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Review

MAGNESIUM OXIDE-REINFORCED ORTHOPAEDIC COMPOSITE MATERIALS: FABRICATION, PERFORMANCE AND CLINICAL APPLICATION PROSPECTS

Haodong Xia[1,§], Wangwei Zhu[1,§], Jiahui Yang[1], Peng Wan[2], Xing Yang[1], Shibo Huang[1], Tianwei Zhang[1], Xiaoyan Chen[1], Junlei Li[1], Weidan Wang[1,3,*] and Dewei Zhao[1,*]

[1]Department of Orthopedics, Affiliated Zhongshan Hospital of Dalian University, 116001 Dalian, Liaoning, China
[2]School of Materials Science and Engineering, Dongguan University of Technology, 523808 Dongguan, Guangdong, China
[3]Institute of Metal Research, Chinese Academy of Sciences, 110016 Shenyang, Liaoning, China
[§]These authors contributed equally.

Abstract

This review systematically discusses the research progress of magnesium oxide (MgO) nanoparticle (NP) composites in orthopaedic implants, focusing on their material characteristics, biological performance, preparation methods and applications. It also analyses their potential and associated challenges in bone repair. The paper first summarises the mechanisms by which MgO NPs enhance the mechanical strength, corrosion resistance, biocompatibility, osteogenic activity, and antibacterial properties of conventional orthopaedic materials. The results show that MgO NPs significantly improve the overall performance of composites by refining grains, filling surface defects, releasing Mg^{2+}, and regulating the local microenvironment. In addition, this paper discusses current applications of MgO-based composites in bone fixation, bone defect repair, and drug delivery while outlining the key challenges hindering clinical translation. Finally, it highlights future research directions, emphasising material design, process optimisation, and intelligent release systems to advance the clinical application of MgO NPs composite in orthopaedic repair and regenerative medicine. Consequently, this review provides a theoretical basis and technical foundation for developing next-generation high-performance bone implant materials.

Keywords: Magnesium oxide, osteogenesis, mechanical property, corrosion resistance, antibacterial.

***Address for correspondence**: Weidan Wang, Department of Orthopedics, Affiliated Zhongshan Hospital of Dalian University, 116001 Dalian, Liaoning, China; Institute of Metal Research, Chinese Academy of Sciences, 110016 Shenyang, Liaoning, China. E-mail: wangweidan@dlu.edu.cn; Dewei Zhao, Department of Orthopedics, Affiliated Zhongshan Hospital of Dalian University, 116001 Dalian, Liaoning, China. E-mail: zhaodewei2016@163.com.

Introduction

The development of orthopaedic implants remains a central objective in bone repair and regenerative medicine and has consistently attracted the attention of researchers and clinicians. Ideal bone repair materials should possess excellent mechanical properties to provide adequate support, together with good biocompatibility, osteogenic activity, antibacterial properties, and controllable biodegradability to meet long-term application demands in complex physiological environments [1,2]. Conventional orthopaedic metallic implants (e.g. stainless steel and Ti alloys) face significant limitations due to mechanical mismatch with native bone tissue, which often induces stress-shielding. Moreover, their bioinert and non-degradable nature frequently leads to insufficient osseointegration and necessitates secondary surgical removal, thereby increasing both the physiological and economic burden on patients [3].

In contrast, magnesium alloys, with densities and elastic moduli similar to those of natural bone and exhibiting good biocompatibility [3–5], are regarded as promising biodegradable materials for bone implants [6,7]. However, bare Mg matrices exhibit high degradation rates and generate hydrogen gas, which may lead to premature loss of mechanical support and fluctuations in local pH levels, thus adversely affecting bone repair [8]. To leverage the advantages of Mg while mitigating its drawbacks, researchers have incorporated MgO nanoparticles (NPs) into alloy matrices, bone cements, and hydrogel systems [6,9,10], thereby achieving synergistic improvements in material design and biological activation in orthopaedic implants.

With a high specific surface area, mild degradation characteristics, and multiple biological activities, MgO NPs have become a key additive for enhancing the performance of composite materials. Previous studies have confirmed that MgO NPs can improve mechanical strength by refining grain sizes, releasing Mg^{2+}, regulating the osteogenic microenvironment, and generating reactive oxygen species (ROS) to inhibit bacterial proliferation [11,12]. However, few reviews have systematically summarised the exceptional properties of MgO-based materials, indicating the need for an integrated and in-depth analysis to consolidate current findings and address existing research gaps. First, most studies focus on a single property of MgO and lack comparative analyses of its mechanisms of action within the body. The role of MgO in bone repair is multifaceted, and identifying its optimal concentration is crucial to ensuring beneficial regulatory effects in various biological processes. Second, existing reviews tend to cover the application of MgO across the broader biomedical field but fail to address the "differentiated needs of metal-, ceramic-, and polymer-based matrices" in orthopaedic implantation scenarios. This gap has resulted in weak alignment between research directions and clinical needs.

A comprehensive literature search was conducted using PubMed, Web of Science, ScienceDirect, Nature and other databases, with keywords including "MgO", "antibiosis", "osteogenesis", "bone", "compatibility", "angiogenesis", and "mechanics". Studies with flawed experimental designs, small sample sizes, or lacking relevance to orthopaedic experiments were excluded. More than 150 articles published within the past decade were selected for analysis. This review addresses the identified research gaps by concentrating on the application scenarios of orthopaedic implants. Particular emphasis is placed on the mechanisms of performance regulation and the functional effects of MgO NPs as reinforcing materials in three primary matrices: metals, ceramics, and polymers. The structural characteristics and performance shortcomings of different matrix types are distinguished to clarify how MgO NPs address the inherent limitations of each matrix in orthopaedic implantation. This is achieved through the synergistic effects of structural optimisation, ion regulation, and microenvironmental modulation. Finally, a clear theoretical framework is proposed to guide matrix selection, MgO incorporation strategies, and clinical scenario adaptation. This framework is expected to support the effective translation of MgO NPs composites from basic research to clinical application.

Material properties of MgO-reinforced composites

Mechanical properties

Materials such as metals and metal oxides have been extensively studied for biomedical applications. Reinforcements used in medical composite materials must meet key criteria, including biocompatibility, an appropriate degradation rate, and ideally, the ability to promote new bone formation to accelerate bone healing. MgO NPs exhibit antibacterial and anti-tumour properties, highlighting their translational potential in the biomedical field [13]. Furthermore, the incorporation of MgO into biodegradable alloys contributes to grain refinement and enhances the mechanical properties of the alloy composites (Table 1) [14]. When used as a reinforcing agent, MgO avoids intense interfacial reactions with the Mg matrix and minimises the formation of intermetallic compounds. These effects collectively provide reliable mechanical support and promote controlled degradation during the initial stage of implantation.

Lin *et al*. [15] investigated the effect of incorporating different weight percentages of MgO into a Mg-3Zn-0.2Ca-based alloy on its mechanical properties. The results showed that the addition of 0.5 wt.% MgO significantly enhanced both the ultimate tensile strength and yield tensile strength of the composite. Similarly, Zhang *et al*. [16] introduced 0.6 wt.% MgO into a Mg-3Zn-0.3Ca composite. This modification increased the compressive fracture strain (CSF) from 14.1% to 34.18%, while the overall strength remained nearly unchanged. Ti and its alloys are among the most commonly used materials for bone substitute implants. However, their bioinert surfaces can delay the healing process, potentially leading to implant loosening, failure, and subsequent tissue damage [17]. Coating Ti alloy matrices with MgO NPs increases cell adhesion and promotes local cellular activity. This modification preserves the mechanical strength of the Ti alloy matrix while enhancing osteogenic capacity due to the presence of MgO NPs on the surface [18]. MgO NPs intrinsically promote osteoblast proliferation and exhibit hydrophilic characteristics. This hydrophilicity enhances cell adhesion and proliferation on the scaffold surface, enabling the implant to retain sufficient mechanical strength while mitigating the surface inertness of the original Ti substrate [19].

