Heliyon 10 (2024) e34673

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Review article

A narrative review on application of metal and metal oxide nanoparticles in endodontics

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A R T I C L E I N F O

Keywords:
Metal nanoparticles
Metal oxide nanoparticles
Dentistry
Endodontics
Human health

A B S T R A C T

The distinct physicochemical and biological characteristics of metal and metal oxide nanoparticles have attracted considerable interest in various branches of dentistry as potential solutions to the problems associated with conventional dental treatments and to promote human health. Many scientists have been interested in nanoparticles for endodontic applications in the last several decades. Endodontic treatment is more likely to be successful when metal and metal oxide nanoparticles are used. Endodontic therapies often make use of nanoparticles made of metals and metal oxides. The effect of nano metals and metal oxide in endodontic treatments has not been published or is not widely available in the literature. Therefore, this paper aims to review recent studies on the development and application of some important metal and metal oxide nanoparticles such as silver and silver oxide, zinc oxide, zirconium oxide, magnesium oxide, titanium dioxide and other metal oxide nanoparticles in endodontic therapeutic procedures.

1. Introduction

Nanotechnology is recognized as a cutting-edge technology due to its rapid advancements [1]. Nanoparticles are central to nanotechnology, exhibiting distinct chemical, physical, mechanical, biological, thermal, and electrical properties that differ from those of their bulk counterparts [2,3]. The reduction in particle size to the nanoscale can also lead to remarkable magnetic and optical properties [4,5]. One way to classify nanoparticles is by their nanosystem, which might be metallic, bimetallic, metal oxide, or magnetic [2,6]. Metal and metal oxide nanoparticles are the most common and are valued for their exceptional properties in various fields, including medicine and biology [7]. The synthesis of metallic nanoparticles typically involves metal salts, and their visible properties are influenced by surface characteristics (size, shape, and morphology) and physicochemical properties, making the choice of synthesis method critical [4]. Various methods can be used to prepare these nanoparticles, including green synthesis, conventional chemical and physical methods such as vapor deposition, thermal precipitation, photodeposition, sputtering, and pulsed electrodeposition [8,9]. These synthesized nanoparticles manifest enormous properties, namely great antimicrobial and anti-inflammatory activity, high stability, easy preparation processes, simple incorporation, and functionalization by various molecules [7]. Au, Ag, iron, Mg, Al, Ti, Pd, Pt, Cu, Al_2O_3, ZnO, TiO_2, CuO, In_2O_3, Co_3O_4, MgO, ZrO_2, SiO_2, Cr_2O_3, Ni_2O_3, Mn_2O_3, and CoO, are the most widely

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https://doi.org/10.1016/j.heliyon.2024.e34673
Received 20 March 2024; Received in revised form 24 June 2024; Accepted 15 July 2024
Available online 16 July 2024

used ones because of providing distinct properties [10–13]. Using metal and metal oxide nanoparticles has great potential in medicine and dentistry. They can be embedded into dental materials to improve properties [14]. The aim of this overview is a general review of metal and metal oxide nanoparticles in endodontics.

2. Metal and metal oxide nanoparticles in medicine

Nanoparticles made of metals or metal oxides are now essential in many areas of biomedicine, such as imaging, medication delivery, prostheses and implants, and diagnostic systems [15]. Beyond these uses, metal and metal oxide nanoparticles are utilized as antibacterial, antioxidant, anti-inflammatory, and anti-angiogenic agents [3]. Metal and metal oxide nanoparticles have been approved for clinical diagnosis and treatment, and they exhibit great promise in research advancement in diagnostic or therapeutic abilities (Schematic 1) [6].

2.1. Diagnostic application

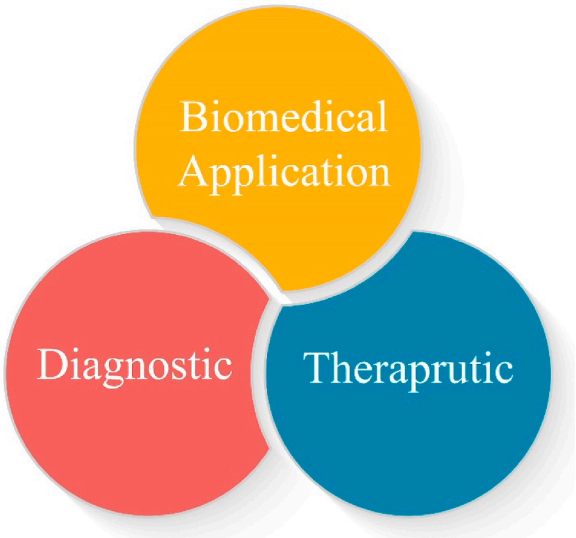
Recent years have seen tremendous advancements in the biomedical use of nanoparticles made of metals and metal oxides for diagnostic purposes, including molecular imaging and cancer diagnostics [7]. Modern diagnostic imaging tools often use metal and metal oxide nanoparticles, such as MRI and fluorescent-labeled particles [7]. One of the most essential uses of nanoparticles in medicine is as contrast agents in bio-imaging procedures like magnetic resonance imaging (MRI) and computed tomography [16]. There has been much interest in the diagnostic potential of manipulating magnetic metal oxide nanoparticles using an external magnetic field since it is a novel approach to remotely controlling their position [17,18].

2.2. Therapeutic application

Several therapeutic applications are possible owing to the metal and metal oxide nanoparticles, including drug delivery, drug release control, hyperthermia, and anti-infection therapy [16]. The therapeutic field has the potential to benefit significantly from metal and metal oxide nanoparticles due to their ability to form nanocarrier structures that have high delivery efficiency, sustained and targeted delivery of multiple therapeutic agents, excellent pharmacological activity, good stability, and bioavailability [7]. To lessen the medication's overall dosage and, by extension, its negative effects, metal oxide nanoparticles can be used for targeted drug delivery [7]. Nanoparticles can effectively increase the drug delivered at the target tissue and tumor site [16].

Several studies showed that some metal oxide nanoparticles have been mostly used due to their great magnetic behavior [9,19]. Magnetic nanoparticles can be applied in hyperthermia therapy [17]. Magnetic hyperthermia, a promising cancer treatment option, aims to raise the temperature to the point where tumor cells die [16,17]. Recently, there have been many studies on hyperthermia therapeutics, all of which have revealed that many different optimized magnetic nanoparticles are helpful for magnetic hyperthermia treatment [6,17].

Nanoparticles can provide effective and broad-range neutralization against viral infection [20]. Most of the metal oxides NPs such as TiO_2, MgO, Zinc oxide, CuO, Al_2O_3, ZrO_2, Co_3O_4, In_2O_3, Cr_2O_3, SiO_2, Ni_2O_3, and Mn_2O_3 NPs could kill bacterial cells [10,21]. Metal oxide NPs have shown promising antibacterial properties in multiple investigations [20].



Schematic 1. Biomedical application of metal and metal oxide nanoparticles.

