REVIEW ARTICLE

Zein-Coated MgO Nanoparticles as a Potential Antimicrobial Agent in Dentistry: A Review

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Abstract

The increasing prevalence of antibiotic resistance and the resurgence of infectious diseases have spurred a critical need for novel antimicrobial solutions. Nanoparticles (NPs) have emerged as a highly promising class of therapeutic agents, distinguished by the unique physicochemical properties that enable them to effectively inhibit the growth of microorganisms. The burgeoning interest in harnessing NPs for their antimicrobial potential has instigated extensive scientific inquiry. Simultaneously, nanotechnology, a multidisciplinary field focused on the design and development of materials, tools, and systems with distinct physical, chemical, and biological attributes at the nanoscale, has garnered significant attention. This interest is largely driven by the potential advantages it offers, particularly in fields like dentistry and medicine. Therefore, it becomes paramount to gain a profound understanding of the fundamental principles underpinning nanotechnology to appreciate its multifaceted applications in our daily lives. Recent advancements in this realm have highlighted Zein-coated Magnesium Oxide Nanoparticles (MgO NPs) as an especially promising antimicrobial agent with considerable potential. These nanoparticles exhibit potent antibacterial properties and can be seamlessly integrated into various dental formulations when combined with other materials. This collaborative approach opens up new avenues for developing innovative dental products that possess enhanced antimicrobial capabilities. The utilization of Zein-coated MgO NPs as a foundational component in dental formulations underscores their significance and underscores the broader implications of nanotechnology in addressing critical healthcare challenges. In light of these breakthroughs, the imperative to delve deeper into the intricacies of nanotechnology becomes evident, as it holds the key to unlocking transformative solutions for the improvement of societal well-being and public health.

Keywords: Antibacterial; Innovative Zein-Coated Magnesium Oxide Nanoparticles; Nanoscale; Therapeutic.

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1. Introduction

Nanotechnology involves the synthesis, characterization, and application of nanomaterials. A nanoparticle is an arrangement of atoms and molecules of one or more single or multiple elements on a nanoscale that range from one to one hundred nanometres (nm) [1].

Preliminary differences between organic and inorganic materials are evident when categorizing nanomaterials. For instance, materials that have organically benign nanostructures; such as ferritin, liposomes, micelles, and dendrimers; are more suitable for the administration of drugs [2]. Meanwhile, materials that are based on metal or metal oxides (MOs) are classified as inorganic materials. Metal-based nanomaterials, that are created from materials such as gold (Au), copper (Cu), selenium (Se), and silver (Ag), are used for the thermal ablation of tissue as well as gene delivery and to improve the efficacy of radiotherapy.

Metal oxides are formed by oxidizing metallic materials [3]. The most significant MOs are Silicon dioxide (SiO_2), Zinc oxide (ZnO), Ferric oxide (Fe_2O_3), Magnesium oxide (MgO), and titanium dioxide (TiO_2). These materials can be used in industries; such as medicine, agriculture, information technology, electronics, energy, and environmental protection; as they possess unique features [4, 5].

Zein; a naturally occurring protein that is found in corn endosperms; is soluble in alcohol. An amorphous polymer with plasticizing viscoelasticity, it also has a glass transition temperature of 165 oC. This potentially advantageous inherent property greatly decreases its hydrophobic attraction and increases its steric repulsion at the molecular level. It also helps stabilize and prevents Zein particles from aggregating [6].

A well-known MO nanoparticle, MgO has garnered widespread scientific interest as it is easy to synthesize and is also chemically stable. Apart from its potent bactericidal activity and tumor inhibition capabilities, MgO NPs are also used as antacids, detoxifiers, and in biomolecular diagnostics in the medical industry. Furthermore, film-coating drugs with metal NPs; such as magnesium oxide and Zein polymer; have yielded positive outcomes [7].

This present study reviewed relevant extant laboratory-based studies that have evaluated the effectiveness of NPs in tissue regeneration [8]. It is important because it addresses the urgent need for novel antimicrobial solutions and therapeutic agents, especially in the context of antibiotic resistance. The innovation lies in the application of nanotechnology and the specific focus on Zein-coated MgO NPs, which have the potential to revolutionize dentistry and medicine by providing enhanced antimicrobial capabilities. Additionally, the exploration of NPs in tissue regeneration opens up new possibilities in the field of regenerative medicine.