Corrosion resistance

Generally, the corrosion behaviour of alloys is primarily governed by the interaction between the metal matrix and the second phase components [20]. Unlike single-phase alloy materials, in Mg-based composites, the Mg matrix serves as the anode during corrosion, while the second phase and reinforcing materials collectively act as the cathode. Reinforcements exert a dual effect on the corrosion behaviour of Mg matrix composites. On one hand, reinforcement can act as a partially protective coating, thereby reducing the corrosion rate of the Mg matrix. When distributed in a network-like pattern, the reinforcement also functions as a physical barrier, preventing corrosive medium from penetrating the matrix and thus hindering the corrosion process. On the other hand, if the electrode potential difference between the reinforcement and the Mg matrix is too large, a micro-galvanic couple may occur. This results in accelerated localised corrosion.

Table 1. Effect of MgO on the mechanical properties of composite materials.

Material	MgO content	Effect on mechanical properties	Ref.
Mg-3Zn-0.2Ca/MgO	0.5 wt.%	Ultimate tensile strength increased to 329.03 MPa; yield tensile strength increased by 22.81%.	[15]
Mg-3Zn-0.3Ca/MgO	0.6 wt.%	Uniformly distributed MgO increases the CSF of the material from 14.1% to 34.18%.	[16]
Mg/MgO	0.5 vol%	Tensile strength increased to 233 MPa; yield strength increased to 151 MPa; macrohardness improved to 41HR15T.	[21]
Polymethyl methacrylate (PMMA)/MgO	15 wt.%	Compressive strength increased from 60.3 to 108 MPa; fracture toughness increased from 5.85 to 9.80 MPa·$m^{1/2}$; Young's modulus increased by 82%.	[22]
SrO-MgO-TCP	1 wt.%	Mechanical strength of the scaffold increased from 6.62 to 9.38 MPa due to grain refinement, densification, and β -crystal-phase stabilisation.	[23]
HA/MgO-H	1 wt.%	Young's modulus increased from 0.14 MPa (pure Cys-H) to 0.21 MPa (nearly 50% improvement); compressive stress at 50% deformation significantly increased.	[24]

MgO NPs exhibit excellent heat resistance and low toxicity [25]. Additionally, their hygroscopic properties enable them to react with water to form $Mg(OH)_2$ [25], which further contributes to corrosion resistance. Study has demonstrated that the interface between the Mg matrix and MgO matrix plays a crucial role in improving the corrosion resistance of composites and the tensile strength of the composite material [26]. MgO NPs can also fill surface defects, which are the primary initiation sites for corrosion in composite materials [27]. Owing to their chemical stability and biodegradability under neutral pH conditions, MgO NPs have attracted significant attention [28–30]. Their barrier properties and stability effectively improve the corrosion resistance of composite systems. Fayyadh and Ahmed [31] prepared MgO NPs and ZnO NPs using a co-precipitation method and applied them to a polymer surface via a soaking technique to compare their corrosion resistance. The results indicated that both materials conferred superior corrosion resistance, with MgO NPs exhibiting better oxidation resistance than ZnO NPs. Rad *et al*. [32] evaluated the influence of MgO NPs on the corrosion behaviour of hot-dip aluminised Zn coatings through salt spray testing, electrochemical impedance spectroscopy (EIS), and potentiodynamic polarisation tests. The results demonstrated that the addition of 1 wt.% MgO reduced the corrosion rate by 32.5% and decreased the corrosion current density by approximately 81%. It is believed that, on one hand, MgO NPs block micropores on the coating surface, with these micropores being potential initiation sites for corrosion. In contrast, OH^- generated by redox reaction react with MgO to form $Mg(OH)_2$. This reaction not only inhibits further corrosion but also helps maintain the surrounding pH and stabilises Zn-containing corrosion products. Yu *et al*. [33] coated Zn powder with MgO NPs and infiltrated the MgO NPs into a Zn matrix using three-dimensional (3D) printing technology. Comparison with pure Zn scaffolds revealed that corrosion initiated from each vertex and gradually expanded, resulting in a rapid corrosion rate. In contrast, corrosion of Zn/MgO composite scaffolds was surface-initiated, and by Day 30, degradation was limited to the outer surface. In addition, the presence of MgO adjusted the pH of the surrounding solution. Notably, after 26 d, the pH in the Zn/MgO was significantly lower than that in the Zn scaffold group, further demonstrating the corrosion resistance imparted by MgO NPs. Owing to their high chemical stability and unique surface properties, MgO NPs exhibit substantial advantages in enhancing the corrosion resistance of composite materials. First, MgO NPs can form a dense protective film on the material surface, effectively blocking the penetration of corrosive media (such as water, oxygen, and corrosive ions) [34]. In addition, the alkaline nature of MgO NPs helps neutralise the surrounding acidic environment, thereby reducing the corrosion rate of the material surface [35]. In metal matrix composites, MgO NPs can enhance material compactness by filling micro-defects and pores, further improving corrosion resistance [36]. Therefore, incorporating MgO NPs into composite systems not only significantly improves the mechanical properties of the material but also provides long-term corrosion protection. This enables implants to effectively provide mechanical support over extended periods. Table 2 summarises the effects of MgO NPs particles on the corrosion resistance of various composite materials.

Biological properties of MgO-reinforced composites

Biocompatibility

MgO has attracted increasing attention in the field of orthopaedic implants due to its excellent biocompatibility and non-toxic biological activity [40–42]. Zhao *et al*. [43] developed polylactic acid/stearic acid modified MgO composites and investigated the influence of MgO morphol-

Table 2. Studies on the corrosion resistance of MgO-reinforced composites.

Body material	Optimal MgO content	Result	Mechanism	Ref.
Mg-3Zn-0.2Ca/MgO	0.3 wt.%	Corrosion rate reduced by 30%.	The $Mg(OH)_2$ formed from Mg degradation covers the surface of the material, increases the thickness and density of the corrosion product layer, and inhibits the infiltration of corrosive media.	[26]
MgO, ZnO	9 wt.%	At the optimal addition level, the corrosion rate over four weeks was 21.3% lower than that of 3 wt.% MgO coating, and 7.9% lower than that of a ZnO coating at the same loading.	MgO has a wider band gap than ZnO, which enhances its electrochemical corrosion resistance.	[31]
Zn-55Al-1.6Si/MgO	1 wt.%	Corrosion rate decreased by 33%; corrosion current density decreased by 81%; total resistance increased by approximately three-fold.	MgO NPs block micropores in the coating; OH^- generated from redox reactions inhibits corrosion and helps maintain environmental pH.	[32]
Zn/MgO	0.2 wt.%	On Day 30, the degradation rate of the Zn/MgO group was 2.3 mg/day compared to 4.6 mg/day in the control group.	MgO NPs form a dense protective film on the surface, effectively preventing the penetration of corrosive media.	[33]
Mg-HA-MgO	10 wt.%	Corrosion resistance increased from 0.25 to 1.23 $k\Omega cm^2$.	$Mg(OH)_2$ is formed as a corrosion product and adheres to the surface, creating a barrier that inhibits further corrosion.	[37]
MgO/Mg-Zn-Ca	1 wt.%	Compared with the control group, the corrosion current density and degradation rate were significantly reduced, and the corrosion product layer exhibited higher stability.	Uniformly distributed MgO acts as a physical barrier against corrosive media. Its degradation product $Mg(OH)_2$ fills corrosion-induced pores , providing further protection.	[38]
AZ31/MgO		Compared to uncoated AZ31, the corrosion current density decreased by 92.7%, indicating a significant improvement in corrosion resistance.	The MgO coating offers both physical barrier properties and chemical stability. A uniform and dense MgO coating effectively reduces the corrosion rate.	[39]

