jaafari, M.R.; Rezayat, S.M.; Bidgoli, S.A. Toxicity assessment of superparamagnetic iron oxide nanoparticles in different tissues. *Artif. Cells Nanomed. Biotechnol.* **2020**, *48*, 443–451. [CrossRef] [PubMed]
48. Malhotra, N.; Lee, J.-S.; Liman, R.A.D.; Ruallo, J.M.S.; Villaflores, O.B.; Ger, T.-R.; Hsiao, C.-D. Potential toxicity of iron oxide magnetic nanoparticles: A review. *Molecules* **2020**, *25*, 3159. [CrossRef] [PubMed]
49. Mann, R.; Mitsidis, D.; Xie, Z.; McNeilly, O.; Ng, Y.H.; Amal, R.; Gunawan, C. Antibacterial activity of reduced graphene oxide. *J. Nanomater.* **2021**, *2021*, 9941577. [CrossRef]
50. Liu, Y.; Wen, J.; Gao, Y.; Li, T.; Wang, H.; Yan, H.; Niu, B.; Guo, R. Antibacterial graphene oxide coatings on polymer substrate. *Appl. Surf. Sci.* **2018**, *436*, 624–630. [CrossRef]
51. Bregnocchi, A.; Zanni, E.; Uccelletti, D.; Marra, F.; Cavallini, D.; De Angelis, F.; De Bellis, G.; Bossù, M.; Ierardo, G.; Polimeni, A.; et al. Graphene-based dental adhesive with anti-biofilm activity. *J. Nanobiotechnology* **2017**, *15*, 89. [CrossRef] [PubMed]
52. Rhazouani, A.; Gamrani, H.; El Achaby, M.; Aziz, K.; Gebrati, L.; Uddin, M.S.; Aziz, F. Synthesis and toxicity of graphene oxide nanoparticles: A literature review of in vitro and in vivo studies. *BioMed Res. Int.* **2021**, *2021*, 5518999. [CrossRef]
53. Abedi, M.; Ghasemi, Y.; Nemati, M.M. Nanotechnology in toothpaste: Fundamentals, trends, and safety. *Heliyon* **2024**, *10*, e24949. [CrossRef]
54. Loesche, W.J. *Microbiology of Dental Decay and Periodontal Disease. Medical Microbiology*, 4th ed.; Wiley: Hoboken, NJ, USA, 1996.
55. Rezaei, T.; Mehramouz, B.; Gholizadeh, P.; Yousefi, L.; Ganbarov, K.; Ghotaslou, R.; Taghizadeh, S.; Kafil, H.S. Factors associated with Streptococcus mutans pathogenicity in the oral cavity. *Biointerface Res. Appl. Chem.* **2023**, *13*, 368.
56. Carrouel, F.; Viennot, S.; Ottolenghi, L.; Gaillard, C.; Bourgeois, D. Nanoparticles as Anti-Microbial, Anti-Inflammatory, and Remineralizing Agents in Oral Care Cosmetics: A Review of the Current Situation. *Nanomaterials* **2020**, *10*, 140. [CrossRef] [PubMed]
57. Abadi, M.F.; Mehrabian, S.; Asghari, B.; Namvar, A.E.; Ezzatifar, F.; Lari, A.R. Silver nanoparticles as active ingredient used for alcohol-free mouthwash. *GMS Hyg. Infect. Control* **2013**, *8*, Doc05. [CrossRef]
58. Ahmed, O.A.K.; Sibuyi, N.R.S.; Fadaka, A.O.; Maboza, E.; Olivier, A.; Madiehe, A.M.; Meyer, M.; Geerts, G. Prospects of Using Gum Arabic Silver Nanoparticles in Toothpaste to Prevent Dental Caries. *Pharmaceutics* **2023**, *15*, 871. [CrossRef] [PubMed]
59. Bruna, T.; Maldonado-Bravo, F.; Jara, P.; Caro, N. Silver Nanoparticles and Their Antibacterial Applications. *Int. J. Mol. Sci.* **2021**, *22*, 7202. [CrossRef] [PubMed]
60. Saliminasab, M.; Jabbari, H.; Farahmand, H.; Asadi, M.; Soleimani, M.; Fathi, A. Study of antibacterial performance of synthesized silver nanoparticles on Streptococcus mutans bacteria. *Nanomed. Res. J.* **2022**, *7*, 391–396. [CrossRef]
61. Sathiyaraj, S.; Suriyakala, G.; Gandhi, A.D.; Babujanarthanam, R.; Almaary, K.S.; Chen, T.-W.; Kaviyarasu, K. Biosynthesis, characterization, and antibacterial activity of gold nanoparticles. *J. Infect. Public Health* **2021**, *14*, 1842–1847. [CrossRef]
62. Al-Fahham, B.M.; Mohamed, R.A.; Al-Talqani, J.M.T.; Fahad, A.H.; Haider, J. Evaluating Antimicrobial Effectiveness of Gold Nanoparticles against Streptococcus oralis. *Int. J. Dent.* **2023**, *2023*, 9935556. [CrossRef]
63. Punniyakotti, P.; Panneerselvam, P.; Perumal, D.; Aruliah, R.; Angaiah, S. Anti-bacterial and anti-biofilm properties of green synthesized copper nanoparticles from Cardiospermum halicacabum leaf extract. *Bioprocess Biosyst. Eng.* **2020**, *43*, 1649–1657. [CrossRef]
64. Ramyadevi, J.; Jeyasubramanian, K.; Marikani, A.; Rajakumar, G.; Rahuman, A.A. Synthesis and antimicrobial activity of copper nanoparticles. *Mater. Lett.* **2012**, *71*, 114–116. [CrossRef]
65. Agarwal, H.; Shanmugam, V. A review on anti-inflammatory activity of green synthesized zinc oxide nanoparticle: Mechanism-based approach. *Bioorganic Chem.* **2020**, *94*, 103423. [CrossRef]

66. Matsumoto-Nakano, M. Role of *Streptococcus mutans* surface proteins for biofilm formation. *Jpn. Dent. Sci. Rev.* **2018**, *54*, 22–29. [CrossRef] [PubMed]
67. Emad, M.; Salama, K. A comparison of the effects of lemon peel-silver nanoparticles versus brand toothpastes and mouthwashes on staphylococcus spp. isolated from teeth caries. *Iraqi J. Sci.* **2020**, *61*, 1894–1901. [CrossRef]
68. Junevičius, J.; Žilinskas, J.; Česaitis, K.; Česaitienė, G.; Gleiznys, D.; Maželienė, Ž. Antimicrobial activity of silver and gold in toothpastes: A comparative analysis. *Stomatologija* **2015**, *17*, 9–12.