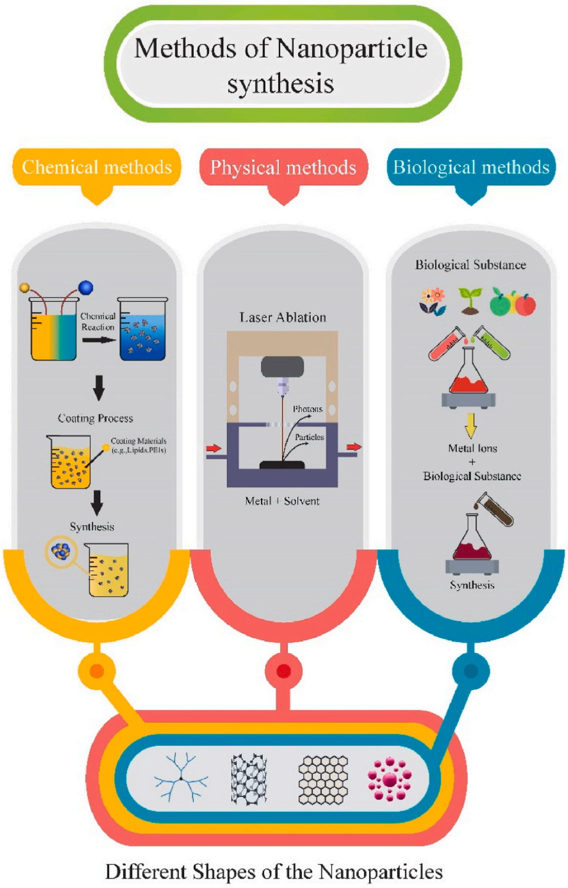
3. Synthesizes of metal and metal oxide

Physiochemical characteristics, size, shape, and morphology are all affected by nanoparticle synthesis [19,22]. Nanoparticle production uses various techniques, the most common of which fall into one of three broad categories: physical, chemical, or biological (Schematic 2) [19,22]. These methods can prepare different nanoparticles with various sizes and morphologies [15]. Physical synthesis methods are commonly used to synthesize highly pure and ultra-thin nanostructures and nano-alloys [19]. The chemical synthesis of ions through a succession of reactions is the conventional way of producing nanoparticles and has been used to synthesize several nanoparticles [19]. New approaches to biological synthesis have recently evolved, addressing the issues of reaction complexity, high cost, and safety that have plagued traditional methods [4]. One appropriate synthesis process can be chosen for the manufacture of nanoparticles, depending on the desired nanoparticle qualities [4,19].

Two main ways to approach synthesis are top-down and bottom-up [23]. Synthesis of complex nanostructures from atoms and molecules is known as a bottom-up technique while downsizing bulk particles to create small nano-sized particles with various properties is known as a top-down approach [19]. Nanostructured metal and metal oxide materials were synthesized using different concepts and processes [24]. Nanoparticle production of metals and metal oxides is detailed here, along with some of the most critical steps in the process.

3.1. *Chemical method*

As part of the chemical synthesis process, a reaction mixture is gradually heated from room temperature to a high temperature [15]. The chemical properties of surfactants, precursors, and high-boiling solvents are crucial to this process [15]. The chemical synthesis approach [15,24] can create metal oxide nanoparticles. It is possible to chemically produce nanoparticles of many metal oxides, including Fe_2O_3, Fe_3O_4, zinc oxide, magnesium oxide, titanium dioxide, cadmium oxide, cenoxite, and vanadium oxide [24].



Schematic 2. Methods of nanoparticle synthesis.

3.2. Sol-gel procedure

Traditional and widely used in industry, the sol-gel process can produce nano and microstructures of excellent quality [4]. Zinc oxide, MgO, TiO_2, ZrO_2, CuO, Al_2O_3, TiO_2–SiO_2, and SiO_2–Al_2O_3 with aluminum oxide are all manufactured using this system [2]. This process includes the steps of crystallization, aging, condensation, and drying [2].

A) Hydrolysis, which involves combining solvents with metal alkoxide (MA) precursors
B) The removal of solvents (condensation) leads to the formation of a polymer network composed of metal oxide connections.
b) As the solution ages, it forms a gel-like network with liquid and solid components.
d) Gels that dry, with the hydroxyl groups on their surfaces removed (drying)
c) Pressing it into a solid ceramic form or crystallizing it into a crystalline substance

3.3. Co-precipitation technique

This process involves dissolving the salt precursor (metal salts such as nitrates or chlorides) in an aqueous solution and then converting it to metal hydroxide by adding ammonium or sodium hydroxide [24]. The resulting salt is washed, and the metal oxide nanoparticles are obtained by heating to remove hydroxides [15]. For example, the co-precipitation approach can produce Fe_3O_4, $BiVO_4$, SnO_2, Co_3O_4, NiO, and ZrO_2 nanoparticles [24]. Low synthesis temperature, simplicity of processing and scaling up, low cost, and flexibility in modulating core and surface properties are some of the possible benefits of this approach [24].

3.4. Hydrothermal method

Hydrothermal methods allow for the creation of binary metal oxide nanoparticles, such as CuO, by reacting vapors from aqueous solutions with solid materials at high temperatures and vapor pressures, resulting in the deposition of microscopic particles [15].

3.5. Sonochemical method

Sonochemical synthesis involves preparing nanomaterials for a chemical reaction using high-intensity ultrasound sonication of metal salts in solution with oxygen [15]. The sonochemical preparation of nanoparticles of metal oxides, including CuO, ZnO, NiO, and MnO, is somewhat recent [24].

3.6. Laser ablation method

A process known as laser ablation uses the irradiation of colloidal solution targets dissolved in solvents to reduce particle size to the nanometer range [25]. A number of factors, including laser wavelength, pulse duration and energy, ablation time, laser fluency, and surfactant effects, determine the characteristics of the metal particles that are created [4]. Cu, CuO, Cu_2O, ZrO_2, ZnO, Fe_3O_4, NiO, Al_2O_3, SnO_2, and Au–SnO_2 have also been synthesized by the laser ablation method [24].

3.7. Biosynthesis methods

Many different types of metal oxide nanoparticles can be synthesized by nature in natural settings [24]. The low energy need of biological synthesis compared to its physicochemical alternatives has recently piqued much interest in producing metal oxide nanoparticles employing various plant extracts, fungi, and bacteria [20]. Compared to physical and chemical approaches, the inability to achieve nanoparticles of desirable size and shape with a low yield is the greatest obstacle in biological synthesis [24]. many metal and metal oxide nanoparticles such as Au, Ag, Fe_3O_4, CuO, ZnO, MgO, and TiO_2 can be synthesized by biosynthesis [15].

3.8. Other methods

Depending on the properties of the metal/metal oxide nanoparticles required for application, many other synthetic strategies such as the electrochemical method, polyol method, wet chemical method, microwave method, physical vapor deposition method, solvothermal method, microemulsion method, and combustion method can be used [4,16,20,23]. Choosing the right synthesis method for creating metal oxide nanostructures significantly affects their size, toxicity, monodispersity, and stability, as mentioned before [24].

4. Properties of metal oxide nanoparticles

Due to their exceptional physical and chemical characteristics, metal oxide nanoparticles are promising candidates for use in various biomedical contexts [26]. Several factors significantly impact the characteristics of metal oxide nanoparticles, including their toxicity, magnetic and optical properties, antibacterial capabilities, porosity, crystallinity, concentration, pH, temperature, and pressure (10). Nanoparticles' antibacterial activity can be enhanced by subjecting them to high heat conditions, large surface area, and low pH [10].

The antibacterial activity is enhanced due to the tiny particles' increased contact with bacteria and their bigger surface area [27].

Variations in nanoparticle concentration, shape, porosity, and surface roughness can affect the surface area-to-volume ratio [10].

Numerous studies have shown that their form can affect nanoparticles' antibacterial activity [10]. By manipulating the solvents employed, the concentration of those solvents, the temperature and pH of the preparation environment, and the synthesis procedure, a variety of nanoparticle shapes, sizes, and configurations can be created [10]. Nanoparticles in higher concentrations indicate better antibacterial activity [10].

Evidence shows poorly soluble compounds might induce a reduced cytotoxic response [28]. Acidic pH enhances Zinc oxide NP solubility, which in turn improves their hazardous characteristics, as demonstrated by *Saliani* et al. [29]. The antibacterial action of nanoparticles is improved when the pH of the medium is decreased to an acidic range, which releases ions from the nanoparticles. Bacteria also have their amino acids and peptides augmented when the nanoparticles dissolve in their bodies [29]. Hence, each nanostructure with different production conditions has unique antibacterial and toxicity properties [30].

4.1. Antibacterial properties

The antibacterial properties of some metal and metal oxide nanoparticles, such as gold, silver, copper, titanium dioxide, zinc oxide, magnesium oxide, iron oxide, and cerium oxide, show great potential against various microorganisms [3]. Since microbial pathogens are unable to build resistance to them, they are extremely effective against bacteria that have developed resistance to different kinds of antibiotics [15]. Metal oxides can have antibacterial effects in both bulk powder and nanoparticulate form; iron oxide, for example, is solely bactericidal in its nanoparticulate form [31].