ogy (specifically, NPs and whiskers) on the *in vitro* and *in vivo* degradation behaviour of the composites. The results demonstrated that MgO effectively regulates the degradation rate of the polylactic-acid matrix and improves its biological activity, indicating that MgO possesses favourable biocompatibility for biomedical applications. Owing to its exceptional biocompatibility, MgO can better interact with human tissues, thereby reducing immune rejection and inflammatory responses [44]. As a bone implant material, MgO facilitates the adhesion and growth of bone cells and accelerates bone regeneration. Yu *et al.* [33] evaluated the effect of MgO on the biocompatibility of 3D-printed Zn scaffolds both *in vitro* and *in vivo*. The study demonstrated that the addition of MgO NPs increased the degradation rate of the scaffold while enhancing biocompatibility and cellular adhesion. Experimental evidence confirms that MgO NPs enhance the biocompatibility of Zn scaffolds. High biocompatibility is critical for minimising adverse reactions, improving therapeutic outcomes, and ensuring patient safety [45,46]. These benefits facilitate bone tissue regeneration and repair, lower the risk of infection, and provide adequate mechanical support. As a result, the bone healing process is accelerated, thereby increasing the success rate of bone implants and improving patient rehabilitation outcomes [47].

Osteogenesis

Mg plays an important role in bone metabolism [48]. It not only promotes osteogenesis but also inhibits osteoclast formation and bone resorption through multiple mechanisms [49]. Study has demonstrated that Mg promotes the maturation and differentiation of osteoblasts and enhances

bone formation by activating signalling pathways such as PI3K/Akt and Wnt [50]. The PI3K/Akt pathway serves as a key phosphorylation catalyst[51]. It directly inhibits pro-apoptotic and growth inhibitory factors (such as Bad, GSK-3β , and FoxO) while activating growth-promoting pathways (such as mTORC1) by phosphorylating a series of key downstream proteins [51–53]. This regulation supports the core functions of promoting cell survival, proliferation, and growth. Wang *et al*. [54] reported that Mg^{2+} significantly increased Akt phosphorylation in osteoblasts. However, when the PI3K/Akt pathway was blocked by maltin, osteoblast formation was considerably suppressed. Similarly, Liu *et al*. [55] revealed that osteoblast differentiation was significantly accelerated by knocking out the Akt inhibitor gene Pten via Cre-mediated recombination. In addition, the TRPM7/PI3K signalling pathway has been shown to induce osteoblast migration, enabling osteoblasts to migrate from low Mg^{2+} concentration to areas with high Mg^{2+} levels [56]. This migration increases the expression level of chemotaxis-related genes (MMP2, MMP9, and VEGF). Moreover, classical Wnt-β -catenin signalling can promote osteogenic activity by activating the Src-ERK and PI3K-Akt signalling pathways [57]. In recent years, Mg^{2+} has been found to enhance the differentiation of human bone marrow stromal cells into osteoblasts by regulating Runx2/Osx via the MAPK signalling pathway. It also activates the p38/Osx/Runx2 signalling pathway to promote osteogenic differentiation in mouse mesenchymal stem cells. Furthermore, Mg^{2+} facilitates the osteogenic differentiation of bone marrow-derived mesenchymal stem cells (BMSCs) by downregulating miR-381 in macrophage-derived exosomes [58]. In addition, Mg^{2+} inhibits the differentiation and fusion of osteoclast precursor cells by regulating the local pH environment. It also regulates the OPG/RANK/RANKL and NF-κB signalling pathways, thereby suppressing downstream signalling in the OPG/RANK/RANKL pathway. The expression and up-regulation of cathepsin K, tartrate-resistant acid phosphatase, c-Src, β3 integrin, and related proteins are closely associated with osteoclast activity. The NF-κB signalling pathway regulates more than 150 downstream target genes. In bone metabolism, this pathway functions not only as a downstream effector of the RANKL signal but also independently regulates immune and inflammatory responses. Upon activation, NF-κB enters the nucleus to directly regulate the expression of a wide range of target genes. These include pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6), chemokines (IL-8 and MCP-1), anti-apoptotic proteins (Bcl-2, Bcl-xL, and cIAP1/2), enzymes (COX-2), and other downstream proteins [59,60]. Through this large-scale transcriptional regulation, the NF-κB pathway establishes an inflammatory microenvironment that supports osteoclast formation and activity by up-regulating pro-inflammatory, pro-survival, and immune cell recruitment-related proteins. Inhibition of osteoclast formation and activity can reduce bone resorption [61,62]. Researchers co-cultured osteoclast precursor cells with extracts from Mg-coated Ti material. The results showed that the alkaline environment produced by the degradation of the Mg coating significantly inhibited the differentiation of bone marrow macrophages into osteoclasts [61]. These mechanisms highlight the potential of Mg in preventing and treating bone metabolic disorders such as osteoporosis. Fig. 1 shows the mechanism by which MgO influences the osteogenic function of bone implants.

High osteoinductive potential offers several advantages. It can significantly accelerate osseointegration, shorten the healing period, and promote new bone ingrowth into the microporous structure of implants [63], thereby reducing the risk of implant loosening during bone regeneration. Moreover, MgO also addresses the issue of large-volume graft necrosis by promoting angiogenesis. Additionally, it accelerates patient recovery by promoting bone formation, shortening treatment duration, and reducing treatment costs. As an inorganic nanomaterial with excellent biocompatibility, MgO NPs can directly activate osteoblast differentiation pathways through the sustained release of Mg^{2+}. They also facilitate hydroxyapatite (HAp) deposition and accelerate osseointegration by modulating the surface microenvironment of implants [64,65]. Mao *et al*. [66] developed a shape memory fibre cellulose/MgO (SF/MgO) composite scaffold. *In vitro* studies demonstrated enhanced adhesion, proliferation, and migration of ME3T3-E1 pre-osteoblasts, as well as promoted osteogenic differentiation of BMSCs. In a rat skull defect model, the SF/MgO scaffold significantly promoted bone regeneration. Similarly, Huang *et al*. [67] fabricated a biomimetic active scaffold via chemical cross-linking of $CaCO_3$/MgO NPs, carboxymethyl chitosan (CMC), and bone morphogenetic protein-2 (BMP-2). This scaffold exhibited superior modulus and compressive strength compared to the CMC scaffold. *In vitro* experiments revealed that the composite scaffold possessed strong mineralisation capacity and promoted robust bone differentiation ability. The in situ defect repair experiment of the rat skull showed that the composite scaffold achieved excellent bone regeneration outcomes. Liu *et al*. [68] developed a MgO NPs composite hydrogel scaffold (P-G-C-MgO) with a bionic trabecular bone structure for the repair of critical-sized bone defects. This scaffold significantly enhanced cell recruitment, osteogenic differentiation, and mineralisation through the combined effects of sustained Mg^{2+} release, a bionic porous structure, and bioactive components. It exhibited strong osteogenic potential in both *in vitro* and *in vivo* studies. Similarly, Guo *et al*. [69] verified that Mg^{2+} released from MgO-containing hydrogels promotes bone regeneration by up-regulating osteogenic gene expression and enhancing mineralisation, as demonstrated through *in vitro* and *in vivo* experiments. These findings underscore the potential of MgO-based materials for applications in bone defect repair. Table 3 summarises representative stud-