2. Biomedical Applications of Metal Oxide Nanoparticles (MONPs)

Metal oxide nanoparticles must meet certain criteria to be used in specific applications. For example, a MONP must possess the kinetic properties required to satisfy the conditions required to treat a specific infection. It must also be biodegradable to eliminate the need for subsequent surgical intervention [9].

2.1. Internal Tissue Therapy

The efficacy of internal tissue therapy largely depends on its ability to influence the several molecular signaling pathways that govern the division, differentiation, migration, and death of cells as well as the expression of cellular growth factors [7]. One of the key advantages of using nanomedicine for disease therapy is the ability to develop nanocarriers for the most efficient delivery of medications. The use of nanocarriers in a drug delivery system can increase pharmacological activity and prolong the targeted administration of several therapeutic medicines. Furthermore, patients experience fewer adverse effects when engineering materials are used to increase the specificity of nano-systems [10].

As they target specific areas, NPs decrease the total dosage required of a drug and, in turn, adverse side effects. However, some of the challenges of using NPs for targeted therapies include decreasing unwanted molecular interactions, harmful effects on healthy tissue, and increasing selectivity for target cells such as cancer cells. Some of the natural polymers that are used as drug delivery and targeted nanocarriers include polysaccharides, polyesters, Deoxyribonucleic Acid (DNA), Ribonucleic Acid (RNA), polypeptides, enzymes, and proteins. Synthetic polymer materials are materials that have been conjugated with inorganic NPs such as silica [11].

Increasing the ability of MONPs to localize medications and target cells may significantly improve their use by decreasing the total dosage required and tissue damage. Nanohybrid material shells can stabilize MONPs as well as vary how long they remain in the body. This not only makes them tissue-specific but eliminates the toxicity that NPs cause by producing Reactive Oxygen Species (ROS). When nanocarriers are taken up by the target cells, they should be able to escape through the endosomes, and the total NPs should show good accumulation and penetration [12].

2.2. Nano-Oxides and Anti-Inflammatory Properties

Nanoparticles (NPs) have increasingly been recognized as promising anti-inflammatory agents as they are more effective at blocking inflammation-enhancers; such as cytokines; and inflammation-assisting enzymes due to their larger surface area-to-volume ratio. Magnesium Oxide (MgO), among other metals and MONPs, has been proven to possess anti-inflammatory characteristics [13].

Inflammation is the body's initial response to an accident, disease, hormonal imbalance, internal organ malfunction, or external factors; such as an invasion of harmful bacteria or alien particles. An inflammatory response occurs when a pathogen damages or attacks tissues which, in turn, induces the recruitment of macrophages, killer cells, and stem cells that aid in addressing the response [14]. Macrophages are crucial for the autoregulation of the inflammatory process. Large, heterogeneous, mononucleated macrophages are produced in the bone marrow and circulate in the bloodstream as monocytes, which are movable white blood cells [15].

Metal NPs can enter the body through the nasal, oral, or cutaneous pathways. They can easily cross most biological barriers, such as mucous linings, as they are small. As such, they can even access sensory organs. Nanoparticles first enter the body through the circulatory system and directly interact with the blood plasma proteins found in plasma; which form part of the blood in the circulatory system. This interaction causes the proteins to form a corona around the NPs. Several common proteins; such as immunoglobulin, immunoglobulin M, and fibrinogen; are found in almost all NPs [16].

Although most NPs can enter a cell via holes in the cell membrane or ion channels, this method of ingress largely depends on the size of the NP. In the absence of membrane receptors, NPs are absorbed by cells via adhesive contacts; such as those caused by electrostatic interactions, Van der Waals forces, or steric interactions. Various cellular reactions occur depending on the location of the NPs within the cell, which again depends on their size [17].

Most cellular vesicles can quickly endocytose metal NPs at higher concentrations. Phagocytosis and macro-pinocytosis are processes that are carried out by neutrophils and macrophages, respectively. The protein corona that surrounds the NPs first comes into contact with receptors on the cell surface when the protein-coated metal NPs interact with the macrophages or neutrophils at sites of inflammation [18].