An assortment of Gram-negative and Gram-positive bacteria, including *A. actinomycetemcomitans, C. jejuni, E. coli, S. aureus, S. mutans, S. salivarius, S. sanguis,* and *P. gingivalis*, have been demonstrated to exhibit antimicrobial activity by metal oxide nanoparticles in several investigations conducted during the last twenty years [31]. There are two potential ways in which these substances kill bacteria: (i) when the metal oxide comes into touch with the bacterial cell wall, destroying it through an oxidation reaction, and (ii) by producing more reactive oxygen species (ROS), primarily hydroxyl radicals and superoxide ions [8].

Factors affecting metal oxide nanoparticles' antibacterial efficacy include their size, shape, crystal structure, distribution, agglomeration, synthesis parameters, pH, and zeta [28].

There was a significant improvement in the inhibition of bacterial growth by smaller, more surface-to-volume-ratio metal oxide nanoparticles when compared to larger ones [10,15]. The difference in antimicrobial efficiency based on the size of the nanoparticles is due to an electrochemical interaction between the nanoparticles and the cell walls [28]. The contact between metal oxide nanoparticles and bacterial membranes is enhanced by their zeta potential, leading to the breakdown of membranes and the loss of intracellular contents [15].

4.2. Toxicity properties

There have been serious concerns about the toxicity of nanomaterials with increasing nanomaterial production rates [19, 32]. Developing novel nanomaterials that provide low toxicity and high biomedical performance is essential to achieve more efficacious therapy [19]. The leading cause of toxicity is producing reactive oxygen species, which can lead to inflammation, oxidative stress, and DNA, cell membrane, and protein damage [33]. Particle size, shape, distribution, aggregation mode, charge, chemical makeup, morphology, surface area, chemistry, and intrinsic qualities are among the several factors that significantly impact the hazardous effects [5]. Hence, creating nanoparticles with little or no toxicity requires careful regulation of their physicochemical characteristics. The toxicity phenomenon is very complicated, and nanoparticles with the same physical condition and chemical composition show other toxicological behaviors [5].

Since nanoparticle toxicity is strongly proportional to their size, bigger nanoparticles are safer than smaller ones [1]. The electrostatic interaction between the positively charged nanoparticles and the negatively charged cell membrane makes them far more hazardous than their negatively charged counterparts [15].

It is believed that the different crystal structures of the same nanoparticles can show different toxicity [5]. For example, among the different crystal structures of TiO_2, the rutile form has more toxicity, while the anatase form does not show considerable toxicity [5].

The general absence of toxicity in the bulk material leads most scientists to conclude that metal oxide nanoparticles are not harmful [34].

According to Dasai et al. the toxicity ranking in low-light settings was as follows: $ZnO > CuO > Co_3O_4 > TiO_2$ [35]. It was also demonstrated that, when exposed to light, the toxicity was as follows: $ZnO > CuO > TiO_2 > Co_3O_4$ [35].

5. Metal and metal oxide nanoparticles in endodontic treatment

Utilizing nanoparticles as innovative dental materials offers a solution to numerous issues linked to conventional methods of treating oral disorders, thanks to their unparalleled physicochemical and biological characteristics [36,37]. Dental cavities, periodontal disease, sensitivity to the teeth, and precancerous and malignant mouth diseases can all develop due to an oral infection [36].

Potentially more effective antibacterial and antibiofilm treatment techniques based on metal oxide nanoparticles might be implemented in the dental field [38]. In recent years, many researchers have examined metal oxide nanoparticles as a novel treatment modality in dentistry. These nanoparticles have shown great promise in light polymerization composite resins and bonding systems, bioceramics, endodontic sealers, and coating materials for dental implants. Additionally, they have demonstrated superior antibacterial efficacy against pathogens [39].

Research in endodontics has demonstrated that certain metal oxide nanoparticles can enhance antibacterial effectiveness, restore mechanical integrity to damaged dentin matrix, and promote tissue regeneration [38]. Bacterial biofilms cause primary and secondary root canal infections [40].

The treatment may not be successful when germs remain in the root canal system after an endodontic treatment [41]. Consequently, antimicrobial irrigation and mechanical instrumentation are essential for effective endodontic therapy [41]. A root canal irrigation protocol, along with root canal cleaning and shaping, is crucial for reducing the number of microorganisms in the canal. However, it is impossible to eliminate dental infections due to the polymicrobial nature of endodontic infections, which include actinomyces, enterococcus, streptococcus, peptostreptococcus, and countless more [42,43].

Improving the eradication of endodontic infections and treatment requires the employment of novel nanomaterials [44]. Endodontic irrigants, endodontic sealers, and intracanal medicaments utilizing various carriers have been developed over the past ten years, employing multiple metal and metal oxide antibacterial nanoparticles [42]. Schematic 3 displays a selection of the crucial metal oxides utilized in endodontic treatment. There has been much interest in using nanoparticles to improve the mechanical characteristics and antibacterial capabilities of materials and in using these materials to regenerate sick tissue [45].

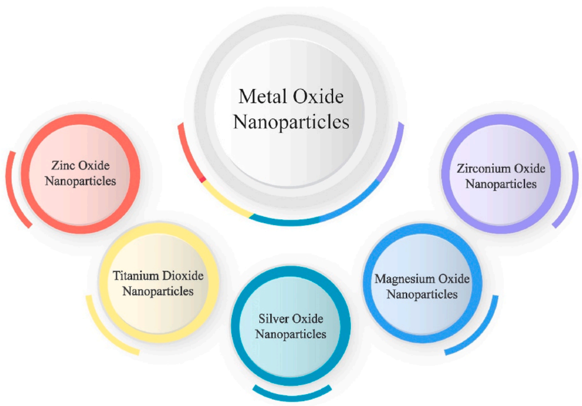
5.1. *Zinc oxide nanoparticles*

Root canal sealers made of zinc oxide nanoparticles are popular because they prevent pulp chamber and apical microbiome leakage and invasion [38,46,47]. Zinc oxide nanoparticles are also shown to exhibit antibiofilm activity against many strains, such as *Enterococcus faecalis*. According to Kishen et al. antibacterial nanoparticles such as zinc oxide, chitosan/zinc oxide, or chitosan-layer-zinc oxide significantly decreased *E. faecalis* adhesion [48]. Regarding primary endodontic infections, *S. aureus* is among the most commonly isolated species [49]. Kozuszko et al. [49] made it easier for zinc oxide nanoparticles and graphite-type carbon microparticles to fight *S. aureus* bacteria while being biocompatible. One area where zinc oxide nanoparticles showed promise was in regenerative endodontics [49]. Zinc oxide nanoparticles were potential material in the regenerative endodontic field [49].

Endodontic treatment makes use of a variety of root canal sealers [50]. Through intra-canal administration, zinc oxide nanoparticles combined with polyethylene glycol and either calcium hydroxide or neither exhibited antibacterial action against *Escherichia coli*, Candida albicans, *Klebsiella pneumoniae*, Pseudomonas aruginosa, and *Staphylococcus aureus* [39]. Researchers Versiani et al. examined how adding zinc oxide nanoparticles to Grossman sealer changed its physicochemical characteristics. Grossman sealer's flowability, solubility, dimensional stability, and radiopacity were all enhanced, and the setting time was reduced when 25 % of the usual zinc oxide powder was substituted with zinc oxide nanoparticles [46]. Hadi et al. sought to determine whether endodontic sealers containing zinc oxide nanoparticles could inhibit the growth of Candida and *E. faecalis* [51]. Antibacterial activity against Candida and *E. faecalis* strains was very good at all concentrations of zinc oxide nanoparticles [51].

The concentration of zinc oxide nanoparticles determines their antibacterial impact; a larger concentration shows a greater bactericidal action [45].