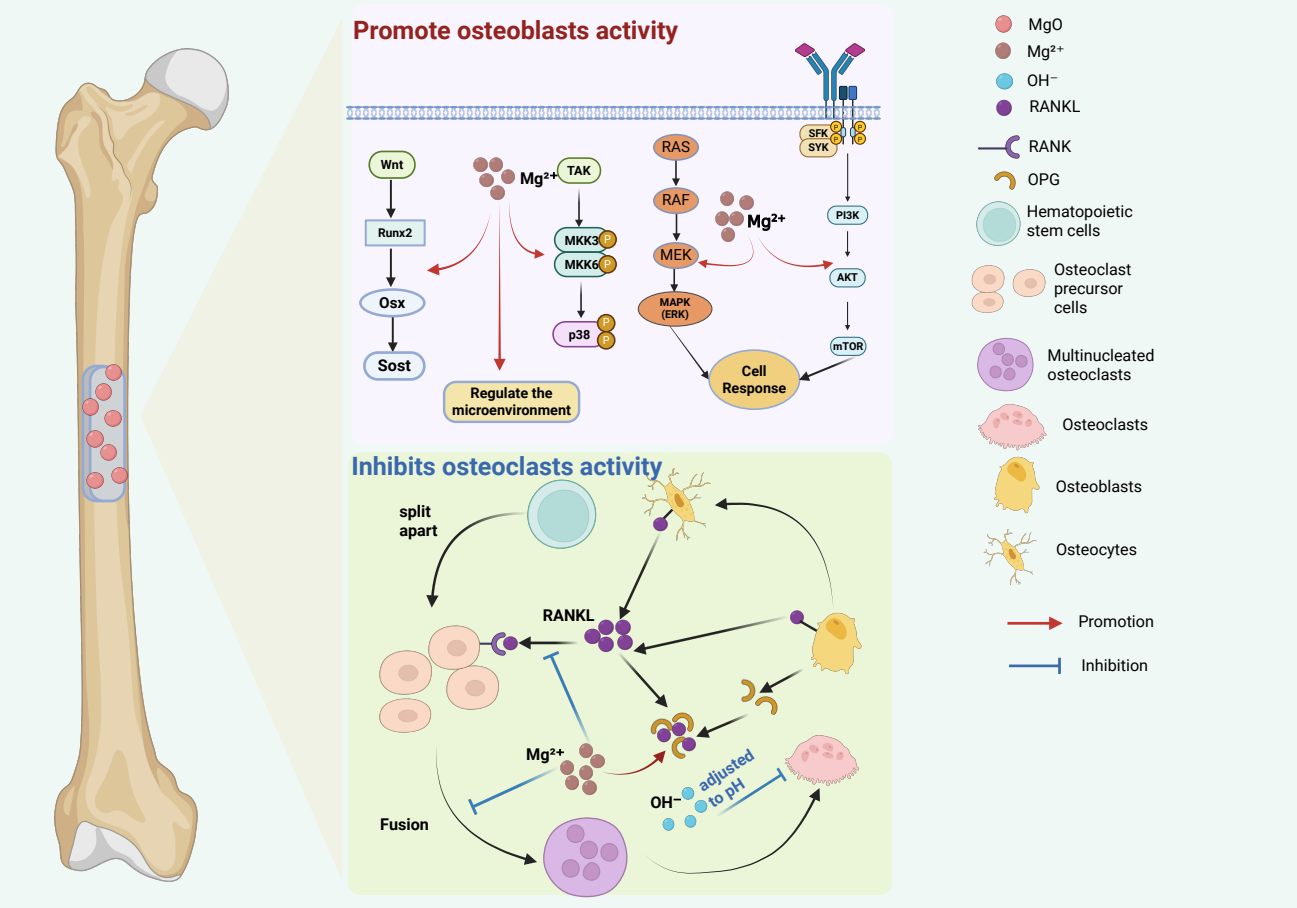

Fig. 1. Osteogenic mechanism of MgO-reinforced composites. The degradation of MgO NPs during bone repair releases Mg^{2+}, which promotes osteoblast activity via multiple signalling pathways, including Wnt, PI3K/AKT, RAS/MAPK, and P38. Concurrently, Mg^{2+} inhibits osteoclast activity through the OPG/RANK/RANKL signalling pathway, thereby contributing to bone regeneration. Created in BioRender. hao, X. (2026) https://BioRender.com/2wlnfll.

ies on osteogenesis mechanisms of MgO-incorporated composites.

Angiogenesis

The repair and regeneration of bone tissue require an adequate blood supply to deliver oxygen, nutrients, and cells (such as osteoblasts) essential for healing [73,74]. Numerous studies [65,75] have confirmed that MgO effectively addresses the challenge of "insufficient blood supply" in the bone repair area by promoting angiogenesis, thereby accelerating bone regeneration. This pro-angiogenic capability is one of the core factors contributing to the effectiveness of MgO as a bone repair material. The angiogenic ability of MgO is primarily attributed to the sustained release of Mg^{2+} during its degradation and the corresponding formation of an alkaline microenvironment. First, Mg^{2+} promotes the proliferation, migration, and survival of vascular endothelial cells, key processes in the formation of new blood vessels [76]. Secondly, it up-regulates the expression of crucial pro-angiogenic factors, such as VEGF and basic fibroblast growth factor [77]. These factors act as "signal cues" for angiogenesis by promoting endothelial cell recruitment and guiding their organisation into tubular structures. Additionally, the alkaline microenvironment generated by the degradation of MgO neutralises acidic by-products from inflammation or cellular metabolism in the bone defect site, thereby establishing a suitable pH environment for angiogenesis [69]. Moreover, the porous structure of the MgO NP-reinforced composite provides structural support and spatial guidance for neovascularisation, facilitating the early ingrowth and organisation of new blood vessels.

Antibacterial properties of MgO-reinforced composites

Boo *et al.* [78] confirmed that bone defect infections often involve Gram-positive bacteria (such as Staphylococcus aureus) and Gram-negative bacteria (such as Pseudomonas aeruginosa and Escherichia coli). In implant surgeries, ensuring the sterility of the implant site is crucial for early rehabilitation. This is particularly important within the first 24 h post-implantation, during which the elimination of residual bacteria is essential to support guided bone

Table 3. Representative studies on the osteogenic mechanisms of MgO-reinforced composites.