The corona, which primarily comprises serum proteins, functions as a ligand for the macrophage receptors. This triggers the macrophages, which play a crucial role in the uptake of NPs. The findings suggest that macrophages exhibit a stronger and quicker absorption of NPs in the presence of serum proteins [19].

3. Magnesium Oxide Nanoparticles

Magnesium (Mg), an essential element, is the primary intracellular metal in the human body. More than half of the Mg content of the human body is stored in the bones, with the rest stored in the soft tissues and muscles. Mg is present in the blood and interstitial fluids at a concentration of 1% or less. Approximately 300 enzymes are activated by magnesium, which also contributes to the inactivation of many other enzymes. Mg is an important cofactor in hundreds of enzymatic reactions, of which, protein and nucleic acid synthesis, mitochondrial integrity, plasma membrane permeability, and cell cycle are crucial physiological functions [20]. It has many medical applications in orthopedic implants due to its biocompatibility, low weight, and low modulus of elasticity, which make it both physically and medically compatible with bone [21].

Magnesium (Mg)is non-toxic to human cells as it is a component of the human body. The development of nanotechnology has revealed that certain metals, including Ag and Au among others, have numerous uses in their nanoforms. In addition to retaining the characteristics of the metals involved, MOs can also possess other characteristics, such as catalytic qualities in the case of Titanium (Ti) and ZnO. Unlike simple metal NPs, MONPs exhibit a variety of special qualities, and therefore, are utilized more frequently. MgO NPs operate as excellent catalysts and absorbents and are used in a variety of industries, including electronics, optics, and ceramics. As they have an, hitherto, unrivaled ability to remove contaminants, they are used in the toxic and chemical industries [22].

3.1. Synthesis Methods

Magnesium oxide nanoparticles can be easily created using several techniques. Often, these procedures are bottom-up approaches in which precursors are used to create MgO NPs. The sol-gel method is one of the most popular methods of producing MgO NPs. In the simplest sol-gel method, a precursor; such as sodium hydroxide; is added to an Mg-based precursor; such as magnesium nitrate ($Mg(NO_3)_2$); to create a magnesium hydroxide (Mg(OH)2) gel or precipitate. Once this has been filtered, a calcination or annealing process is conducted [23].

The hydrothermal reaction method is also widely used to produce MgO NPs. Unlike the sol-gel method, this is a straightforward method that requires calcination and heating in its later stages. In this method, an Mg precursor is introduced to a solvent system to produce Mg $(OH)_2$ crystals, which are then calcined to produce MgO NPs that have a high surface area and uniform distribution. The main benefit of this method is that the form and size of the resulting NPs can be adjusted by combining several Mg precursors and solvents [24].

Zinc (Zn), Manganese (Mn), and Strontium (Sr) are added as alloying elements to Mg-based composites to improve their mechanical properties and resistance to corrosion [25]. Organic acids can also be used to produce MgO NPs, thus, effectively lowering the overall cost of synthesis. In this method, a variety of organic acids; such as oxalic acid ($C_2H_2O_4$), tartaric acid ($C_4H_6O_6$), and citric acid ($C_6H_8O_7$); are combined with glycine ($C_2H_5NO_2$). Magnesium oxide nanoparticles (MgO NPs) are produced when the precipitates are dried and strengthened. The resulting NPs have excellent catalytic and anticancer activities. Organic precursors also influence the properties of the NPs, and these qualities can be altered to control them [26].

The chemical bath method can also be used to synthesize MgO NPs [27]. However, some of the drawbacks of chemical synthesis are that it requires expensive and poisonous chemicals and produces waste, which is bad for the environment. On the other hand, green synthesis, which is the production of NPs from non-toxic, environmentally friendly sources such as plants and microbes, is more affordable and cost-effective. As such, there is significant research interest in the development of environmentally friendly methods of producing NPs. For instance, rambutan (Nephelium lappaceum) fruit extract has been used in a similar way as the sol-gel synthesis method to create MgO NPs. The precipitate is separated from the extract through centrifugation and then heated for calcination [2].