Researchers found that adding zinc oxide nanoparticles to silymarin-mediated HAP increased its antibacterial efficacy against several oral infections [52]. The success or failure of endodontic treatment is heavily dependent on endodontic sealers [43]. A sealer made of zinc oxide and silver and zinc oxide nanoparticles was tested for its antibacterial activity against *Escherichia coli* [43]. Research has shown that different nanoparticles add different levels of antibacterial activity to sealer. For example, sealer mixed with silver nanoparticles had the most potent antibacterial effect, while sealer mixed with zinc oxide nanoparticles had the weakest [43]. The effectiveness of a sealer containing calcium hydroxide, chitosan nanoparticles, and zinc oxide nanoparticles in inhibiting the growth of two different strains of *Escherichia coli* was assessed by Nair et al. [53]. Calcium hydroxide sealers containing zinc oxide nanoparticles had a much lower optical density value than those containing chitosan nanoparticles. Regarding endodontic sealers, zinc oxide nanoparticles have better antibiofilm efficacy than chitosan nanoparticles against both *E. faecalis* strains [53]. According to some



Schematic 3. Metal oxide nanoparticles in endodontic treatment.

reports, endodontic infection removal may be aided by irrigants' chemical characteristics and concentration [54]. Novel nanoparticle solutions have been developed during endodontic therapy due to the restricted disinfection activity induced by regularly used root canal irrigants [55]. Researchers Kishan et al. tested the efficacy of irrigant solutions containing zinc oxide nanoparticles and sealers based on zinc oxide against *E. faecalis* biofilms that develop on root dentin [48]. The results showed that the presence of zinc oxide nanoparticles increased the antibacterial activity of the zinc oxide-based sealer and reduced bacterial adhesion to the dentine wall by 95 % [48]. Furthermore, Sridevi et al. [56] also found similar outcomes. Here, Shertha et al. assessed the efficacy of zinc oxide nanoparticles as an irrigant solution against both planktonic and biofilm forms of *Escherichia coli*. The authors saw a decrease in biofilm thickness.

Core root filling products made of gutta-percha cones are popular because they are biocompatible, inexpensive, have a long shelf life in the clinic, and may have antibacterial qualities [57,58]. After endodontically treated roots were filled with gutta-percha and AH Plus sealer, Jowkar et al. tested the fracture resistance of the treated roots using root canal irrigants consisting of titanium dioxide nanoparticles, zinc oxide nanoparticles, and silver nanoparticle solution [54]. Endodontically treated roots were more resistant to fracture after nanoparticle irrigation of the channels [54]. In addition, Almeida et al. showed that traditional endodontic irrigants, solutions with silver and zinc oxide nanoparticles, and other antibacterial agents were effective against the root canal biofilm of *Enterococcus faecalis* [55]. Comparable to traditional endodontic irrigants, they discovered that 1 % Ag and 26 % Zinc oxide nanoparticles effectively removed *E. faecalis* biofilm [55]. Using a rapidly dissolving nanofibrous film, Chachlioutaki et al. assessed the efficacy of intracanal coadministration of zinc oxide nanoparticles, an anti-inflammatory drug, and ketoprofen [59]. Among the most common microorganisms found in the root canal area, they demonstrated that nanofibrous film was efficient against *E. faecalis*. Among the most common microorganisms found in the root canal area, they showed that nanofibrous film was efficient against *E. faecalis* [59]. According to Wang et al. zinc oxide nanoparticles have low cell cytotoxicity in vitro and exhibit outstanding antibacterial activity against P. gingivalis and A. naeslundii [60].

The success of root canal therapy depends on using an endodontic sealer with appropriate mechanical qualities [61]. The results showed no discernible change in the mechanical properties of dental adhesives and composite resins after adding zinc oxide nanoparticles [62]. The push-out binding strength of fiber posts to root dentin utilizing resin cement was investigated and compared by Jowkar et al. when intraarticular dentin pretreatment with silver, zinc oxide, and titanium oxide nanoparticles was applied [62]. Regarding the fiber posts, there were no discernible variations in push-out bond strength between the zinc oxide and titanium oxide nanoparticles, and the silver nanoparticles demonstrated the highest values compared to the other two types of nanoparticles [62].

Table 1
Research reviews on the use of zinc oxide nanoparticles for endodontic.

Formulations NPs	Applications	Findings	ref
a sealer made of zinc oxide that contains nanoparticles of both zinc oxide and silver	Antibacterial properties of nanoparticles have recently come into the spotlight in endodontic therapy	Although the difference was insignificant, silver nanoparticles had superior antibacterial activity to zinc oxide nanoparticles.	[43]
Small carbon particles with a graphite-type structure and zinc oxide nanoparticles	Antibacterial effect and biocompatibility of Zinc oxide nanoparticles and graphite-type carbon microparticles against *S. aureus*	Nanoparticles of zinc oxide showed promise as a material for regenerative endodontics.	[49]
Zinc oxide nanoparticles with endodontic sealers	Antibacterial activity of combination zinc oxide nanoparticles with endodontic sealers against *E. faecalis and Candida*	All concentrations of Zinc oxide nanoparticles showed perfect antibacterial activity on *E. faecalis* and Candida strains.	[51]
Zinc oxide nanoparticles and silymarin-mediated HAP	Striking out *S. aureus*, S. mutans, *E. faecalis*, and Candida albicans as antibacterial agents	Silymarin-mediated HAP and zinc oxide nanoparticles had antimicrobial activity against oral pathogens.	[52]
Silicone sealant with chitosan and zinc oxide nanoparticles	Effectiveness of a sealer including calcium hydroxide, chitosan nanoparticles, and zinc oxide nanoparticles against biofilms	The efficacy of a sealant including nanoparticles of zinc oxide, chitosan, and calcium hydroxide in the presence of biofilms	[53]
zinc oxide, Silver, and titanium dioxide nanoparticles	Endodontically treated root fracture resistance as a function of three different nanoparticle solutions administered as final root canal irrigants	Endodontically treated roots had improved fracture resistance. Among the tested substances, NaOCl had the lowest FR value.	[54]
Silver and zinc oxide nanoparticles	Endodontic irrigants formulated with silver and zinc oxide nanoparticles exert antibacterial action against the *E. faecalis* biofilm in root canals.	*E. faecalis* biofilm was effectively inhibited by 1 % Ag nanoparticles and 26 % ZnO nanoparticles.	[55]
nanoparticles of zinc oxide and fluorinated graphene combined with a ZnO-based sealant	The effectiveness of a sealer including zinc oxide, fluorinated graphene, and zinc oxide nanoparticles against microorganisms	Compared to pure ZnO-based sealer, the antibacterial impact of sealer blended with various nanoparticles was significantly better.	[56]
Nanofibrous film of zinc oxide nanoparticles and ketoprofen	Investigate the feasibility of intracanal coadministration of zinc oxide nanoparticles, an antibacterial, and ketoprofen, an anti-inflammatory, using the rapidly dissolving nanofibrous film.	The nanofibrous film was effective against *E. faecalis*,	[59]
zinc oxide nanoparticles	Zinc oxide nanoparticles' impact on cell function, biofilm formation, and antibacterial activity in an infected root canal	Zinc oxide nanoparticles had excellent antibacterial activity against *P. gingivalis* and *A. naeslundii* and had low cell cytotoxicity in vitro	[60]
Zinc oxide nanoparticles	Find out how well zinc oxide nanoparticles kill all the microbes in a root canal system, including *E. faecalis* and candida.	An increase in concentration increased bacterial sensitivity to zinc oxide nanoparticles.	[66]

According to Eskandarinezhad et al. zinc oxide nanoparticles added to mineral trioxide aggregate did not reduce the aggregate's compressive strength, and these nanoparticles can be utilized to alter the aggregate's other characteristics as well [63]. According to the measurements taken by Elkateb et al. [64], the zinc oxide-based Pulp Canal Sealer was found to have a deeper tubular penetration when combined with nanoparticles of zinc oxide, Ag, and doped zinc oxide-Ag. Their results demonstrated that the flowing qualities of endodontic sealer materials were enhanced by nanoparticle addition, with Ag nanoparticles exhibiting the deepest penetration [65]. Grossman Sealer's physicochemical characteristics were studied by Versiani et al. who studied the addition of zinc oxide nanoparticles in varying concentrations [47]. Comparatively, sealers containing 25 % zinc oxide nanoparticles exhibited far lower solubility levels and dimensional alteration [46]. The research on the use of zinc oxide nanoparticles in endodontic treatment is summarized in Table 1. Even though zinc oxide nanoparticles are one of the most cutting-edge new dental materials, using them as a root canal sealant to eradicate infected microbes during endodontic treatment is still challenging.