Material	Optimal content of Mg	Mechanism	Ref.
Zn-MgO	0.2 wt.%	Released Mg^{2+} activate the PI3K/STAT7 pathway, enhancing osteoblast-related gene expression.	[33]
SF/MgO	10 wt.%	The slow sustained release of Mg^{2+} promotes adhesion, proliferation, migration, and differentiation of osteoblasts and BMSCs.	[66]
$CaCO_3$/MgO/CMC/BMP-2	5 vol%	Mg and BMP-2 synergistically activate the signalling pathway through multi-pathway cross-talk, thereby significantly enhancing osteogenic differentiation.	[67]
P-G-C-MgO2	2 wt.%	MgO maintains the pH level and optimises the microenvironment. It synergises with gelatin and type I collagen to enhance cell adhesion, proliferation, and extracellular matrix deposition.	[68]
PEG-BSA/a-RGD@MgONPs	10 mg/mL	Released Mg^{2+} promote the growth of osteoblasts by up-regulating the genes related to vascular endothelial growth factor (VEGF) and osteogenesis.	[69]
PCL-MgO NPs	PCL: MgO = 1 : 0.3	Degradation of OH^- stimulates the release of BMP-2 and ALP, further promoting bone formation. MgO NPs extend the release time of parathyroid hormone (PTH), so that PTH continues to act on osteoblasts.	[70]
PCL-MgO NPs	10%	Induces macrophage polarisation to the M2 phenotype, enhancing the paracrine effect. Promotes the proliferation and migration of endothelial cells while up-regulating angiogenesis-related factors.	[71]
CpTi-MgO-Cu	1 wt.%	By regulating pH levels, MgO contributes to the recruitment, proliferation, and differentiation of osteoblasts. It also participates in regulating gene expression.	[72]

regeneration. Bacterial adhesion to implant membranes can occur as early as 4 h after stent implantation, marking a key stage in biofilm formation and subsequent infection risk [79]. MgO is considered a promising antibacterial agent due to its environmental friendliness, non-toxicity, low cost, and excellent photostability [80]. As NPs, MgO can exert antibacterial effects by inducing oxidative stress via the generation of ROS [12]. These ROS trigger apoptosis and cause damage to membrane lipids, membrane proteins, and nuclear membranes [81]. Pugazhendhi *et al.* [82] synthesised MgO NPs using Sargassum wighitii as both a reducing and capping agent. The resulting MgO NPs exhibited potent bactericidal activity against Gram-positive bacteria (such as Streptococcus pneumoniae, MRSA11, and MRSA56), Gram-negative bacteria (including E. coli and P. aeruginosa), and fungal strains in a dose-dependent manner. *In vitro*, both the minimum bactericidal concentration and minimum inhibitory concentration for Gram-positive bacteria were 256 μg/mL. For Gram-negative bacteria, the minimum inhibitory concentration was 256 μg/mL, while the minimum bactericidal concentration was 1024 μg/mL. Notably, MgO NPs at 30 μg/mL demonstrated antibacterial effects comparable to or exceeding those of fluconazole in the positive control group. These findings highlight the strong antibacterial potential of MgO NPs.

When incorporated into composite materials at the nanoscale, the unique physical and chemical properties of MgO are fully utilised. Nanoscale MgO exhibits a large specific surface area, enabling extensive contact with bacterial cells. It interferes with bacterial physiological metabolism through the release of Mg^{2+}, disrupts cell membrane integrity, and subsequently inhibits bacterial growth and proliferation [29]. This nanoscale antibacterial mechanism is both efficient and durable, enabling composite materials to retain the mechanical properties of conventional materials while imparting robust antibacterial functionality. The antibacterial efficacy of MgO NPs composites is dose-dependent. As the MgO NPs content increases, a greater number of active sites become available for bacterial contact, resulting in increased Mg^{2+} release that disrupts bacterial physiological processes. Additionally, more ROS are generated, further damaging bacterial structures [36]. Fig. 2 illustrates the antibacterial mechanism of MgO NPs. Furthermore, the OH^- ions produced during the degradation of MgO NPs can bind to the H^+ expelled by the proton pump [12]. In general, the normal functioning of the proton pump is essential for maintaining the electrochemical gradient across the bacterial membrane. OH^- ions generated during the degradation of MgO bind with a large amount of H^+ expelled by the proton pump, thereby disrupting membrane potential balance. This disruption impairs critical life activities of bacteria, including nutrient uptake, ATP synthesis, and flagellar motility. Additionally, Mg^{2+} acts as a metal cofactor [83,84], necessary for maintaining the structure and function of ribosomes. It is essential for the assembly of large and small ribosomal sub-

units, the stabilisation of ribosomal 3D structure, and the precise alignment of mRNA and tRNA during translation. Excessive concentrations of Mg^{2+} can disrupt intracellular balance, resulting in abnormal changes in ribosomal conformation or competitive inhibition at binding sites of other essential metal ions (such as Mn^{2+} [12] and K^{+}), thereby suppressing protein synthesis [85,86]. Khatua *et al*. [87] synthesised MgO NPs using centella asiatica extract as a reducing and stabilising agent, and investigated the antibacterial and antifungal effects of Ca-MgO NPs in human prostate cancer cells (PC3). The experimental results showed that the half minimum inhibitory concentration (MIC50) for the highly sensitive strains was 80 μg/mL, for moderately sensitive strains was 160 mg/mL, and for low-sensitivity strains was 320 mg/mL. In contrast, the MIC50 values for the control group generally ranged between 320 and 1280 μg/mL, which were considerably higher than those observed for Ca-Mg NPs. Ghaffari *et al*. [88] investigated the antibacterial properties of CaO and MgO NPs both *in vivo* and *in vitro*, focusing on their alkaline and ROS release capacity. The toxic effects of these two nanomaterials on *E. coli* mother cells, protoblasts, and macrophages were evaluated using the counting method and the MTT method. The results showed that the IC_{50} values of CaO NPs, MgO NPs, and MgO–CaO NPs over 72 h were 7.9, 10.3, and 8.0 μg/mL, respectively. CaO NPs, MgO NPs, and MgO–CaO NPs induced approximately 7.8%, 53.57%, and 12.8% apoptosis in protozoa, respectively, indicating that all materials can trigger protozoal apoptosis. Notably, the apoptotic rate induced by MgO NPs was more than seven times higher than that of Ca NPs, demonstrating their strong efficacy in reducing lesion area. Dong *et al*. [70] fabricated coaxial electrospun nanofibers comprising a PTH core and MgO NPs as the shell (MgO NPs-PCL/PTH-PCL), which inhibited bacterial growth and promoted bone formation. The antibacterial activity of MgO NPs-PCL/PTH-PCL against *S. aureus* and *E. coli* was subsequently evaluated. The results showed that the killing rate of MgO NPs-PCL/PTH-PCL against *S. aureus* and *E. coli* exceeded 85% after 24 h, demonstrating strong antibacterial efficacy. The release of free Mg^{2+} induced uncontrolled generation of reactive ROS in bacteria, leading to excessive oxidative stress, cell membrane distortion, and cellular damage. Consequently, MgO NPs-PCL/PTH-PCL can effectively prevent postoperative infection. Moreover, MgO NPs enhance the antibacterial properties of composite materials, providing reliable protection for bone repair implants against bacterial invasion in complex physiological environments. Fig. 2 illustrates the antibacterial mechanisms and bacterial species affected by MgO, while Table 4 summarises the advantages of MgO NP-reinforced composites.

MgO-reinforced composites for orthopaedic application

Fabrication

Preparation of MgO

The difficulty of preparing MgO varies with the preparation method, leading to differences in purity, particle diameter, uniformity, and production cost. Table 5 summarises the main preparation methods for MgO intended for use as a bone implant material. Based on its final application form, MgO can be prepared in two ways: as a coating or as a powder/bulk material. The coating approach primarily involves constructing an MgO film on the surface of existing bone implant substrates (such as metal or polymer) to impart material biological activity and antibacterial properties. In contrast, powder or bulk MgO is directly synthesised to produce particles or porous scaffolds, which can be used to fill bone defects or as reinforcing phases in composite materials.