69. O'hagan-Wong, K.; Enax, J.; Meyer, F.; Ganss, B. The use of hydroxyapatite toothpaste to prevent dental caries. *Odontology* **2021**, *110*, 223–230. [CrossRef] [PubMed]
70. Shang, R.; Kaisarly, D.; Kunzelmann, K.-H. Tooth whitening with an experimental toothpaste containing hydroxyapatite nanoparticles. *BMC Oral Health* **2022**, *22*, 331. [CrossRef] [PubMed]
71. Shang, R.; Kunzelmann, K.-H. Biomimetic tooth-whitening effect of hydroxyapatite-containing mouthrinses after long-term simulated oral rinsing. *Am. J. Dent.* **2021**, *34*, 307–312. [PubMed]
72. Florea, A.-D.; Dobrota, C.T.; Carpa, R.; Racz, C.-P.; Tomoaia, G.; Mocanu, A.; Avram, A.; Soritau, O.; Pop, L.C.; Tomoaia-Cotisel, M. Optimization of Functional Toothpaste Formulation Containing Nano-Hydroxyapatite and Birch Extract for Daily Oral Care. *Materials* **2023**, *16*, 7143. [CrossRef] [PubMed]
73. Ionescu, A.C.; Cazzaniga, G.; Ottobelli, M.; Garcia-Godoy, F.; Brambilla, E. Substituted Nano-Hydroxyapatite Toothpastes Reduce Biofilm Formation on Enamel and Resin-Based Composite Surfaces. *J. Funct. Biomater.* **2020**, *11*, 36. [CrossRef] [PubMed]
74. Amaechi, B.T.; Lemke, K.C.; Saha, S.; Luong, M.N.; Gelfond, J. Clinical efficacy of nanohydroxyapatite-containing toothpaste at relieving dentin hypersensitivity: An 8 weeks randomized control trial. *BDJ Open* **2021**, *7*, 23. [CrossRef] [PubMed]
75. Barma, M.D.; Kannan, S.D.; Indiran, M.A.; Rajeshkumar, S.; Kumar, R.P. Antibacterial Activity of Mouthwash Incorporated with Silica Nanoparticles against S. aureus, S. mutans, E. faecalis: An in-vitro Study. *J. Pharm. Res. Int.* **2020**, *32*, 25–33. [CrossRef]
76. Wang, S.; Fang, L.; Zhou, H.; Wang, M.; Zheng, H.; Wang, Y.; Weir, M.D.; Masri, R.; Oates, T.W.; Cheng, L.; et al. Silica nanoparticles containing nano-silver and chlorhexidine respond to pH to suppress biofilm acids and modulate biofilms toward a non-cariogenic composition. *Dent. Mater.* **2024**, *40*, 179–189. [CrossRef]
77. Aspinall, S.R.; Khutoryanskiy, V.V. Surface Modification of Silica Particles with Adhesive Functional Groups or Their Coating with Chitosan to Improve the Retention of Toothpastes in the Mouth. *Langmuir* **2023**, *39*, 1677–1685. [CrossRef]
78. Parnia, F.; Yazdani, J.; Javaherzadeh, V.; Dizaj, S.M. Overview of nanoparticle coating of dental implants for enhanced osseointegration and antimicrobial purposes. *J. Pharm. Pharm. Sci.* **2017**, *20*, 148–160. [CrossRef] [PubMed]
79. Rasouli, R.; Barhoum, A.; Uludag, H. A review of nanostructured surfaces and materials for dental implants: Surface coating, patterning and functionalization for improved performance. *Biomater. Sci.* **2018**, *6*, 1312–1338. [CrossRef]
80. Memarzadeh, K.; Sharili, A.S.; Huang, J.; Rawlinson, S.C.; Allaker, R.P. Nanoparticulate zinc oxide as a coating material for orthopedic and dental implants. *J. Biomed. Mater. Res. A* **2015**, *103*, 981–989. [CrossRef] [PubMed]
81. Li, N.; Liu, Z.; Liu, G.; Wang, Z.; Guo, X.; Guo, C.; Han, J. TiO_2 Nanocoatings with Controllable Crystal Type and Nanoscale Topography on Zirconia Implants to Accelerate Bone Formation. *Bioinorg. Chem. Appl.* **2022**, *2022*, 8650659. [CrossRef]
82. Hammad, S.M.; El-Wassefy, N.A.; Shamaa, M.S.; Fathy, A. Evaluation of zinc-oxide nanocoating on the characteristics and antibacterial behavior of nickel-titanium alloy. *Dent. Press J. Orthod.* **2020**, *25*, 51–58. [CrossRef] [PubMed]
83. Zhang, Y.; Gulati, K.; Li, Z.; Di, P.; Liu, Y. Dental implant nano-engineering: Advances, limitations and future directions. *Nanomaterials* **2021**, *11*, 2489. [CrossRef]
84. Besinis, A.; Hadi, S.D.; Le, H.R.; Tredwin, C.; Handy, R.D. Antibacterial activity and biofilm inhibition by surface modified titanium alloy medical implants following application of silver, titanium dioxide and hydroxyapatite nanocoatings. *Nanotoxicology* **2017**, *11*, 327–338. [CrossRef] [PubMed]
85. Pang, K.; Seo, Y.-K.; Lee, J.-H. Effects of the combination of bone morphogenetic protein-2 and nano-hydroxyapatite on the osseointegration of dental implants. *J. Korean Assoc. Oral Maxillofac. Surg.* **2021**, *47*, 454–464. [CrossRef] [PubMed]
86. de Oliveira, P.G.F.P.; de Melo Soares, M.S.; Silveira e Souza, A.M.M.; Taba Jr, M.; Palioto, D.B.; Messora, M.R.; Ghiraldini, B.; Nunes, F.A.d.S.; de Souza, S.L.S. Influence of nano-hydroxyapatite coating implants on gene expression of osteogenic markers and micro-CT parameters. An in vivo study in diabetic rats. *J. Biomed. Mater. Res. Part A* **2021**, *109*, 682–694. [CrossRef] [PubMed]
87. Lamkhao, S.; Phaya, M.; Jansakun, C.; Chandet, N.; Thongkorn, K.; Rujijanagul, G.; Bangrak, P.; Randorn, C. Synthesis of Hydroxyapatite with Antibacterial Properties Using a Microwave-Assisted Combustion Method. *Sci. Rep.* **2019**, *9*, 4015. [CrossRef] [PubMed]
88. De Stefani, A.; Bruno, G.; Preo, G.; Gracco, A. Application of Nanotechnology in Orthodontic Materials: A State-of-the-Art Review. *Dent. J.* **2020**, *8*, 126. [CrossRef] [PubMed]
89. Ilić, B.; Petrović, B.; Marinković, J.; Miletić Vukajlović, J.; Stevanović, M.; Potočnik, J.; Jokanović, V. Investigation of Ion Release and Antibacterial Properties of TiN-Cu-Nanocoated Nitinol Archwires. *Coatings* **2023**, *13*, 1587. [CrossRef]
90. Selvaraj, A.; George, A.M.; Rajeshkumar, S. Efficacy of zirconium oxide nanoparticles coated on stainless steel and nickel titanium wires in orthodontic treatment. *Bioinformation* **2021**, *17*, 760–766. [CrossRef]