5.2. Titanium dioxide nanoparticles

Nanosized titanium dioxide particles are biocompatible, nontoxic, and highly stable, with suitable photocatalytic and antibacterial properties [67]. Titanium dioxide nanoparticles are increasingly used in endodontic and root canal therapy (68). Developing nanoparticles in endodontics aims to enhance mechanical characteristics and antibacterial activity [38].

Table 2 summarizes the research on root canal treatment with titanium dioxide nanoparticles. According to many investigations, titanium dioxide nanoparticles enhanced traditional glass ionomer cement's mechanical and bactericidal properties [68]. Elsaka et al. demonstrated that conventional glass ionomers exhibited enhanced fracture toughness, flexural strength, and compressive strength characteristics, in addition to enhanced antibacterial capabilities against S. mutans, when 3 % and 5 % (w/w) titanium dioxide nanoparticles were added to them [68]. However, their mechanical characteristics were drastically diminished when glass ionomers were combined with 7 % (w/w) titanium dioxide nanoparticles [68]. The compressive strength of the modified calcium silicate-based cement may not be affected by the addition of nano-scale titanium dioxide particles within a concentration range of 1 %–5 %, according to specific reports [69]. Given the high failure rate of endodontic treatments, restoring teeth that have undergone this procedure is a significant concern [70]. *Sihivahanan* et al. improved the mechanical properties of MultiCore Flow and everX Flow composite resin by incorporating 2.5 % titanium dioxide nanoparticles as a filler [70]. Mineral trioxide aggregates are used in many challenging endodontic procedures [71].

Zinc, silver, and titanium dioxide nanoparticles have been added to mineral trioxide aggregate to enhance its characteristics [71].

Table 2
Review of research on titanium dioxide's use in endodontic.

Formulations NPs	Applications	Findings	ref
Silver/Zinc oxide/and Titanium dioxide	Test the fracture resistance of roots that have undergone endodontic treatment using three different nanoparticle solutions that are utilized as final irrigants in root canals.	Endodontically treated roots were more resistant to breakage after final treatment with nanoparticles.	[54]
Silver/Zinc oxide/Titanium oxide nanoparticles + resin cements	Evaluate the push-out bond strength of fiber posts with silver/zinc oxide/titanium oxide nanoparticles	Intraradicular dentin pretreatment with silver/zinc oxide/titanium oxide nanoparticles did not interfere with using fiber posts' push-out bond strength	[63]
Titanium dioxide nanoparticles + composite resin with everX Flow and MultiCore Flow	Evaluation of the mechanical properties of composite resins using nanoparticles of titanium dioxide	The mechanical characteristics of composite resin were enhanced when 2.5 % titanium dioxide nanoparticles were added.	[70]
Titanium dioxide nanoparticles + conventional glass-ionomer	Evaluate the physical and antibacterial properties	GI-containing 3 % (w/w) TiO_2 nanoparticles improved mechanical and antibacterial properties	[68]
Titanium dioxide nanoparticles + calcium silicate-based cement	Test the impact of adding titanium dioxide nanoparticles to modified cement made of calcium silicate on its compressive strength.	Incorporating titanium dioxide nanoparticles in a concentration range of 1 %–5 % does not affect the improved calcium silicate-based cement's compressive strength.	[69]
Titanium dioxide nanoparticles + mineral trioxide aggregate	Titanium dioxide nanoparticle biocompatibility testing with mineral trioxide aggregate	The addition of TiO_2 nanoparticles at a weight percentage of 1 wt% did not affect the biocompatibility of mineral trioxide aggregate.	[71]
Titanium dioxide nanoparticles + mineral trioxide aggregate	Analyze the titanium dioxide nanoparticle-aggregated mineral trioxide's physical characteristics.	Setting time, working time, compressive strength, and push-out bond strength of mineral trioxide aggregate were all enhanced by adding titanium dioxide nanoparticles with a weight ratio of 1 %.	
Silver and titanium dioxide nanoparticles + mineral trioxide aggregate	Analyzing the cytotoxic effects of aggregates of mineral trioxide with nanoparticles of titanium dioxide and silver	Mixing silver or titanium dioxide nanoparticles with mineral trioxide aggregate can improve antibacterial activity.	[72]
Titanium dioxide nanoparticles + fiber-reinforced composite	The strength of fiber micro-tensile bonds was assessed. Surface treated with nanoparticles of titanium dioxide	Out of all the materials tested, the composite resin with 5 % titanium dioxide nanoparticles bonded the best to the fiber-reinforced composite post.	[73]
Titanium dioxide nanoparticles	Root canal walls treated with a 4 % titanium tetrafluoride solution were examined for their impact. walls	Endodontics might benefit from this framework.	[74]

Samiei et al. found that including titanium dioxide nanoparticles at a weight ratio of 1 % improved the mineral trioxide aggregate's compressive strength, push-out bond strength, setting time, and working time [75].

Samiei et al. explored the biocompatibility of mineral trioxide aggregate with 1 wt% titanium dioxide nanoparticles with human gingival fibroblasts [71]. According to their findings, titanium dioxide nanoparticles added to mineral trioxide aggregate at a concentration of 1 wt percent did not compromise its biocompatibility [71]. Endodontically treated teeth lacking coronal structure are the most common candidates for fiber-reinforced composite post-placement [63]. Jowkar et al. [63], with the help of silver, zinc oxide, and titanium dioxide nanoparticles, studied the influence of fiber posts on the push-out bond strength to root canal dentin. The group that used silver nanoparticles outperformed the others [63]. A similar result was obtained by *Dsouza* et al., they exhibited that the addition of titanium dioxide nanoparticles into mineral trioxide aggregate showed favorable cell viability and biocompatibility [72].

Fiber posts have several desirable qualities, making them an excellent choice for endodontically treated tooth restoration. These include resistance to corrosion, improved dentin bonding, and a reduced risk of vertical root fracture [73]. Sihivahanan et al. assessed the experimental dental composite resin's micro tensile bond strength using fiber posts filled with titanium dioxide nanoparticles [73]. Compared to other conventional composite resins, such as Multicore Flow, the experimental resin with 5 % titanium dioxide nanoparticles formed a stronger bind to the fiber-reinforced composite post [73].

According to Ramya and Rajaseka [76], titanium dioxide nanoparticles have shown promising antimicrobial and antifungal effects against a variety of gram-positive and gram-negative bacteria. They also showed promising antibacterial action against S. mutans and lactobacillus.

The root canal space can be effectively cleaned, and biofilms can be better removed using root canal irrigation solutions [54]. Endodontists have long relied on a variety of irrigation treatments, but a new, non-toxic option has emerged: titanium dioxide nanoparticles [54]. Researchers Jowkar et al. found that endodontically treated roots were more resistant to fracture when final root canal irrigants made of silver, zinc oxide, and titanium dioxide nanoparticle solutions were utilized [54].

In endodontics, titanium dioxide nanoparticles improve mechanical properties and remineralization of the tooth structure. This is achieved by lowering biofilm formation, inhibiting demineralization, and counteracting the ever-growing microorganisms related to caries and endodontics.

Table 3
Summary of studies that evaluated the application of silver and silver oxide in endodontic.