When producing MgO NPs via green synthesis, the size of the particles is decreased by ultrasonically treating the MgO NPs, which enables them to be used as antibacterial agents [28]. Another study used Southernwood (Artemisia abrotanum) plant extract to produce MgO NPs that had exceptional photocatalytic activity. The plant was chosen due to its medicinal qualities, which can treat many disorders. The artificial NPs had a spherical shape and were about 10 nm in size on average [29].

3.2. Antimicrobial Activity of Magnesium Oxide Nanoparticles (MgO NPs)

Magnesium oxide nanoparticles (MgO NPs) exhibit greater antibacterial activity due to their small size and highly active wide surface area for metal and MONPs, with their diminutive size serving as the key factor of their antibacterial ability [30]. The alkalinity of MgO NPs contributes significantly to their antibacterial activity as it enables them to dissolve in a variety of liquids easily. Metal oxide nanoparticles (MONPs), such as MgO NPs, have an edge over traditional antibiotics due to their distinct processes and ability to be active against antibiotic-resistant strains [31].

Their antibacterial action depends on their size and dosage, with higher concentrations of MgO NPs showing a stronger inhibition. The physical interaction between bacterial strains and MgO NPs causes profound morphological changes in cells and interferes with normal cellular processes, thereby, inhibiting cell growth and, ultimately, leading to cell death [32].

Although their antibacterial activity is unknown, most of it can be attributed to their ability to produce ROS and damage cell membranes. This explains why an increase in MgO NP concentration enhances antibacterial efficacy as the accompanying increase in oxygen (O_2) concentration more effectively ruptures the cell wall of the bacteria. Furthermore, its alkalinity may play a significant role in its antibacterial activities [33].

Magnesium oxide nanoparticles (MgO NPs) make Gram-positive bacteria more sensitive than Gram-negative bacteria. Several Gram-positive and Gram-negative microorganisms; such as Escherichia coli (E. coli) and Staphylococcus aureus (S. aureus); have been used to investigate the efficacy of MgO NPs. It has been discovered that inhibition is dependent on the size of the NPs, where smaller NPs exhibit larger inhibition zones than larger NPs. It is also influenced by the duration of the calcination process, which increases the size of the NPs during their synthesis [34].

Magnesium oxide nanoparticles (MgO NPs) have been found to cause cell death and the contents of cells to leak, thereby disrupting and disintegrating cell walls. The production of ROS has also been found to cause DNA damage and genotoxicity. Nanoparticles (NPs) are believed to inhibit biofilm formation. This three-component process is one of the best alternatives for managing phytopathogens in the future [35]. The antibacterial activity of MgO NPs against the Gram-positive S. aureus and Pseudomonas aeruginosa (P. aeruginosa) and the Gram-negative E. coli was assessed using the resazurin incorporation method. The resazurin method relies on the metabolic activity of live cells to drive enzyme activity, which makes the MgO NPs bactericidal [36].

Sequential oxidation-reduction events can occur on the surface of MgO NPs and result in the production of ROS: such as superoxide radicals (O2-), hydrogen peroxide molecules (H_2O_2), and hydroxyl groups [37]. Superoxide radicals (O2-) are created when MgO NPs react with O_2 molecules to create these common oxide catalysts. Many peptide connections can be found in the proteins of cell walls. An attack by the superoxide on the carbonyl carbon atoms in the peptide links will result in the death of the bacteria [38].

Differential toxicity occurs when all the examined bacteria can produce Superoxide Dismutase (SOD); a cellular antioxidant defense enzyme that may react with the O2 created by the MgO NPs to produce H2O2. This enables them to penetrate E. coli. Meanwhile, P. aeruginosa and S. aureus are responsible for producing Catalase (CAT); an antioxidant enzyme that converts H_2O_2 into H_2O and O_2 and decreases its sensitivity to other antioxidant enzymes. There are cellular toxicity mechanisms that include increased ROS production that surpasses the ability of the cellular antioxidant defense system to prevent cells from going into a state of oxidative stress, which damages cellular components such as lipids. Fatty acid oxidation also results in the production of lipid peroxides, which set off a series of events that break cell membranes and cause cell death [39].