91. Golshah, A.; Feyli, S.A. Effect of zirconium oxide nano-coating on frictional resistance of orthodontic wires. *J. Orthod. Sci.* **2022**, *11*, 35. [CrossRef]
92. Chen, Y.; Chen, Z.; Zheng, Z.; Xia, Y. Bio-inspired nanocomposite coatings on orthodontic archwires with corrosion resistant and antibacterial properties. *Front. Bioeng. Biotechnol.* **2023**, *11*, 1272527. [CrossRef]

93. Gracco, A.; Dandrea, M.; Deflorian, F.; Zanella, C.; De Stefani, A.; Bruno, G.; Stellini, E. Application of a Molybdenum and Tungsten Disulfide Coating to Improve Tribological Properties of Orthodontic Archwires. *Nanomaterials* **2019**, *9*, 753. [CrossRef] [PubMed]
94. Aminoroaya, A.; Neisiany, R.E.; Khorasani, S.N.; Panahi, P.; Das, O.; Madry, H.; Cucchiarini, M.; Ramakrishna, S. A review of dental composites: Challenges, chemistry aspects, filler influences, and future insights. *Compos. Part B Eng.* **2021**, *216*, 108852. [CrossRef]
95. Gholampour, S.-S.; Zoorazma, G.; Shakouri, E. Evaluating the effect of dental filling material and filling depth on the strength and deformation of filled teeth. *Dent. Mater. Tech.* **2016**, *5*, 172–180. [CrossRef]
96. Ab Rahman, I.; Padavettan, V. Synthesis of Silica Nanoparticles by Sol-Gel: Size-Dependent Properties, Surface Modification, and Applications in Silica-Polymer Nanocomposites—A Review. *J. Nanomater.* **2012**, *2012*, 132424. [CrossRef]
97. Zhang, M.Q.; Rong, M.Z.; Yu, S.L.; Wetzel, B.; Friedrich, K. Effect of particle surface treatment on the tribological performance of epoxy based nanocomposites. *Wear* **2002**, *253*, 1086–1093. [CrossRef]
98. Pinto, D.; Bernardo, L.; Amaro, A.; Lopes, S.M.R. Mechanical properties of epoxy nanocomposites using titanium dioxide as reinforcement—A review. *Constr. Build. Mater.* **2015**, *95*, 506–524. [CrossRef]
99. Carballeira, P.; Haupert, F. Toughening effects of titanium dioxide nanoparticles on TiO_2/epoxy resin nanocomposites. *Polym. Compos.* **2010**, *31*, 1241–1246. [CrossRef]
100. Moreau, J.L.; Weir, M.D.; Giuseppetti, A.A.; Chow, L.C.; Antonucci, J.M.; Xu, H.H.K. Long-term mechanical durability of dental nanocomposites containing amorphous calcium phosphate nanoparticles. *J. Biomed. Mater. Res. Part B Appl. Biomater.* **2012**, *100*, 1264–1273. [CrossRef]
101. Fathy, A.; Elkady, O.; Abu-Oqail, A. Production and properties of Cu-ZrO_2 nanocomposites. *J. Compos. Mater.* **2018**, *52*, 1519–1529. [CrossRef]
102. Velo, M.M.d.A.C.; Filho, F.G.N.; Nascimento, T.R.d.L.; Obeid, A.T.; Castellano, L.C.; Costa, R.M.; Brondino, N.C.M.; Fonseca, M.G.; Silikas, N.; Mondelli, R.F.L. Enhancing the mechanical properties and providing bioactive potential for graphene oxide/montmorillonite hybrid dental resin composites. *Sci. Rep.* **2022**, *12*, 10259. [CrossRef] [PubMed]
103. Aati, S.; Chauhan, A.; Shrestha, B.; Rajan, S.M.; Aati, H.; Fawzy, A. Development of 3D printed dental resin nanocomposite with graphene nanoplatelets enhanced mechanical properties and induced drug-free antimicrobial activity. *Dent. Mater.* **2022**, *38*, 1921–1933. [CrossRef]
104. Chen, J.; Zhao, Q.; Peng, J.; Yang, X.; Yu, D.; Zhao, W. Antibacterial and mechanical properties of reduced graphene-silver nanoparticle nanocomposite modified glass ionomer cements. *J. Dent.* **2020**, *96*, 103332. [CrossRef] [PubMed]
105. Barot, T.; Rawtani, D.; Kulkarni, P. Physicochemical and biological assessment of silver nanoparticles immobilized Halloysite nanotubes-based resin composite for dental applications. *Heliyon* **2020**, *6*, e03601. [CrossRef] [PubMed]
106. Comeau, P.; Burgess, J.; Malekafzali, N.; Leite, M.L.; Lee, A.; Manso, A. Exploring the Physicochemical, Mechanical, and Photocatalytic Antibacterial Properties of a Methacrylate-Based Dental Material Loaded with ZnO Nanoparticles. *Materials* **2022**, *15*, 5075. [CrossRef]
107. Javed, R.; Rais, F.; Fatima, H.; Haq, I.U.; Kaleem, M.; Naz, S.S.; Ao, Q. Chitosan encapsulated ZnO nanocomposites: Fabrication, characterization, and functionalization of bio-dental approaches. *Mater. Sci. Eng. C* **2020**, *116*, 111184. [CrossRef] [PubMed]
108. Rodrigues, R.A.A.; Silva, R.M.F.d.C.e.; Ferreira, L.d.A.Q.; Branco, N.T.T.; Ávila, D.S.; Peres, A.M.; Fernandes-Braga, W.; Sette-Dias, A.C.; Andrade, L.; Palma-Dibb, R.G.; et al. Enhanced mechanical properties, anti-biofilm activity, and cytocompatibility of a methacrylate-based polymer loaded with native multiwalled carbon nanotubes. *J. Mech. Behav. Biomed. Mater.* **2022**, *136*, 105511. [CrossRef] [PubMed]
109. Kumar, M.; Kumar, R.; Kumar, S. Synergistic effect of carbon nanotubes and nano-hydroxyapatite on mechanical properties of polyetheretherketone based hybrid nanocomposites. *Polym. Polym. Compos.* **2021**, *29*, 1365–1376. [CrossRef]
110. Priyadarsini, S.; Mukherjee, S.; Mishra, M. Nanoparticles used in dentistry: A review. *J. Oral Biol. Craniofacial Res.* **2018**, *8*, 58–67. [CrossRef]
111. Mandhalkar, R.; Paul, P.; Reche, A. Application of Nanomaterials in Restorative Dentistry. *Cureus* **2023**, *15*, e33779. [CrossRef]
112. Azmy, E.; Al-Kholy, M.R.Z.; Fattouh, M.; Kenawi, L.M.M.; Helal, M.A. Impact of Nanoparticles Additions on the Strength of Dental Composite Resin. *Int. J. Biomater.* **2022**, *2022*, 1165431. [CrossRef]
113. Saridou, M.; Nikolaidis, A.K.; Koulaouzidou, E.A.; Achilias, D.S. Synthesis and Characterization of Dental Nanocomposite Resins Reinforced with Dual Organomodified Silica/Clay Nanofiller Systems. *J. Funct. Biomater.* **2023**, *14*, 405. [CrossRef]