Preparation of MgO-containing materials

Various approaches have been developed to incorporate MgO into bone repair materials. To fully exploit the advantages of composite materials while minimising drawbacks associated with mixing, researchers have continuously refined mixing technology. To date, five principal preparation methods have been reported, as summarised in Table 6. The selection of a specific method depends on the desired material properties and application requirements [96]. Surface modification and in-situ synthesis generally provide stronger antibacterial activity and enhanced osteogenic ability. In contrast, in-situ synthesis and 3D-printing techniques yield composites with superior mechanical strength and structural integrity. For applications requiring personalised customisation or complex pore structures, 3D-printing technology remains the only viable option [97]. Therefore, selecting an appropriate approach for combining MgO with the base materials is critical to ensuring the full functionality of MgO within the composite system.

MgO-reinforced bone repair materials

MgO has attracted considerable attention in the field of bone implants due to its favourable physical, chemical, and biological properties. When used as bone fixation materials, such as in bone plates and bone nails [103], MgO-based composites stabilise the fracture site while gradually degrading over time. The Mg released during degradation promote fracture healing and eliminates the need for secondary surgical removal. When applied as a bone repair scaffold for treating bone defects, the 3D porous structure of MgO composites provides an optimal microenvironment for osteocyte proliferation and guides the growth of new bone tissue. Additionally, the biological activity and degradability of MgO contribute to the regeneration and re-

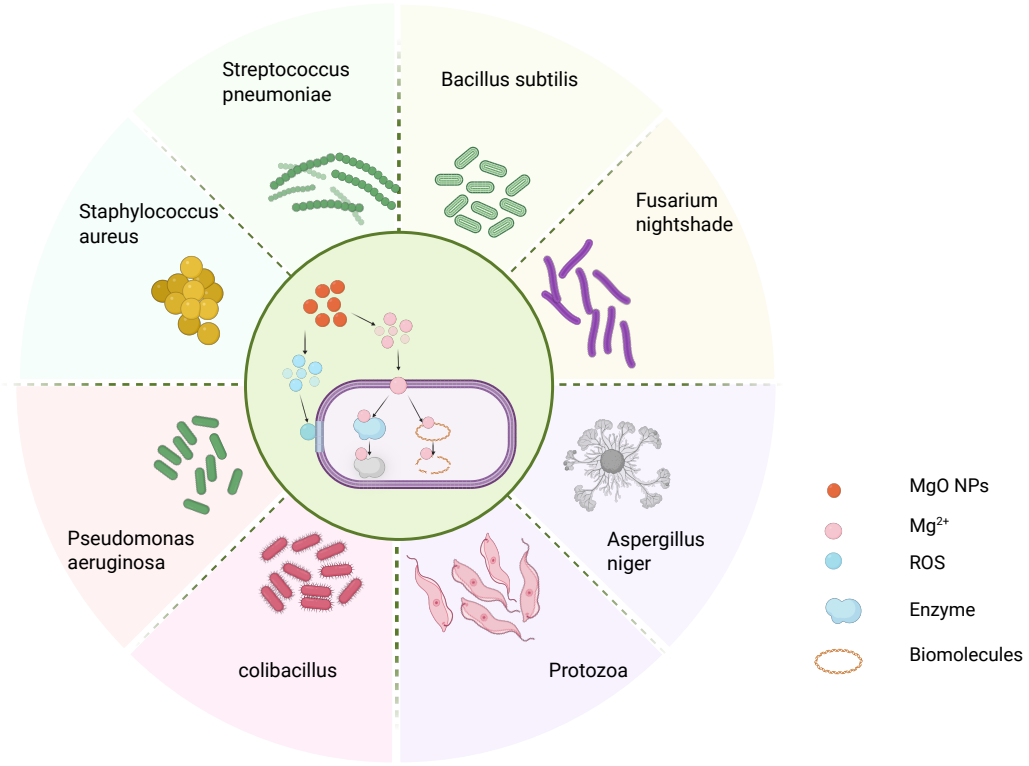

Fig. 2. Antibacterial mechanisms of MgO NPs. ROS generated during the degradation of MgO NPs damage bacterial cell membranes, while the released Mg^{2+} penetrate the cells and disrupts essential enzymes and biomolecules, leading to bacterial death. The figure also illustrates representative bacterial species susceptible to MgO NPs. Created in BioRender. hao, X. (2026) https://BioRender.com/msm19pa.

construction of bone tissue [64].

MgO-reinforced alloys

Biodegradable Mg alloys possess excellent biocompatibility, suitable mechanical strength, and remarkable osteogenic potential; however, their high degradation rate hinders the broader application of pure Mg alloys [104]. When MgO is incorporated with Mg as an alloying material, it reduces the degradation rate of pure Mg alloy [105]. Moreover, the robust biocompatibility and biological activity of MgO promote osteoblast proliferation and differentiation, thereby promoting new bone formation [43,67]. The incorporation of MgO NPs modifies the local microenvironment of the alloy changes. MgO NPs gradually release Mg^{2+} and increase the local pH value, creating an alkaline microenvironment that inhibits osteoclast activity while enhancing osteoblast function. In addition, the high specific surface area and nano-scale effect of MgO NPs strengthen the alloy by improving its hardness, and overall mechanical stability. These characteristics also ensure controlled degradation and excellent performance throughout the biodegradation process [28]. At present, most studies have introduced additional metallic elements to Mg alloys to improve mechanical strength and corrosion resistance. However, the addition of these elements inevitably induces a galvanic corrosion effect [106–108]. Alloying pure Mg with MgO NPs avoids this issue. The resulting Mg–MgO NPs alloy exhibits a refined structure and increased mechanical strength. Moreover, the presence of MgO NPs reduces gas production during degradation, thereby preventing delayed healing caused by the physical separation between the material and the surrounding tissue. Goh *et al.* [21] prepared approximately 1 vol% Mg/MgO NPs composites using the melt deposition method. They reported significant improvements in hardness, tensile strength, and elastic modulus. Periosteum-derived stem cell (PDSC)-mediated subperiosteal osteogenesis represents a crucial pathway for repairing bone defects, with higher potential for fracture repair and regeneration than that of BMSCs [109]. Study has shown that Mg^{2+} released from Mg-based implants stimulate the release of calcitonin gene-related peptide from dorsal root ganglion neurons in the peripheral cortical bone, thereby promoting fracture healing in rats through the osteogenic differentiation of PDSCs [110]. Osteogenesis in

Table 4. Summary of the advantages of MgO-reinforced composite materials.