3.3. Cytocompatibility

The toxicity of nanomaterials; such as NPs, quantum dots, nanotubes, and nanowires; has come to light in recent years. Many researchers have addressed the toxicity of MgO NPs. Human astrocytoma (astrocyte-like) U87 cells were treated with MgO NPs for 48 hours. However, Lai *et al.* found that this did not significantly affect the survival of the cells until the next treatment at a concentration of 50 g/mL. Other studies on the cytotoxicity and neurotoxicity of MgO NPs discovered that MgO NPs did not harm either undifferentiated or differentiated SH-SY5Y cells. A 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay was used to evaluate cell viability [40, 41].

In terms of their effect on fibroblasts, while examining the effect of MgO NPs on cell viability, morphology, adhesion, dose-dependency, and the sensitivity of different cell responses, Liu *et al.* (2020) discovered that lower concentrations of MgO (0.5 to 1%) significantly promoted cell proliferation while high concentrations (2%) suppressed cell growth. In comparison to fibroblasts, rat bone marrow mesenchymal stem cells (rBMSCs) appeared to be more responsive to a magnesium-rich milieu [7].

According to research, MgO NPs are not hazardous to human skin. In another investigation, MgO NPs were shown to be safe when exposed to human fibroblasts. Magnesium oxide nanoparticles (MgO NPs) have unique cytotoxic effects on the human liver cancer cell line (HepG2) and the human foreskin cell line (BJ). More studies on the toxicity of MONPs are necessary due to a lack of toxicological data on the effects of MgO NPs on human neural cells [10].

4. Zein Particles

Zein, which accounts for 35 to 60% of all the proteins in corn, is the main storage protein in corn or maize. It is considered a prolamin due to its unique solubility [42]. Zein is a composite protein or polypeptide that comprises many proteins, that are often categorized according to their solubility, charge, and molecular weight. To date, alpha- (α), beta- (β), and gamma- (ɣ) zein fractions are the three primary fractions that have been identified based on their molecular weight and solubility [43].

Most of the Zein in the core (75-85%) is composed of the α-zein fraction, whereas the β- and ɣ-Zein fractions make up just 10 to 15% and 5 to 10%, respectively, depending on the genotype. The α-zein has a molecular weight of between 21 and 25 kDa with a minor subfraction of 10 kDa. It can be dissolved in alcohols ranging from 50 to 95% without the need for a reducing agent or buffer, unlike the other two fractions, which can only be dissolved with the help of a reducing agent and/or buffer. When all the component fractions of Zein were considered, the solvent with the highest solubility for extracting the entire Zein from dry-milled maize was an aqueous solution of 70% ethanol [44, 45].

Zein is a corn polymer that has been proven to have several positive qualities, including biocompatibility, low toxicity, and high in vivo absorbability of the degraded end products. Due to its excellent resilience to heat, humidity, and abrasion, and the ability to cover up unpleasant tastes or strong odors, Zein has numerous pharmaceutical applications, particularly when used to coat tablets with sugar. Zein has also been considered for use in regulating or sustaining the release of drugs in dosage form due to its insolubility in water and its ability to swell [46].

Alpha- (α) Zein, which is the most abundantly available, is the most extensively used prolamin in maize. It is also the only Zein that is found and produced industrially as it has numerous possible industrial uses due to its distinctive amino acid structure and sequence. More specifically, more than half of the amino acid residues are nonpolar, and it has 9 to 10 tandem repeats of the helical segments of these nonpolar residues connected by polar turns that are high in glutamine [47].

Its poor solubility of Zein in water and its negative nitrogen balance render Zein unsuitable for direct human consumption. However, it can be quickly transformed into spherical colloidal particles. Zein has been used in modified-release systems for the administration of enzymes, medications, and essential oils among other things because of its high coating capacity, biodegradability, and biocompatibility [48].

4.1. Zein Nanoparticles for Drug Delivery

Zein NPs have been used to encapsulate a range of hydrophobic bioactive molecules; such as DNA; and medications; such as abamectin and ciprofloxacin; to target active macrophages. Two antioxidant proteins (enzymes); CAT and SOD; were enclosed in Zein NPs and substantial amounts of sorbitol and glycerol surfactants were used to enhance the stability and re-dispersibility of the Zein NPs as well as the miscibility of the encapsulated proteins in an aqueous alcohol solution [49].