Formulations NPs	Applications	Findings	ref
Silver nanoparticles	Evaluate the cytotoxicity of different types of silver nanoparticles	Silver nanoparticles had no cytotoxic at 25 mg/mL or lower concentrations.	[77]
Silver oxide with graphene oxide nanocomposite	Evaluation of antibacterial activity	They are promising antibacterial and antibiofilm agents	[79]
Silver nanoparticle confined mesoporous structured bioactive powder.	Evaluation of antibacterial activity of silver nanoparticle against *E. faecalis*	-Antibacterial activities depended on the confining of silver nanoparticle position - In a root canal infection, they were effective against *E. faecalis* bacteria.	[80]
A combination of silver nanoparticles and a Nd-YAG laser	TThe combination of silver nanoparticles with Nd-YAG lasers has a bactericidal effect against *Enterococcus faecalis*.	The presence or absence of Nd: YAG laser irradiation did not affect the efficacy of silver nanoparticles in killing *E. faecalis*.	[81]
Silver nanoparticles	The Inhibitory action of silver nanoparticles on microorganisms in the root canal, necrosis	The use of these nanoparticles as an endodontic irrigation agent or sealer successfully decreased inflammation in the root canal.	[82]
Dimethylaminohexadecyl methacrylate + silver nanoparticles	Evaluation of long-lasting antibiofilm effects of new root canal sealer	Endodontic sealer demonstrated strong antibiofilm capabilities while retaining its physical and sealing characteristics.	[83]
Chitosan and silver nanoparticles coated Gutta-percha	Evaluation of antibacterial activity for endodontic applications	Higher antibacterial potency for a higher increase in the success rate of root canal therapies was accompanied by a rise in antibacterial potency.	[84]
Silver nanoparticles are synthesized on an aqueous graphene oxide matrix.	Evaluation of antimicrobial efficacy of silver nanoparticles synthesized on an aqueous graphene oxide matrix	Graphene oxide nanoparticles produced in water significantly decreased total biovolumes.	[85]
Silver and gold nanoparticles	Evaluation of the *En-face* optical coherence tomography analysis of silver and gold nanoparticles as irrigating solutions used in endodontic treatment.	Because of their optical opacity, both nanoparticles are used as root canal irrigants.	[86]
Silver nanoparticles	Detection of genes related to resistance to silver nanoparticles in bacteria from secondary endodontic infections	A high frequency of silCBA silver resistance genes (73.3 %) was attained.	[87]
Silver oxide nanoparticles	Evaluation of physical and mechanical properties of glass-ionomer cements	Both GICs had their surface roughness improved by adding nanofillers.	[88]
Silver nanoparticles	Assessing the antimicrobial efficacy of photodynamically activated silver nanoparticles in root canal infections	As an auxiliary tool for root canal system disinfection, it shows promise.	[89]

5.3. Silver and silver oxide nanoparticles

Silver and silver oxide nanoparticles were used in various medical areas because of their broad antimicrobial activity and low toxic effects on cells and tissues [77,78]. According to *Takamiya* et al., silver nanoparticles showed no cytotoxic effects at 25 mg/mL or lower concentrations [77]. Numerous studies have illustrated the potency of silver and silver oxide nanoparticles in endodontic therapy (Table 3).

By interacting with oxygen, silver forms various phases, such as Ag_2O, AgO, Ag_2O_3, and Ag_3O_4. In the past decade, Ag_2O nanoparticles have been widely investigated as interesting materials owing to their unique properties [90]. Silver oxide nanoparticles were found to have good antimicrobial activity [78]. In their investigation, Sondi and Salopek-Sondi demonstrated that silver oxide nanoparticles effectively inhibited the growth of *E. coli* bacteria. A graphene oxide nanocomposite adorned with silver oxide exhibited remarkable antibacterial and antibiofilm properties, as shown by Khan et al. [79]. This material could potentially be employed to impede the proliferation of human bacterial pathogens linked to long-term illnesses. Researchers Vithiya et al. [90] examined how well silver oxide nanoparticles killed harmful germs. Regarding effectiveness against bacteria, they demonstrated that silver oxide nanoparticles are on par with silver nanoparticles [90,91].

One potential endodontic use for silver nanoparticles is disinfection, specifically, their use in root canal procedures to flush out bacteria and other debris [77]. To avoid infection or re-infection of the root canal space, several endodontic materials, such as cement, root canal sealers, and gutta-percha, have silver nanoparticles added to them [92]. Kung et al. assessed the antimicrobial efficacy of a bioactive powder containing silver nanoparticles in a mesoporous structure against *E. faecalis*, a bacteria that infects root canal systems [80]. They found that the antibacterial effects of silver nanoparticles were location-dependent, with intermesopore confinement producing the best results against *E. faecalis* infections in root canals [80]. When tested against S. mutans, other studies found that silver nanoparticles were more efficient than chlorhexidine as an antibacterial agent [93]. Combining silver nanoparticles with a Nd:YAG laser demonstrated antimicrobial properties, effectively eliminating biofilms and resistant bacteria lodged deep within the dentinal tubules, which are inaccessible to traditional disinfection methods [81].

An endodontic sealer's antibacterial properties can help eliminate those pesky root canal germs [94]. In endodontics, silver nanoparticles were used as a sealer or irrigating agent to eradicate specific bacterial and fungal species, such as Streptococcus sp., *Staphylococcus aureus* sp., Candida sp., Actinomyces sp., Actinobacillus sp., and Bacillus sp [94]. A novel root canal sealer was created by combining dimethylaminohexadecyl methacrylate with silver nanoparticles. Baras et al. [83] found that adding silver nanoparticles enhanced the biofilm-inhibition performance of the sealer. According to their findings, a sealer containing 0.15 % silver nanoparticles and 5 % dimethylaminohexadecyl methacrylate significantly improved microbial clearance, warding off additional endodontic infections and potential root canal system recontamination in the future [83].

Because of its biocompatibility, pliability, dimensional stability, radio-opacity, and ease of removal, gutta-percha has been extensively investigated in endodontics as a root canal filler material [95,84]. As an antibacterial agent against *E. faecalis*, *S. aureus*, C. albicans, and *E. coli*, gutta-percha coated with silver nanoparticles has been developed for root canal treatment [96,97]. Adding chitosan and Ag nanoparticles to Gutta-percha demonstrated significant antibacterial effectiveness against *E. faecalis* [84]. covering gutta-percha with Ag nanoparticles has greater antibacterial activity than covering it with chitosan nanoparticles, according to Mohan et al. [84].

In addition, mineral trioxide aggregate is one bioactive endodontic cement that can be enhanced with silver nanoparticles to make it more efficient against endodontic pathogens [98]. To improve the effectiveness of pulp-capping, apexification, and closing perforations in teeth, mineral trioxide aggregate containing silver nanoparticles can inhibit bacterial recolonization [98]. Researchers Bahador et al. found that adding silver nanoparticles to mineral trioxide aggregate increased its antibacterial activity against anaerobic periodontal/endodontic bacteria [99].

There have been many attempts to make root canal irrigants more effective against germs by adding antibacterial chemicals to them [100]. Ag nanoparticles are a great option for endodontic treatment for intracanal irrigation [98]. Here, Ioannidis et al. compared sterile saline, EDTA 17 %, CHX 2 %, NaOCl 1 %, and 2.5 % as root canal irrigants against endodontic biofilms, as well as the antibacterial and biofilm disruption capabilities of a nano silver-graphene oxide combination [85]. While the authors found that 2.5 % NaOCl killed more microbes than the control groups, Ag-graphene could be a good substitute for NaOCl in root canal irrigation [85]. Another study evaluated the bactericidal activity of low-concentration Ag nanoparticles with that of 5.25 % NaOCl as an irrigation solution against *E. faecalis*, and the results showed that both solutions had comparable efficacy [101]. In a study conducted by Charannya et al. the antimicrobial effects of various solutions were compared. The results showed that the combination of 15 μg/mL Ag nanoparticles and 2 % CHX solution had the strongest antimicrobial effect, along with 85 % saline (control), 5 % NaOCl, 1 % NaOCl, 1 % Ag nanoparticles, and 26 % Zinc oxide nanoparticles solutions [102]. Topala et al. [86] assessed the efficacy of endodontic irrigating solutions containing gold and Ag nanoparticles using en-face optical coherence tomography. Endodontic irrigating solutions containing gold and Ag nanoparticles were used to clean and shape the root canal, as reported in the paper [86].