Characteristic	Mechanism	Advantages	Ref.
Biocompatibility	Controlled release of Mg^{2+}.	MgO interacts better with surrounding tissues, reducing immune rejection and inflammation.	[42,44,47]
Mechanical property	MgO NPs refine grains and enhance bonding between the alloy and bone tissue, thereby improving structural support.	Increases compressive and flexural strength.	[14,15]
Corrosion resistance	MgO forms a protective surface layer that prevents the penetration of corrosion media. During degradation, $Mg(OH)_2$ is generated, providing additional protection against further corrosion.	Reduces degradation rate, prolongs service life, and prevents early accumulation of degradation products.	[25,31–33]
Osteogenic activity	Activates PI3K/Akt, Wnt, and other signalling pathways to promote osteoblast maturation and differentiation; regulates local pH value and inhibits differentiation and fusion of osteoclast precursors.	Exerts dual regulatory effects by promoting osteogenesis and inhibiting osteoclasts in bone metabolism, indicating potential for preventing and treating bone metabolic diseases such as osteoporosis.	[50,54,66–68]
Antibacterial property	Through the oxidative stress effect induced by ROS, MgO NPs destroy the bacterial membrane lipids, membrane proteins, and nuclear membrane structures, ultimately leading to cell necrosis.	Robust antibacterial properties help maintain sterility at the early implant site and prevent the adverse effects of residual bacteria on bone regeneration.	[70,81,82,87,88]

the subperiosteal region plays a vital role in bone regeneration. Periosteum-guided regeneration have shown to play a vital role in the repair of bone defects. New bone formation depends on both the extent of bone marrow overflow and the maintenance of adequate membrane space. The periosteum serves as a biological medium for cell and growth factor attachment, providing a protected and stable environment that supports new bone formation. However, continuous gas evolution during degradation can alter the membrane space, thereby inhibiting bone repair [111]. Alloying with MgO effectively mitigates gas production, accelerates early periosteal healing, and enables Mg-based alloys to release Mg^{2+} that regulates the local microenvironment and promotes osteogenesis [112]. Shen *et al.* [113] prepared Mg-1Zn-xCaO composites through in situ synthesis of MgO from CaO to improve the mechanical and corrosion resistance of low alloy Mg-1Zn alloy. The incorporation of MgO NPs particles refined the grain structure of the alloy and significantly enhanced the mechanical performance of the alloy .

MgO-reinforced bone cements

Polymethyl methacrylate (PMMA) is the most widely used bone cement material in orthopaedic fixation; however, it is a non-degradable and bioinert material that cannot induce new bone formation. The limited biological activity of PMMA limits its application in bone tissue regeneration [114]. Incorporating metallic components into bone cement to confer biological activity has proven to be an effective strategy for enhancing its performance [115]. Several biologically active inorganic bone cements, such as $Mg_3(PO_4)_2$ bone cement, exhibit osteoinductive properties, demonstrating that the inclusion of metallic element materials can impart biological functionality to bone cement [116]. However, enhancing bone cement to improve osteogenic activity remains a major challenge. To address the issue of heat release during the polymerisation of PMMA, Khandaker *et al.* [117] incorporated NPs such as MgO, HAp, and chitosan (CS) into PMMA to examine the influence of these additives on thermal behaviour. The maximum curing temperature of PMMA samples containing MgO was significantly lower than that of other samples, which substantially reduced curing time. Ricker *et al.* [118] reported that incorporating nanomaterials such as MgO and $BaSO_4$ into PMMA not only mitigated the harmful exothermic reaction and enhanced radiation ability but also increased osteoblast adhesion compared with unmodified PMMA. These findings indicate that the addition of MgO NPs can significantly improve the suitability of bone cement for orthopaedic bone repair applications. Firstly, the incorporation of MgO NPs increased the surface roughness and specific surface area of PMMA, creating additional anchoring sites for cell attachment. Secondly, the presence of MgO imparted hydrophilicity to PMMA, and the resulting hydrophilic surface facilitated closer cell contact and enhanced secretion of adhesion proteins. In addition, Mg^{2+} released during degradation participates in various physiological processes and induces the formation

Table 5. Preparation principles, advantages, and disadvantages of MgO.

Method	Principle	Advantage	Disadvantage	Application	Ref.
Preparation as powder or bulk material					
Hydrothermal method	The Mg source and precipitant are placed in a high-pressure reactor, wherein the reaction is carried out at high temperature and high pressure to directly crystallise MgO or its precursor.	Controllable morphology and good crystallinity.	Requires high-pressure equipment and incurs a high cost.	Research on nanomaterials with specific morphologies.	[89]
Solid-state reaction	Mg compounds are calcined directly in a high-temperature furnace and decomposed into MgO.	Simple process, low cost, and high yield.	Produces large particle size and low reactivity.	Economical raw materials for bone repair composites.	[90]
Biological template method	Using the porous structure of natural biological materials as a template, MgO materials with a hierarchical pore structure are replicated by impregnating Mg-salt solution, followed by calcination to remove the template.	Generates a biomimetic porous structure, which is beneficial for cell growth and nutrient transport.	Complex process with limited reproducibility.	Preparation of biomimetic structural materials.	[91]
Sol-gel process	Using Mg salt as a precursor, hydrolysis and condensation are conducted in solution to yield sol, which is subsequently coated on the substrate.	Controllable composition, simple equipment requirements, and porous microstructure.	Prone to cracking, weak interfacial binding, and easy particle agglomeration.	Fabrication of bioactive coating and nanopowders.	[92]
As coating preparation					
Atomic layer deposition	Self-limiting chemical reactions are alternately performed between the substrate surface by the precursor and the reactant on the substrate surface, enabling layer-by-layer deposition.	Produces uniform, dense, and high-precision coatings at low temperature.	High cost and slow deposition rate.	Surface functionalisation of high-end implants.	[93]
Electrochemical deposition	In an electrolyte containing Mg^{2+}, $Mg(OH)_2$ hydroxide or basic salt is deposited on the cathode surface under an external electric field, followed by heat treatment to convert it into MgO.	Rapid process at room temperature; suitable for complex shapes.	Limited process stability and moderate binding force.	Surface modification of metallic implants.	[94]
Plasma-spray discharge	MgO powder is injected into a high-temperature plasma jet, melted or semi-melted, and then sprayed onto the substrate surface at high speed to form a coating.	Produces coatings with strong adhesion, rapid deposition, and substantial thickness.	High-temperature processing may cause phase decomposition and porosity.	Fabrication of friction-resistant coatings.	[95]

of a bone-like apatite layer on the material surface [119]. This mineral phase, similar to the inorganic components in human bones, provides a highly biocompatible and easily identifiable surface for osteoblasts, thereby greatly promoting cell adhesion and functional activity [120,121]. With the progressive ageing of the population, the incidence of osteoporotic fractures has increased in recent years [122]. Unlike other fracture types, the fixation of osteoporotic fractures presents considerable difficulties. The fracture site is brittle due to bone loss, and secondary fractures often occur after fixation [123]. Therefore, effective repair of bone at the fracture site is essential. MgO, as a bone repair material, can both inhibit osteoclast formation and promote osteoblast production, offering a promising approach for the treatment of osteoporotic fractures. Huang *et al.* [124] added MgO NPs and alendronate (ALN) to calcium phos-

Table 6. Preparation methods of MgO-containing materials.