114. Toledano, M.; Vallecillo-Rivas, M.; Aguilera, F.S.; Osorio, M.T.; Osorio, E.; Osorio, R. Polymeric zinc-doped nanoparticles for high performance in restorative dentistry. *J. Dent.* **2021**, *107*, 103616. [CrossRef]
115. Alshamrani, A.; Alhotan, A.; Kelly, E.; Ellakwa, A. Mechanical and Biocompatibility Properties of 3D-Printed Dental Resin Reinforced with Glass Silica and Zirconia Nanoparticles: In Vitro Study. *Polymers* **2023**, *15*, 2523. [CrossRef]
116. Rudolf, R.; Popović, D.; Tomić, S.; Bobovnik, R.; Lazić, V.; Majerič, P.; Anžel, I.; Čolić, M. Microstructure Characterisation and Identification of the Mechanical and Functional Properties of a New PMMA-ZnO Composite. *Materials* **2020**, *13*, 2717. [CrossRef] [PubMed]
117. Ebrahim, M.I.; Ahmed, M.A.; Felemban, N.H. Effect of Nanoparticles Reinforced Adhesive Layers on Microleakage of Tooth Restorations. *World J. Nano Sci. Eng.* **2016**, *06*, 64–69. [CrossRef]

118. Balhaddad, A.A.; Garcia, I.M.; Mokeem, L.; Alsahafi, R.; Collares, F.M.; de Melo, M.A.S. Metal Oxide Nanoparticles and Nanotubes: Ultrasmall Nanostructures to Engineer Antibacterial and Improved Dental Adhesives and Composites. *Bioengineering* **2021**, *8*, 146. [CrossRef]
119. Xiao, Z.; Zhao, Q.; Niu, Y.; Zhao, D. Adhesion Advances: From Nanomaterials to Biomimetic Adhesion and Applications. *Soft Matter* **2022**, *18*, 3447–3464. [CrossRef] [PubMed]
120. Khan, A.S.; Alhamdan, Y.; Alibrahim, H.; Almulhim, K.S.; Nawaz, M.; Ahmed, S.Z.; Aljuaid, K.; Ateeq, I.S.; Akhtar, S.; Ansari, M.A.; et al. Analyses of Experimental Dental Adhesives Based on Zirconia/Silver Phosphate Nanoparticles. *Polymers* **2023**, *15*, 2614. [CrossRef]
121. Melo, M.A.S.; Cheng, L.; Zhang, K.; Weir, M.D.; Rodrigues, L.K.; Xu, H.H. Novel dental adhesives containing nanoparticles of silver and amorphous calcium phosphate. *Dent. Mater.* **2013**, *29*, 199–210. [CrossRef] [PubMed]
122. Rao, A.C.; Kondas, V.V.; Nandini, V.; Kirana, R.; Yadalam, P.K.; Eswaramoorthy, R. Evaluating the effect of poly (amidoamine) treated bioactive glass nanoparticle incorporated in universal adhesive on bonding to artificially induced caries affected dentin. *BMC Oral Health* **2023**, *23*, 810. [CrossRef] [PubMed]
123. Kreutz, M.; Kreutz, C.; Kanzow, P.; Tauböck, T.T.; Burrer, P.; Noll, C.; Bader, O.; Rohland, B.; Wiegand, A.; Rizk, M. Effect of Bioactive and Antimicrobial Nanoparticles on Properties and Applicability of Dental Adhesives. *Nanomaterials* **2022**, *12*, 3862. [CrossRef] [PubMed]
124. Mirhashemi, A.; Akhondi, M.S.A.; Sodagar, A.; Jalali, Y.F.; Jazi, L. Effect of nano-zinc oxide and nano-chitosan particles on the shear bond strength of dental composites used as orthodontic adhesive. *J. World Fed. Orthod.* **2021**, *10*, 172–176. [CrossRef] [PubMed]
125. Binhasan, M.; Al-Habeeb, K.M.; Almuqbil, A.S.; Alhaidary, T.A.; Alfawaz, Y.F.; Farooq, I.; Vohra, F.; Abduljabbar, T. Assessment of the Physical Properties of an Experimental Adhesive Dentin Bonding Agent with Carbon Nanoparticles. *Crystals* **2022**, *12*, 1441. [CrossRef]
126. Allende, J.B.; Nascimiento, F.D.; Damasceno, M.; Chiari, S.; Aliaga-Galvez, R.; Ñaupari-Villasante, R.; Miranda, C.B.; Pardo-Díaz, C.; FelipeGutiérrez, M.; Covarrubias, C.; et al. Evaluation of adhesive properties and enzymatic activity at the hybrid layer of a simplified adhesive loaded with 0.2% Cu and 5% ZnO nanoparticles: A Randomized Clinical Trial and ex vivo analysis. *J. Dent.* **2024**, *149*, 105283. [CrossRef]
127. Roig-Soriano, X.; Souto, E.B.; Elmsmari, F.; Garcia, M.L.; Espina, M.; Duran-Sindreu, F.; Sánchez-López, E.; Sánchez, J.A.G. Nanoparticles in Endodontics Disinfection: State of the Art. *Pharmaceutics* **2022**, *14*, 1519. [CrossRef] [PubMed]
128. Capuano, N.; Amato, A.; Dell'annunziata, F.; Giordano, F.; Folliero, V.; Di Spirito, F.; More, P.R.; De Filippis, A.; Martina, S.; Amato, M.; et al. Nanoparticles and Their Antibacterial Application in Endodontics. *Antibiotics* **2023**, *12*, 1690. [CrossRef]
129. Raura, N.; Garg, A.; Arora, A.; Roma, M. Nanoparticle technology and its implications in endodontics: A review. *Biomater. Res.* **2020**, *24*, 21. [CrossRef] [PubMed]
130. Haseeb, R.; Lau, M.; Sheah, M.; Montagner, F.; Quiram, G.; Palmer, K.; Stefan, M.C.; Rodrigues, D.C. Synthesis and Characterization of New Chlorhexidine-Containing Nanoparticles for Root Canal Disinfection. *Materials* **2016**, *9*, 452. [CrossRef] [PubMed]
131. Parolia, A.; Kumar, H.; Ramamurthy, S.; Madheswaran, T.; Davamani, F.; Pichika, M.R.; Mak, K.-K.; Fawzy, A.S.; Daood, U.; Pau, A. Effect of Propolis Nanoparticles against *Enterococcus faecalis* Biofilm in the Root Canal. *Molecules* **2021**, *26*, 715. [CrossRef]
132. Elmsmari, F.; Delgado, L.M.; Duran-Sindreu, F.; Pérez, R.A.; García, M.L.; Trull, M.T.; Afrashtehfar, K.I.; González, J.A.; Sánchez-López, E. Novel strategies enhancing endodontic disinfection: Antibacterial biodegradable calcium hydroxide nanoparticles in an ex vivo model. *Int. J. Pharm.* **2023**, *648*, 123627. [CrossRef]
133. Marín-Correa, B.M.; Guzmán-Martínez, N.; Gómez-Ramírez, M.; Pless, R.C.; Mundo, J.R.; García-Ramos, J.C.; Rojas-Avelizapa, N.G.; Pestryakov, A.; Bogdanchikova, N.; Fierros-Romero, G. Nanosilver gel as an endodontic alternative against Enterococcus faecalis in an in vitro root canal system in Mexican dental specimens. *New Microbiol.* **2020**, *43*, 166–170.