Xu *et al.* (2013) were the first to use phase separation to create 48 hollow zein NPs, which enhances the ability of Zein NPs to encapsulate and deliver anti-cancer and anti-tumor drugs [50]. Various active chemicals can be loaded into Zein NPs once they have been prepared using a variety of techniques; such as nanoprecipitation, liquid-liquid dispersion, phase separation, and electro-spraying. These methods, based on the annealing precipitation processes, include encapsulation [51].

Several strategies have been used to improve the stability of Zein NPs. One was a thermal treatment that examined how temperatures of 25 to 70°C affected the secondary and tertiary structures of Zein. Treatment at 70°C for 15 minutes was found to affect the primary structure and lower the number of α helices in the secondary structure. These changes were undone when the temperature stabilized at 25°C. However, treatment with Zein proteins at 90°C led to documented irreversible structural changes in the α helices [52].

The findings showed that a brief heat treatment of 15 minutes largely disassembled the tertiary structures of the Zein molecule to produce a monodispersed formula with reduced nanoparticle sizes. After being heated for a longer period and at a higher temperature, the Zein molecules were completely unraveled. The contacts between the polypeptide chains of various protein molecules were increased as the Zein molecules were then able to cluster [53].

5. Zein-Coated Magnesium Oxide Nanoparticles (zMgO NPs)

Zein molecules are better than many other natural and synthetic polymers because of their special physicochemical properties and nanostructure. An enhanced Zein-based nano-structured delivery system will increase the range of potential applications because the field of Zein-based delivery systems is expanding rapidly [46]. However, MgO NPs tend to cluster and aggregate, which may have an impact on their use in dental applications. Hence, a Zein polymer was added to the formulation of MgO NPs to produce a covering that prevents the agglomeration of MgO particles. The inherent features of this polymer help stabilize the NPs against aggregation by lowering the hydrophobic qualities of the particles [54].

It has been demonstrated that a Zein coating boosts the affinity of MgO NPs for bacterial cell walls, blocks bacterial metabolism, and enhances their antibacterial capabilities [55]. Metal oxides (MOs) can be combined with the Zein polymer to create hybrid metal polymers, which have unique chemical properties, including cross-linking. This may have an impact on the optical and physical characteristics of these new compounds [56].

5.1. Application of Zein-coated Magnesium Oxide Nanoparticles

Zein-MgO nanoparticles are a type of composite material that has gained attention in recent years due to their potential applications in various fields such as medicine, food, pharmaceuticals, and packaging as in Table 1.

One study published in the journal Food Chemistry investigated the use of Zein-MgO nanoparticles as a carrier for curcumin, a natural compound with anti-inflammatory properties. The researchers found that the Zein-MgO nanoparticles effectively protected the curcumin from degradation and improved its bioavailability [57].

Another study published in the journal Industrial Crops and Products looked at the use of Zein-MgO nanoparticles as a coating material for packaging applications. The researchers found that the Zein-MgO nanoparticles improved the mechanical and barrier properties of the packaging material, making it more effective at preserving food quality and shelf life [45].

Dental disorders; such as caries, periodontal disease, and candida infection; are the most common illnesses that affect the oral cavity. The primary culprits are bacteria and fungi such as Streptococcus mutans (S. mutans) and Candida albicans (C. albicans) [58]. As the surface contact area of metal ions determines their antibacterial characteristics, NPs increase surface areas and, as a result, increase interactions with both organic and inorganic substances. It has been shown that the bactericidal activity of nano-MgO against both Gram-positive and Gram-negative bacteria is directly proportional to the size and concentration of the particles [59].

In a recent study, Naguib *et al.* found that the alkaline nature of MgO NPs and the antimicrobial capabilities of zMgO-infused cement may potentially reduce the aggregation of microorganisms at the restoration interface as well as neutralize the acid created by cariogenic bacteria. This was proposed as a feasible method of decreasing the likelihood of developing recurring caries and gingival infections [60].