Despite all this research, Orozco et al. [87] found that endodontic bacteria can develop a resistance to Ag nanoparticles over time. Few studies have investigated the potential of silver nanoparticles for the long-term removal of bacteria from endodontic biofilms [100]. Hence, research into the potential uses of silver nanoparticles in endodontics needs to be maintained [103].

5.4. Magnesium oxide nanoparticles

The antibacterial action of magnesium oxide nanoparticles makes them a promising antimicrobial agent for treating endodontic infections [39].

While investigating the inhibitory effects of calcium hydroxide on *E. faecalis* species, Yousefshahi et al. compared the effects of copper, silver, magnesium oxide, and zinc oxide nanoparticles. Copper nanoparticles exhibited the best antibacterial properties when combined with calcium hydroxide, and combining 1 % of nanoparticles greatly enhanced antibacterial properties [104]. Dental cement that had been treated with zein-coated magnesium oxide nanoparticles was tested by Naguib et al. [105] for their antibacterial capabilities against *S. mutants*, *S. aureus*, *E. faecalis*, and *C. albicans*. The specific initial cement substrate influenced the antibacterial characteristics of dental cement incorporating Zein-modified magnesium nanoparticles [105]. According to a research study by Wu et al. modified resin composites with magnesium nanoparticles exhibited great antibacterial activity against *S. mutans* [106]. *Zhu* et al. reported that the silver-magnesium oxide nanocomposite exhibited effective antibacterial activity against *E. coli*, compared to pure magnesium oxide nanoparticles and equivalent silver nanoparticles alone [107].

Because of its outstanding physicochemical qualities, AH Plus has become the sealer of choice for root canal treatment [108]. Sun et al. enhanced AH Plus sealer's mechanical and bioactive properties by incorporating magnesium hydroxide nanoparticles. Their results demonstrated that modified AH Plus samples, particularly those containing 3 % magnesium hydroxide nanoparticles, exhibited remarkable biocompatibility and osteogenic characteristics, suggesting a high potential for use in endodontics [108]. Research by Meng et al. on the antibacterial properties of magnesium hydroxide nanoparticles and modified AH Plus sealer with these nanoparticles found that the latter exhibited better antimicrobial activity against S. mutans [109]. At the same time, the former could be used to eliminate residual bacteria and prevent reinfection. Using *S. mutans* and *S. sobrinus* as examples, Noori et al. showed that GIC with up to 1 wt percent MgO nanoparticles had great antibacterial action [110,111].

The antimicrobial properties of magnesium oxide nanoparticles in water were demonstrated to be [112]. To combat endodontic infections such as *Candida albicans*, *Staphylococcus aureus*, and *Enterococcus faecalis*, Monzavi et al. tested aqueous solutions of magnesium oxide nanoparticles at concentrations of 10 and 5 mg/L [113]. Magnesium oxide nanoparticle solutions (10 and 5 mg/L), 5.25 % NaOCl solutions, and 2 % CHX gluconate solutions did not differ significantly in their antibacterial efficacies against the endodontic pathogens studied [113]. But compared to NaOCl (5.25 %), magnesium oxide nanoparticles (5 mg/L) demonstrated statistically significant long-term efficacy in *E. faecalis* removal in the root canal system, suggesting that these nanoparticles may be a novel option for root canal irrigation [113]. According to another study, the endodontic pathogen *E. faecalis* was successfully eradicated in endodontic therapy using magnesium oxide nanoparticles as an irrigant solution [114]. Table 4 shows that there is currently a lack of research in this area; hence, more studies are necessary.

5.5. Zirconium oxide nanoparticles

Due to their unusual characteristics, nanoparticles of zirconium oxide, a chemical oxide, have recently attracted much attention in endodontics [67]. Table 5 reviews research on endodontic uses of zirconium oxide nanoparticles.

Nanoparticles of zirconium oxide have impressive physicochemical and mechanical characteristics, including high toughness, strength, corrosion resistance, biocompatibility, and low cytotoxic effects [67]. Viapiana et al. [123] examined the mechanical and physicochemical characteristics of endodontic sealers made of Portland cement that contained nanoparticles of zirconium oxide and niobium oxide. The results demonstrated that the sealers met the necessary criteria for clinical application, including low solubility, appropriate flowability, and compressive strength [123]. Zirconium oxide did not change the physicochemical characteristics of calcium silicate-based cement compared to microparticulate forms, according to Martelo et al. [124]. In their study, Gowri et al. demonstrated that zirconium oxide nanoparticles added to PMMA enhanced mechanical qualities while decreasing *C. albicans*

Table 4
Review of research on the use of MgO nanoparticles in endodontic.

Formulations NPs	Applications	Findings	ref
dental cements modified + magnesium oxide nanoparticles	Evaluation of antimicrobial properties	Magnesium oxide nanoparticle-containing dental cement showed significant antibacterial capabilities against Candida albicans and *Staphylococcus aureus*.	[105]
Light-cured resin composite + magnesium oxide nanoparticles	Evaluation of antimicrobial properties	Nanoparticles of magnesium oxide added remarkable antimicrobial and wear-resistant properties to resin composites.	[106]
AH plus + magnesium oxide nanoparticles	Evaluation of bioactivity	Magnesium oxide nanoparticles with an AH content of 3 % demonstrated excellent osteogenic and biocompatibility characteristics.	[108]
Calcium hydroxide + silver, copper, zinc oxide, or magnesium oxide nanoparticles	Evaluation of antibacterial properties	The antibacterial capabilities are enhanced when 1 % of the nanoparticles are combined.	[104]
Magnesium oxide nanoparticles	Test the efficiency of magnesium oxide nanoparticles as an antibacterial agent against the endodontic pathogen *Enterococcus faecalis*.	Endodontic treatment may soon use magnesium oxide nanoparticles as an alternate irrigating fluid.	[114]
AH Plus sealer + Magnesium Hydroxide nanoparticles	Evaluation of antibacterial activity	The antibacterial action of AH Plus was improved, and the antimicrobial effects were long-lasting when magnesium oxide nanoparticles were added to the solution.	[109]
Magnesium oxide nanoparticles	Evaluation of antimicrobial efficacy against endodontic pathogens	Aqueous solutions of magnesium oxide nanoparticles show promise as an antibacterial agent with low toxicity.	[113]

Table 5
Research summaries on zirconium oxide nanoparticles from endodontic.