134. Gholami, A.; Ghezelbash, K.; Asheghi, B.; Abbaszadegan, A.; Amini, A. An In Vitro Study on the Antibacterial Effects of Chlorhexidine-Loaded Positively Charged Silver Nanoparticles on *Enterococcus faecalis*. *J. Nanomater.* **2022**, *2022*, 6405772. [CrossRef]
135. Razumova, S.; Brago, A.; Serebrov, D.; Barakat, H.; Kozlova, Y.; Howijieh, A.; Guryeva, Z.; Enina, Y.; Troitskiy, V. The Application of Nano Silver Argitos as a Final Root Canal Irrigation for the Treatment of Pulpitis and Apical Periodontitis. In Vitro Study. *Nanomaterials* **2022**, *12*, 248. [CrossRef]
136. Tonini, R.; Giovarruscio, M.; Gorni, F.; Ionescu, A.; Brambilla, E.; Mikhailovna, I.M.; Luzi, A.; Maciel Pires, P.; Sauro, S. In Vitro Evaluation of Antibacterial Properties and Smear Layer Removal/Sealer Penetration of a Novel Silver-Citrate Root Canal Irrigant. *Materials* **2020**, *13*, 194. [CrossRef]
137. Ravi, V.; Kini, S.; Shenoy, N.; Somayaji, K.; Shenoy, P. Comparative Evaluation of the Antimicrobial Efficacy of Sodium Hypochlorite, Silver Nanoparticles, and Zinc Nanoparticles against Candidal Biofilm: An In Vitro Study. *Eng. Proc.* **2023**, *59*, 170.
138. Husein, A.; Said, H.M.; Bakar, W.Z.W.; Farea, M. The effect of different sealer placement techniques on sealing Ability: An in vitro study. *J. Conserv. Dent.* **2012**, *15*, 257–260. [CrossRef] [PubMed]
139. Sharma, D.; Worlikar, N.; Shah, K.; Sharma, Y. Recent advancements in root canal sealers-An overview. *J. Adv. Med. Dent. Sci. Res.* **2023**, *11*, 82–91.

140. Marica, A.; Sipos, L.; Iurcov, R.; Stefanescu, T.; Gabriela, C.; Ioanalucan, A. Current use of nanoparticles in endodontics: A sytematic review. *Rom. J. Oral. Rehabil.* **2022**, *14*, 115–126.
141. Behnaz, M.; Kasraei, S.; Yadegari, Z.; Zare, F.; Nahvi, G. Effects of orthodontic bonding containing TiO_2 and ZnO nanoparticles on prevention of white spot lesions: An in vitro study. *Biointerface Res. Appl. Chem* **2022**, *12*, 431–440.
142. Droepenu, E.K.; Wee, B.S.; Chin, S.F.; Kok, K.Y.; Maligan, M.F. Zinc Oxide nanoparticles synthesis methods and its effect on morphology: A review. *Biointerface Res. Appl. Chem.* **2022**, *12*, 4261–4292. [CrossRef]
143. Choi, J.-W.; Yang, S.-Y. Effect of Zinc Oxide Incorporation on the Antibacterial, Physicochemical, and Mechanical Properties of Pit and Fissure Sealants. *Polymers* **2023**, *15*, 529. [CrossRef]
144. Collares, F.M.; Garcia, I.M.; Klein, M.; Parolo, C.F.; Sánchez, F.A.L.; Takimi, A.; Bergmann, C.P.; Samuel, S.M.W.; Melo, M.A.; Leitune, V.C. Exploring Needle-Like Zinc Oxide Nanostructures for Improving Dental Resin Sealers: Design and Evaluation of Antibacterial, Physical and Chemical Properties. *Polymers* **2020**, *12*, 789. [CrossRef]
145. Zubizarreta-Macho, Á.; Rico-Romano, C.; Fernández-Aceñero, M.J.; Mena-Álvarez, J.; Cabal, B.; Díaz, L.A.; Torrecillas, R.; Moya, J.S.; López-Píriz, R. Adding Two Antimicrobial Glasses to an Endodontic Sealer to Prevent Bacterial Root Canal Reinfection: An In Vivo Pilot Study in Dogs. *Antibiotics* **2021**, *10*, 1183. [CrossRef]
146. Bertacci, A.; Moro, D.; Ulian, G.; Valdrè, G. Development of A Nano-Apatite Based Composite Sealer for Endodontic Root Canal Filling. *J. Compos. Sci.* **2021**, *5*, 30. [CrossRef]
147. Al-Sabawi, N.A.; Al-Jubori, S.H. Preparation and characterization of novel nano-tricalcium silicate-58s bioactive glass-based root canal sealer. *Saudi Endod. J.* **2024**, *14*, 90–99. [CrossRef]
148. Raheem, I.A.A.; Razek, A.A.; Elgendy, A.A.; Labah, D.A.; Saleh, N.M. Egyptian Propolis-loaded nanoparticles as a root canal nanosealer: Sealing ability and in vivo biocompatibility. *Int. J. Nanomed.* **2020**, *15*, 5265–5277. [CrossRef] [PubMed]
149. Ibrahim, B.H.; Al-Huwaizi, H. Evaluation of Antimicrobial Activity and Cytotoxicity of an Epoxy Resin-Based Endodontic Sealer Containing Nanoparticles Amorphous Calcium Phosphate. *Int. J. Dent.* **2023**, *2023*, 8717655. [CrossRef] [PubMed]
150. Nazir, M.A. Prevalence of periodontal disease, its association with systemic diseases and prevention. *Int. J. Health Sci.* **2017**, *11*, 72–80.