The antimicrobial activity of three of the most common types of mouthwashes was able to be determined by incorporating various concentrations of zMgO NPs and testing the mixtures on Gram-positive

Table 1. Some of the studies dealing with this type of composite material

Author, year	Highlights	Study design	Conclusion
Tang, Z.X. and Lv, B.F (2014)	synthesis methods, antibacterial activity, and antibacterial mechanisms of MgO nanoparticles	Review article	the antibacterial activity of MgO nanoparticles is size- and concentration-dependent.
Naguib *et al.* (2018)	this study was to assess the antimicrobial property of MgO nanoparticles when coated with a Zein polymer against several oral bacteria and fungi	In vitro study	Zein-coated MgO nanoparticles are a potent antimicrobial agent that can be incorporated in a variety of dental materials and can provide improvements in dental care and oral health.
Brotons-Canto *et al.* (2021)	this study was conducted to evaluate the effect of curcumin incorporation in Zein nanoparticles on the pharmacokinetic parameters of systemic curcumin in plasma	Experimental animal study	increase in bioavailability improve the curcuminoids' absorption profiles.
Naguib *et al.* (2021)	explore the hepato- and nephrotoxicity of low versus high doses of Zein-coated MgO nanowires in rats.	Experimental animal study	no biochemical- or cytotoxicity. utilized as an effective antimicrobial
Onyeaka *et al.* (2022)	Nanocomposite materials have been used in active packaging to prevent the passage of oxygen, carbon dioxide, and moisture into the food	Review article	organic and inorganic nanoparticles improve food nutritional attributes, safety, and quality.

bacteria; such as S. mutans, S. aureus, Enterococcus faecalis (E. faecalis), and C. albicans [61].

Another study assessed the antimicrobial properties of zMgO NPs against several oral bacteria and fungi. The results showed that 1% or 2% Zein-coated MgO nanowires had a statistically significant antibacterial effect against four organisms studied: Staphylococcus aureus, Streptococcus mutans, Enterococcus faecalis, and Candida albicans. The study concluded that zMgO NPs are a new human-friendly and potent antimicrobial agent that can be incorporated into the formulation of a variety of new dental materials and products to improve dental care and oral health [62]. Furthermore, a study demonstrated that dental cements enhanced with zMgO NPs exhibited antimicrobial properties against various oral bacteria. Notably, the study revealed that concentrations of 0.3% and 0.5% of zMgO NPs consistently yielded antimicrobial efficacy comparable to that of the 1% concentration [63].

A study by Kadam *et al.* (2020) found that adding nanoparticle gel to scaling and root planing for the treatment of chronic periodontitis yields better outcomes than using tetracycline gel [64]. To prevent the growth of biofilms, it has been shown that the rupture of the bacterial cell membrane caused by the production of ROS is the cause of the antibiofilm action of nanoscale materials; such as MgO, ZnO, TiO_2, copper oxide (CuO), carbon nanotubes, chitosan, Au, and quaternary ammonium (NH_4^+) compounds [65].

In a separate study, the hepatic and renal toxicity of varying doses of zein-coated MgO nanowires in rats was examined. The results demonstrated that higher doses of zMgO NPs led to significant changes in specific biochemical markers in the livers and kidneys of both male and female albino rats, indicating potential toxic effects [60]. These investigations showcase the versatility of zMgO NPs in diverse applications, such as dental materials and products. Nevertheless, additional research is essential to gain a comprehensive understanding of their safety and effectiveness.

6. Conclusion

This review provides a comprehensive overview of nanotechnology and its applications, focusing on the potential of zMgO NPs in various fields, including medicine, dentistry, and packaging. It highlights the unique properties of Zein and magnesium oxide nanoparticles, their synthesis methods, and their antimicrobial and cytocompatibility attributes. Notably, zMgO NPs exhibit remarkable antibacterial activity and have the potential to revolutionize dental care and oral health. Their application in dental cement, mouthwashes, and other products has shown promising results in inhibiting the growth of pathogenic microorganisms. Nevertheless, ongoing research is crucial to fully harness their potential while ensuring their safety in different contexts.

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