Formulations NPs	**Applications**	Findings	ref
Epoxy resin mixed with Portland cement and niobium or zirconium oxide nano-and microparticles	Determine whether experimental root canal sealers can bioactivate.	Root canal sealers exhibited a degree of bioactivity	[115]
Adding radio-opacifier micro- and nanoparticles of zirconium oxide or niobium oxide to Portland cement	Evaluate the dentine-root canal sealer interface with two experimental sealers: one made of epoxy-based Portland cement and the other of epoxy resin, AH Plus.	The sealers showed promise and were similar to the AH Plus sealer.	[116]
Calcium phosphosilicate glass named + zirconium oxide nanoparticles	Developing a modern bioactive glass-based root canal sealer	Modern bioactive glass-based root canal sealer as a potential candidate for endodontic treatments	[117]
Portland cement + zirconium oxide nanoparticles	Evaluate the hydration chemistry and biocompatibility	The in vitro biocompatibility of zirconium oxide nanoparticles with MG63 osteosarcoma cells was positively affected.	[118]
Zirconium Oxide and Zinc Oxide Nanoparticles + Calcium Silicate-Based Material	Evaluate the Physicochemical Properties and Antibiofilm Activity	Although adding ZnO (at concentrations of 5 % or 10 %) considerably reduced the materials' compressive strength, it did not affect the antibiofilm action and gave Portland cement radiopacity.	[119]
Portland cement is associated with micro- and nanoparticles of zirconium oxide and niobium oxide	Evaluate the radiopacity, pH, and antimicrobial activity of	-All materials showed antimicrobial activity against the evaluated microorganisms - ZrO2 and Nb2O5 could be alternative radio-opacifiers to be added to calcium silicate materials	[120])
Nanoparticles and microparticles of zirconium oxide (ZrO2) and zinc oxide (ZnO) + white Portland cement	Examine the influence of zirconium oxide (ZrO_2), zinc oxide (ZnO), microparticles (MPs), and nanoparticles (NPs) mixed with white Portland cement.	White Portland cement containing ZnO and ZrO2 enhanced the activity of alkaline phosphatase and the release of calcium ions from human dental pulp stem cells.	[121]
Zirconium oxide/polyacrylamide nanocomposite	Evaluate the characterized effect of zirconium oxide/polyacrylamide nanocomposite as a sealer in root canal treatments.	Root canal-filling solutions made of nanocomposite have much promise. The sealers were clinically suitable, with sufficient setting periods and flowability.	[122]
Experimental endodontic sealers based on Portland cement modified with zirconium oxide and niobium oxide.	Determine the experimental endodontic sealers' physicochemical and mechanical qualities using Portland cement-based zirconium oxide and niobium oxide modifications.	We achieved satisfactory compressive strength and low solubility with the sealers. The setting times and flowability were suitable for clinical application.	[123]
Pulp capping material based on sodium trimetaphosphate + containing zirconium oxide and solution containing either chitosan or titanium oxide nanoparticles	Evaluate the mechanical, physicochemical, and antimicrobial properties	One possible substitute for the pulp complex protector is the cement, which contains nano- or microparticles of zirconium oxide, titanium oxide, and sodium trimetaphosphate.	[122]

adhesion [120].

Zirconium oxide nanoparticles reduce bacterial adhesion because they are insoluble in water [125]. Endodontists frequently use zirconium oxide nanoparticles as an antibacterial agent due to their potent antimicrobial properties against dental pathogens, including *E. faecalis* [67]. Research has shown that using zirconium oxide nanoparticles can differentiate *E. faecalis* and other bacteria [126]. Zirconium oxide nanoparticles showed marginally increased antibacterial activity against *P. aeruginosa* but no change in antimicrobial activity against *S. aureus* and *E. coli*, according to Li et al. [127]. Another study found that MG63 osteosarcoma cells were more viable in vitro when exposed to 20 wt% zirconium oxide nanoparticles. Additionally, the nanoparticles sped up the degree of hydration by 26 % in the first 24 h [118].

Because of its more significant control of root canal disinfection compared to typical calcium hydroxide intracanal medicament, triple or double antibiotic paste has been suggested as a better [128]. The antimicrobial activity of a double antibiotic paste comprising either zirconium oxide or barium sulfate was studied by Verma et al. [128]. Zirconium oxide nanoparticle-containing double antibiotic paste had vigorous antibacterial activity [128]. Using microparticulated and nanoparticulated zirconium or niobium oxide, Tanomaru et al. studied the characteristics of mineral trioxide aggregate and Portland cement, which are calcium silicate materials [119]. All the materials had promising antibacterial action against Candida albicans, *E. faecalis*, *Pseudomonas aeruginosa*, S. mutans, and K. rhizophila, although mineral trioxide aggregate demonstrated the highest radiopacity [119].

One radio-opacifier that has shown promise in endodontic treatment is zirconium oxide nanoparticles added to white Portland cement [129]. A more consistent microstructure over the entire canal length was demonstrated by Viapiana et al. for sealers that incorporate radio-pacifier nanoparticles [116]. Zirconium oxide nanoparticle loading improved the retention and sealing ability of epoxy resin- and Portland-based sealers by allowing them to penetrate dentinal tubules at the apical third [116]. In a study miming real-life oral circumstances, researchers found that root canal-filling materials made of zirconium oxide nanoparticles and polyacrylamide nanocomposite hydrogels performed better regarding radiopacity and stability [122]. According to the research conducted by Hu et al. zirconia oxide nanoparticles have an excellent radiopacity of 3 mm [130], which is in line with the recommendations made by the ISO/ADA.

Root canal sealer and root end filler materials should have bioactivity due to their extended proximity to the periapical connective tissues [115]. By adding nano and microparticles of zirconium oxide radio-opacifiers to innovative root canal sealers made of a combination of Portland cement, epoxy resin, and radio-opacifier, Viapiana et al. enhanced the bioactivity potential of these sealers and compared them to AH Plus and MTA Fillapex. There was little correlation between particle size and chemical characteristics, as demonstrated by the innovative root canal sealers [115]. Research by Huang et al. showed that bioactive glass-based root canals enhanced with zirconia oxide nanoparticles had higher radiopacity, better flow, and thinner sealer films [117]. Researchers Rahimi et al. found that human dental pulp stem cells' alkaline phosphatase activity and calcium ion release improved when combining zirconium oxide and zinc oxide nanoparticles [121]. Additional research is required to make these findings more applicable to endodontic therapy.

5.6. Other metal and metal oxide nanoparticles

Gold, nickel, iron, copper, calcium, and cerium oxide nanoparticles have demonstrated diagnostic and therapeutic potential in dentistry [8,130]. Most of these nanoparticles, consisting of metals and metal oxides, have strong antibacterial properties against both gram-positive and gram-negative bacteria [7]. Nanoparticles' unique physicochemical, biological, and antimicrobial characteristics have piqued interest in using them as dental materials [8]. Metal and metal oxide nanoparticle activity is typically dose- and time-dependent, pH- and mixture concentration, and distribution-dependent [7]. However, there is a lack of information regarding the use of these nanoparticles in dental materials and procedures. Thus, additional research is needed in this area.

6. Conclusion

Metallic and metal oxide nanoparticles, including those of silver, copper, gold, platinum, aluminum oxide (Al_2O_3), titanium dioxide (TiO_2), zinc oxide (ZnO), copper oxide (CuO), cobalt (II, III) oxide (Co_3O_4), indium oxide (In_2O_3), magnesium oxide (MgO), silicon dioxide (SiO_2), zirconium dioxide (ZrO_2), chromium (III) oxide (Cr_2O_3), nickel (III) oxide (Ni_2O_3), manganese (III) oxide (Mn_2O_3), cobalt oxide (CoO), and nickel oxide (NiO), are members of the broader nanomaterial category and have been utilized across various medical fields. The unique physical and chemical properties of metal oxide nanoparticles have garnered significant attention. Generally, when used in sufficient concentrations to eradicate bacteria, these nanoparticles present minimal risk to humans. Due to their biocompatibility and antibacterial properties, some of these metallic and metal oxide nanoparticles are particularly well-suited for applications in nano-dentistry. Despite their numerous advantages, these nanoparticles have a tendency to aggregate and adhere to each other. Nevertheless, additional research is required to develop strategies that minimize the risks associated with the use of metal and metal oxide nanoparticles in dental treatments.

7. Future directions

In summary, nanomaterials offer significant hope for combating diseases caused by oral bacteria, with the possibility of leading to long-term, sustained enhancement of the oral microenvironment. Current research is concentrating on creating disinfectants and sealants at the nanoscale, which aim to eliminate persistent pathogens in endodontic treatments and ensure a durable seal to ward off reinfection. Furthermore, investigations are underway to assess the biocompatibility and bioactivity of these materials, with the goal of confirming that they not only address the disease but also facilitate the regeneration of dental tissues. With the progression of nanotechnology, we anticipate the emergence of more advanced and efficient interventions utilizing nano metals and metal oxide, which are poised to transform the treatment of endodontic diseases. These innovations are likely to provide patients with better results and could decrease the need for more invasive procedures.

Funding

This study was supported by Research Council of Kermanshah University of Medical Sciences.

Availability of data and materials

The data used to support the findings of this study are included within the article.

CRediT authorship contribution statement

Roohollah Sharifi: Writing – review & editing, Supervision, Resources. **Ahmad Vatani:** Writing – original draft, Visualization, Investigation. **Amir Sabzi:** Writing – original draft, Investigation, Conceptualization. **Mohsen Safaei:** Writing – review & editing, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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