151. Rajeshwari, H.R.; Dhamecha, D.; Jagwani, S.; Rao, M.; Jadhav, K.; Shaikh, S.; Puzhankara, L.; Jalalpure, S. Local drug delivery systems in the management of periodontitis: A scientific review. *J. Control. Release* **2019**, *307*, 393–409. [CrossRef]
152. Wei, Y.; Deng, Y.; Ma, S.; Ran, M.; Jia, Y.; Meng, J.; Han, F.; Gou, J.; Yin, T.; He, H.; et al. Local drug delivery systems as therapeutic strategies against periodontitis: A systematic review. *J. Control. Release* **2021**, *333*, 269–282. [CrossRef] [PubMed]
153. Şenel, S.; Özdoğan, A.I.; Akca, G. Current status and future of delivery systems for prevention and treatment of infections in the oral cavity. *Drug Deliv. Transl. Res.* **2021**, *11*, 1703–1734. [CrossRef]
154. Alghanem, S.; Dziurkowska, E.; Ordyniec-Kwaśnica, I.; Sznitowska, M. Intraoral medical devices for sustained drug delivery. *Clin. Oral Investig.* **2023**, *27*, 7157–7169. [CrossRef]
155. Paul, M.; Das Pramanik, S.; Sahoo, R.N.; Dey, Y.N.; Nayak, A.K. Dental delivery systems of antimicrobial drugs using chitosan, alginate, dextran, cellulose and other polysaccharides: A review. *Int. J. Biol. Macromol.* **2023**, *247*, 125808. [CrossRef]
156. Zhang, Y.; Jiang, R.; Lei, L.; Yang, Y.; Hu, T. Drug delivery systems for oral disease applications. *J. Appl. Oral Sci.* **2022**, *30*, e20210349. [CrossRef]
157. Joshi, D.; Garg, T.; Goyal, A.K.; Rath, G. Advanced drug delivery approaches against periodontitis. *Drug Deliv.* **2016**, *23*, 363–377. [CrossRef]
158. Chandramouli, M.; Shivalingappa, R.P.; Basavanna, V.; Doddamani, S.; Shanthakumar, D.C.; Nagarajaiah, S.R.; Ningaiah, S. Oral Thin-films from Design to Delivery: A Pharmaceutical Viewpoint. *Biointerface Res. Appl. Chem.* **2023**, *13*, 2023.
159. Steckiewicz, K.P.; Cieciórski, P.; Barcińska, E.; Jaśkiewicz, M.; Narajczyk, M.; Bauer, M.; Kamysz, W.; Megiel, E.; Inkielewicz-Stepniak, I. Silver Nanoparticles as Chlorhexidine and Metronidazole Drug Delivery Platforms: Their Potential Use in Treating Periodontitis. *Int. J. Nanomed.* **2022**, *17*, 495–517. [CrossRef] [PubMed]
160. Constantin, M.; Lupei, M.; Bucatariu, S.-M.; Pelin, I.M.; Doroftei, F.; Ichim, D.L.; Daraba, O.M.; Fundueanu, G. PVA/Chitosan Thin Films Containing Silver Nanoparticles and Ibuprofen for the Treatment of Periodontal Disease. *Polymers* **2023**, *15*, 4. [CrossRef] [PubMed]
161. Tong, F.; Wang, P.; Chen, Z.; Liu, Y.; Wang, L.; Guo, J.; Li, Z.; Cai, H.; Wei, J. Combined Ferromagnetic Nanoparticles for Effective Periodontal Biofilm Eradication in Rat Model. *Int. J. Nanomed.* **2023**, *18*, 2371–2388. [CrossRef]
162. Sahu, S.A.; Panda, S.; Das, A.C.; Mishra, L.; Rath, S.; Sokolowski, K.; Kumar, M.; Mohanty, R.; Nayak, R.; Satpathy, A.; et al. Efficacy of Sub-Gingivally Delivered Propolis Nanoparticle in Non-Surgical Management of Periodontal Pocket: A Randomized Clinical Trial. *Biomolecules* **2023**, *13*, 1576. [CrossRef]
163. Kadam, P.; Mahale, S.; Sonar, P.; Chaudhari, D.; Shimpi, S.; Kathurwar, A. Efficacy of silver nanoparticles in chronic periodontitis patients: A clinico-microbiological study. *Iberoam. J. Med.* **2020**, *2*, 142–147. [CrossRef]
164. Yıldırım, Y.; İnce, I.; Gümüştaş, B.; Vardar, Ö.; Yakar, N.; Munjaković, H.; Özdemir, G.; Emingil, G. Development of doxycycline and atorvastatin-loaded chitosan nanoparticles for local delivery in periodontal disease. *J. Drug Deliv. Sci. Technol.* **2023**, *82*, 104322. [CrossRef]
165. Tsamesidis, I.; Gkiliopoulos, D.; Pouroutzidou, G.K.; Lymperaki, E.; Papoulia, C.; Reybier, K.; Perio, P.; Paraskevopoulos, K.M.; Kontonasaki, E.; Theocharidou, A. Effect of Artemisinin-Loaded Mesoporous Cerium-Doped Calcium Silicate Nanopowder on Cell Proliferation of Human Periodontal Ligament Fibroblasts. *Nanomaterials* **2021**, *11*, 2189. [CrossRef] [PubMed]

166. Bai, B.; Gu, C.; Lu, X.; Ge, X.; Yang, J.; Wang, C.; Gu, Y.; Deng, A.; Guo, Y.; Feng, X.; et al. Polydopamine functionalized mesoporous silica as ROS-sensitive drug delivery vehicles for periodontitis treatment by modulating macrophage polarization. *Nano Res.* **2021**, *14*, 4577–4583. [CrossRef]
167. Bako, J.; Toth, F.; Gall, J.; Kovacs, R.; Csík, A.; Varga, I.; Sculean, A.; Zelko, R.; Hegedus, C. Combined Release of Antiseptic and Antibiotic Drugs from Visible Light Polymerized Biodegradable Nanocomposite Hydrogels for Periodontitis Treatment. *Pharmaceutics* **2022**, *14*, 957. [CrossRef] [PubMed]
168. Gao, P.; Li, G.; Wang, Z.; Zhang, H.; Shan, Y.; Yuan, X.; Shi, Q.; Dou, X.; Zhou, Q.; Xu, Q. Protease-Loaded CuS Nanoparticles with Synergistic Photothermal/Dynamic Therapy against *F. nucleatum*-Induced Periodontitis. *ACS Appl. Mater. Interfaces* **2023**, *15*, 32215–32225. [CrossRef] [PubMed]
169. Pereira, A.d.S.B.F.; Lima, M.L.d.S.; da Silva-Junior, A.A.; Silva, E.d.S.; Júnior, R.F.d.A.; Martins, A.A.; Alves, J.S.F.; Oliveira, A.d.S.; Ferreira, L.D.S.; Costa, E.C.T.d.A.; et al. In vitro-in vivo availability of metformin hydrochloride-PLGA nanoparticles in diabetic rats in a periodontal disease experimental model. *Pharm. Biol.* **2021**, *59*, 1574–1582. [CrossRef] [PubMed]
170. Parmar, R.; Salman, M.M.; Chauhan, P. Fabrication of Cefixime Nanoparticles Loaded Films and their Ex Vivo Antimicrobial Effect on Periodontitis Patient's Saliva. *Pharm. Nanotechnol.* **2021**, *9*, 361–371. [CrossRef]
171. Cao, B.; Da, X.; Wu, W.; Xie, J.; Li, X.; Wang, X.; Xu, H.; Gao, J.; Yang, H.; Su, J. Multifunctional human serum albumin-crosslinked and self-assembling nanoparticles for therapy of periodontitis by anti-oxidation, anti-inflammation and osteogenesis. *Mater. Today Bio* **2024**, *28*, 101163. [CrossRef]
172. Zong, C.; Bronckaers, A.; Willems, G.; He, H.; de Llano-Pérula, M.C. Nanomaterials for Periodontal Tissue Regeneration: Progress, Challenges and Future Perspectives. *J. Funct. Biomater.* **2023**, *14*, 290. [CrossRef]
173. Hollý, D.; Klein, M.; Mazreku, M.; Zamborský, R.; Polák, Š.; Danišovič, L'.; Csöbönyeiová, M. Stem Cells and Their Derivatives—Implications for Alveolar Bone Regeneration: A Comprehensive Review. *Int. J. Mol. Sci.* **2021**, *22*, 11746. [CrossRef]
174. Huck, O.; Stutz, C.; Gegout, P.-Y.; Özçelik, H.; Benkirane-Jessel, N.; Petit, C.; Batool, F. Nanomedicine and Periodontal Regenerative Treatment. *Dent. Clin. N. Am.* **2022**, *66*, 131–155. [CrossRef]
175. Takallu, S.; Kakian, F.; Bazargani, A.; Khorshidi, H.; Mirzaei, E. Development of antibacterial collagen membranes with optimal silver nanoparticle content for periodontal regeneration. *Sci. Rep.* **2024**, *14*, 7262. [CrossRef] [PubMed]
176. Ren, S.; Zhou, Y.; Zheng, K.; Xu, X.; Yang, J.; Wang, X.; Miao, L.; Wei, H.; Xu, Y. Cerium oxide nanoparticles loaded nanofibrous membranes promote bone regeneration for periodontal tissue engineering. *Bioact. Mater.* **2022**, *7*, 242–253. [CrossRef] [PubMed]
177. Shaikh, M.S.; Zafar, M.S.; Alnazzawi, A.; Javed, F. Nanocrystalline hydroxyapatite in regeneration of periodontal intrabony defects: A systematic review and meta-analysis. *Ann. Anat.-Anat. Anz.* **2022**, *240*, 151877. [CrossRef] [PubMed]
178. Chang, P.C.; Luo, H.T.; Lin, Z.J.; Tai, W.C.; Chang, C.H.; Chang, Y.C.; Cochran, D.L.; Chen, M.H. Regeneration of critical-sized mandibular defect using a 3D-printed hydroxyapatite-based scaffold: An exploratory study. *J. Periodontol.* **2021**, *92*, 428–435. [CrossRef]
179. Tamburaci, S.; Tihminlioglu, F. Development of Si doped nano hydroxyapatite reinforced bilayer chitosan nanocomposite barrier membranes for guided bone regeneration. *Mater. Sci. Eng. C* **2021**, *128*, 112298. [CrossRef] [PubMed]
180. Vani, T.M.S.; Paramashivaiah, R.; Prabhuji, M.L.V.; Peeran, S.W.; Fageeh, H.; Tasleem, R.; Bahamdan, G.K.; Aldosari, L.I.N.; Bhavikatti, S.K.; Scardina, G.A. Regeneration of Intrabony Defects with Nano Hydroxyapatite Graft, Derived from Eggshell along with Periosteum as Barrier Membrane under Magnification—An Interventional Study. *Appl. Sci.* **2023**, *13*, 1693. [CrossRef]
181. Huang, B.; Chen, M.; Tian, J.; Zhang, Y.; Dai, Z.; Li, J.; Zhang, W. Oxygen-Carrying and Antibacterial Fluorinated Nano-Hydroxyapatite Incorporated Hydrogels for Enhanced Bone Regeneration. *Adv. Health Mater.* **2022**, *11*, 2102540. [CrossRef] [PubMed]
182. Wei, L.; Feng, X.; Chen, A.; Zhang, Y.; Wang, J.; Shao, L. Application of dental nanomaterials: Potential toxicity to the central nervous system. *Int. J. Nanomed.* **2015**, *10*, 3547–3565. [CrossRef]
183. Karunakaran, H.; Krithikadatta, J.; Doble, M. Local and systemic adverse effects of nanoparticles incorporated in dental materials-a critical review. *Saudi Dent. J.* **2024**, *36*, 158–167. [CrossRef]
184. Tang, X.; Li, L.; Meng, X.; Liu, T.; Hu, Q.; Miao, L. Cytotoxicity of silver nanoparticles on human periodontal ligament fibroblasts. *Nanosci. Nanotechnol. Lett.* **2017**, *9*, 1015–1022. [CrossRef]
185. Cunningham, B.; Engstrom, A.M.; Harper, B.J.; Harper, S.L.; Mackiewicz, M.R. Silver Nanoparticles Stable to Oxidation and Silver Ion Release Show Size-Dependent Toxicity In Vivo. *Nanomaterials* **2021**, *11*, 1516. [CrossRef] [PubMed]
186. Filip, G.A.; Florea, A.; Olteanu, D.; Clichici, S.; David, L.; Moldovan, B.; Cenariu, M.; Scrobota, I.; Potara, M.; Baldea, I. Biosynthesis of silver nanoparticles using Sambucus nigra L. fruit extract for targeting cell death in oral dysplastic cells. *Mater. Sci. Eng. C* **2021**, *123*, 111974. [CrossRef] [PubMed]
187. Ferdous, Z.; Nemmar, A. Health Impact of Silver Nanoparticles: A Review of the Biodistribution and Toxicity Following Various Routes of Exposure. *Int. J. Mol. Sci.* **2020**, *21*, 2375. [CrossRef] [PubMed]
188. Vandebriel, R.J.; De Jong, W.H. A review of mammalian toxicity of ZnO nanoparticles. *Nanotechnol. Sci. Appl.* **2012**, *5*, 61–71. [CrossRef] [PubMed]
189. Kim, K.-B.; Kim, Y.W.; Lim, S.K.; Roh, T.H.; Bang, D.Y.; Choi, S.M.; Lim, D.S.; Kim, Y.J.; Baek, S.-H.; Kim, M.-K.; et al. Risk assessment of zinc oxide, a cosmetic ingredient used as a UV filter of sunscreens. *J. Toxicol. Environ. Health Part B* **2017**, *20*, 155–182. [CrossRef] [PubMed]

190. Luo, Z.; Li, Z.; Xie, Z.; Sokolova, I.M.; Song, L.; Peijnenburg, W.J.; Hu, M.; Wang, Y. Rethinking nano-TiO_2 safety: Overview of toxic effects in humans and aquatic animals. *Small* **2020**, *16*, 2002019. [CrossRef] [PubMed]
191. Tang, M.; Zhang, T.; Xue, Y.; Wang, S.; Huang, M.; Yang, Y.; Lu, M.; Lei, H.; Kong, L.; Wang, Y.; et al. Metabonomic studies of biochemical changes in the serum of rats by intratracheally instilled TiO_2 nanoparticles. *J. Nanosci. Nanotechnol.* **2011**, *11*, 3065–3074. [CrossRef]
192. Lammel, T.; Mackevica, A.; Johansson, B.R.; Sturve, J. Endocytosis, intracellular fate, accumulation, and agglomeration of titanium dioxide (TiO_2) nanoparticles in the rainbow trout liver cell line RTL-W1. *Environ. Sci. Pollut. Res.* **2019**, *26*, 15354–15372. [CrossRef]
193. Vranic, S.; Shimada, Y.; Ichihara, S.; Kimata, M.; Wu, W.; Tanaka, T.; Boland, S.; Tran, L.; Ichihara, G. Toxicological Evaluation of SiO_2 Nanoparticles by Zebrafish Embryo Toxicity Test. *Int. J. Mol. Sci.* **2019**, *20*, 882. [CrossRef]
194. Zhang, Z.; Zhao, L.; Ma, Y.; Liu, J.; Huang, Y.; Fu, X.; Peng, S.; Wang, X.; Yang, Y.; Zhang, X.; et al. Mechanistic study of silica nanoparticles on the size-dependent retinal toxicity in vitro and in vivo. *J. Nanobiotechnol.* **2022**, *20*, 146. [CrossRef]
195. Lee, S.Y.; Kim, I.Y.; Heo, M.B.; Moon, J.H.; Son, J.G.; Lee, T.G. Global proteomics to study silica nanoparticle-induced cytotoxicity and its mechanisms in HepG2 cells. *Biomolecules* **2021**, *11*, 375. [CrossRef] [PubMed]
196. Putthanuparp, T.; Rirattanapong, P.; Ruangsawasdi, N. The cytotoxicity of silver nanoparticles on human gingival fibroblast cells: An in vitro study. *Mahidol Dent. J.* **2023**, *43*, 107–114.
197. Wang, Z.; Zhang, C.; Liu, X.; Huang, F.; Wang, Z.; Yan, B. Oral intake of ZrO_2 nanoparticles by pregnant mice results in nanoparticles' deposition in fetal brains. *Ecotoxicol. Environ. Saf.* **2020**, *202*, 110884. [CrossRef] [PubMed]
198. Barbasz, A.M.; Dyba, B. Direct Interaction of Zirconia Nanoparticles with Human Immune Cells. *Biophysica* **2024**, *4*, 83–91. [CrossRef]
199. Chen, F.-C.; Huang, C.-M.; Yu, X.-W.; Chen, Y.-Y. Effect of nano zinc oxide on proliferation and toxicity of human gingival cells. *Hum. Exp. Toxicol.* **2022**, *41*, 09603271221080236. [CrossRef] [PubMed]
200. Youssef, M.M.; El-Mansy, M.N.; El-Borady, O.M.; Hegazy, E.M. Impact of biosynthesized silver nanoparticles cytotoxicity on dental pulp of albino rats (histological and immunohistochemical study). *J. Oral Biol. Craniofacial Res.* **2021**, *11*, 386–392. [CrossRef] [PubMed]
201. Ullah, A.; Al-Saeed, F.A.; Abduallah, A.M.; Ahmed, A.E.; Shahzad, A.; Amjad, N.; Ali, A.; Mostafa, M.S.; Hussain, R. Calcium Nanoparticles Induce Oxidative Stress in Erythrocytes, Neurotoxicity and Testicular Toxicity in Albino Rats (*Rattus norvegicus*). *Pak. Vet. J.* **2023**, *43*, 241–247. [CrossRef]
202. Solanki, L.A.; Sundari, K.S.; Rajeshkumar, S. In-vitro cytotoxicity evaluation of green synthesized gold nanoparticles and its indigenous mouthwash. *J. Pure Appl. Microbiol.* **2021**, *15*, 735–742. [CrossRef]
203. Khanna, N.; Chokkattu, J.J.; Neeharika, S.; Ramakrishnan, M.; Shanmugam, R.; Thangavelu, L. Anti-inflammatory Activity and Cytotoxic Effect of Ginger and Rosemary-mediated Titanium Oxide Nanoparticles-based Dental Varnish. *World J. Dent.* **2023**, *14*, 761–765. [CrossRef]
204. Kakakhel, M.A.; Wu, F.; Sajjad, W.; Zhang, Q.; Khan, I.; Ullah, K.; Wang, W. Long-term exposure to high-concentration silver nanoparticles induced toxicity, fatality, bioaccumulation, and histological alteration in fish (*Cyprinus carpio*). *Environ. Sci. Eur.* **2021**, *33*, 14. [CrossRef]
205. Mohammadpour, R.; Cheney, D.L.; Grunberger, J.W.; Yazdimamaghani, M.; Jedrzkiewicz, J.; Isaacson, K.J.; Dobrovolskaia, M.A.; Ghandehari, H. One-year chronic toxicity evaluation of single dose intravenously administered silica nanoparticles in mice and their Ex vivo human hemocompatibility. *J. Control. Release* **2020**, *324*, 471–481. [CrossRef] [PubMed]
206. Bengalli, R.; Colantuoni, A.; Perelshtein, I.; Gedanken, A.; Collini, M.; Mantecca, P.; Fiandra, L. In vitro skin toxicity of CuO and ZnO nanoparticles: Application in the safety assessment of antimicrobial coated textiles. *NanoImpact* **2021**, *21*, 100282. [CrossRef] [PubMed]