Preparation methods	Core principle	Advantages	Disadvantages	Substrate	Ref.
Physical mixing	Mechanical mixing of MgO with the base material.	Simple operation and easy control of the additive concentration amount.	Particles are prone to agglomerating, resulting in uneven distribution and possible formation of stress concentration points.	Bone cements and polymer powders.	[98]
Solution blending	MgO is dispersed in a liquid medium, followed by moulding and solvent removal.	Particles are more uniformly distributed compared to those obtained via physical mixing.	Some particle agglomeration may still occur during solvent removal.	Polymer solutions and hydrogels.	[99]
In-situ synthesis	MgO is generated through a controlled chemical reaction within the matrix.	Particle size is small, distribution is uniform, agglomeration does not occur easily, and interfacial bonding is strong, which improves the mechanical properties of the composite.	The chemical reaction process is complex and requires precise control.	Hydrogels and bioceramics.	[100]
Coating/surface modification	Functional MgO-based coatings are constructed on the material surface.	Does not affect the macroscopic mechanical properties of the material; imparts direct antibacterial and osteogenic functions at the surface.	Potential issues with long-term coating stability and interfacial bonding strength.	Metal implants and porous scaffolds.	[101]
3D printing	Composite materials are processed for additive manufacturing.	Enables personalised customisation with precise control over porosity and pore size, facilitating nutrient transport and the growth of blood vessels.	The production process is relatively complex.	Various types of printable composite materials.	[102]

phate cement (CPC). The addition of MgO addressed the issues of slow degradation and high brittleness, while simultaneously promoting osteogenic differentiation and angiogenesis of BMSCs. In combination with ALN, MgO also inhibited osteoclast formation. These findings suggest that MgO/ALN-reinforced CPC represents a promising candidate material for the repair of osteoporotic bone defects. Li *et al*. [125] developed a bioactive NP (MDA-NPs) comprising a core of MgO NPs and a polydopamine shell grafted with 2-aminoethyl methacrylate, and investigated its application in post-injury osteosarcoma repair. The Mg component in the scaffold exerted an inhibitory effect on osteosarcoma cells through the photothermal effect, while Mg^{2+} released from the composite material exhibited osteogenic activity in mouse embryonic osteoblast precursor cells. The composite material also demonstrated strong bone repair ability in a skull defect model. In summary, MgO composites have emerged as promising orthopaedic implant materials due to their ability to regulate environmental pH during degradation, continuously release Mg^{2+} to promote bone formation, and to enhance the physical and chemical properties of the host material.

MgO-reinforced hydrogel

Mg is an essential trace element in the human body, and an appropriate concentration of Mg^{2+} can promote cellular biological activity [126]. In patients with bone defects, promoting bone formation over resorption is critical. The key process involves the proliferation and differentiation of osteoblast lineages, which accelerate osteoblast activity and shorten bone repair time. Lin *et al*. [127] developed a hydrogel-based monodisperse core-shell microsphere delivery system containing MgO NPs, capable of continuously releasing Mg^{2+} to support the differentiation of osteogenic precursor cells (MC3T3-E1) and the formation of Ca nodules. The analysis of mechanical results showed that the average modulus of new bone in poly(lactic-co-glycolic acid) (PLGA)/MgO sodium alginate microsphere group was 12.5 ± 1.2GPa, while that of mature bone was 13.1 ± 2.0GPa, indicating that PLGA/MgO hydrogels effectively promote bone defect repair. Chen *et al*. [65] incorporated MgO NPs into a water-soluble phosphocreatine-functionalised CS (CSMP) aqueous solution and fabricated an injectable hydrogel (CSMP–MgO) through supramolecular binding between the phosphate groups in CSMP and the Mg groups in MgO NPs. The hydrogel acted as a reservoir for the controlled release of Mg^{2+}. The hydrogel CSMP–MgO exhibited superior compressive strength and

reduced brittleness compared with the control group while also promoting osteogenesis and angiogenesis. These findings highlight the strong potential of MgO NPs in enhancing bone regeneration. Jiang *et al*. [128] further developed an injectable porous Mg^{2+} hydrogel for repairing alveolar bone defects. This hydrogel exhibited high osteogenic activity and effective inhibition of osteoclast activity.

MgO-reinforced coating

The application of coatings to the surface of bone implant materials can improve biocompatibility, osseointegration, and mechanical properties while imparting antibacterial characteristics, thereby optimising the therapeutic performance of implants and reducing post-operative complications. Such surface modifications play a crucial role in bone repair and regeneration [129,130]. Basati *et al*. [131] fabricated a coating composed of MgO NPs and carbon quantum dots on the surface of 316L alloy and investigated its antibacterial performance. Minimum inhibitory concentration and minimum bactericidal concentration tests demonstrated that the addition of MgO significantly enhanced antibacterial efficacy against S. aureus. These results highlight the strong potential of MgO in bone repair applications and emphasise the importance of maintaining a sterile environment post-surgery to facilitate early bone recovery. To further enhance the osteoinductivity of HAp coatings on Ti implant surfaces, Ke *et al*. [132] incorporated 1 wt.% MgO into HAp to fabricate a novel coating material. Upon implantation of this scaffold into the distal femoral defect site of rats, it was observed that MgO addition markedly improved osteogenesis, osseointegration, and bone mineralisation ability. Furthermore, the shear modulus increased from 83 to 149 MPa, indicating a substantial enhancement in mechanical properties. The incorporation of MgO into coatings is critical for shortening fracture healing times and providing enhanced mechanical support in orthopaedic applications. Table 7 summarises the outcomes and underlying mechanisms of MgO applications in bone implant materials.

Clinical research and development of Mg-modified materials

In 1906, Albin Lambotte conducted the first clinical experiment using an Mg plate and a steel screw to repair tibia and fibula fractures in a 17-year-old male patient. However, due to the rapid electrochemical corrosion of the Mg plate and insufficient stability, revision surgery was required [135]. This event marked the initial application of Mg-based materials in bone repair. By the mid-twentieth century, as understanding of these materials advanced, Mg and its alloys were applied in autologous bone-graft fixation devices and prosthetic joint surgeries, achieving favourable repair outcomes. Since the beginning of the 21^{st} century, with the progress in material science and technology, the clinical research of Mg-based materials has been renewed and significantly accelerated. In 2013, Windhagen *et al*. [136] demonstrated that magnesium–yttrium–rare earth–zirconium (MgYREZr) alloy screws are biodegradable and safe for clinical use. When applied to the treatment of mild hallux valgus deformity, MgYREZr screws demonstrated imaging and clinical outcomes comparable to those of traditional Ti screws. In 2015, Zhao *et al*. [137] evaluated the treatment of femoral head necrosis using Mg screw fixation combined with vascularised bone transplantation. Imaging revealed good corrosion resistance, with screw diameter reduced by approximately 25% 12 months after surgery. Patients treated with Mg screws achieved significantly higher Harris hip scores than those in the control group (without Mg screw), indicating superior therapeutic efficacy. In May 2025, the Mg-containing biodegradable polymer bone repair material: Bojilie, fabricated through ultra-low temperature 3D printing, was officially approved for clinical use by the National Drug Administration. This 3D interconnected porous scaffold consists of PLGA, β -tricalcium phosphate, and Mg. The successful approval of this product signifies growing recognition of Mg-based materials as effective and reliable options in the field of bone repair. Although most current research on MgO-incorporated composite materials remains at the preclinical stage, extensive findings and a solid theoretical foundation demonstrate the important role of MgO in bone repair. Given the limited scope of clinical application, this study aims to emphasise the potential of MgO-based materials and encourage greater research attention and clinical exploration in this field.

Challenges and prospects

The moderate degradation rate of MgO NPs allows the degradation process of composite materials to synchronise with osteogenesis. Incorporating MgO NPs into composite systems can address non-degradability issues associated with traditional metallic alloys such as stainless steel and Ti alloys while also reducing infection risk and economic burden of secondary surgeries [138,139]. In addition, the slower and more controlled degradation rate ensures adequate mechanical support during fracture healing. In addition, Mg^{2+} released during the degradation of MgO NPs promotes osteoblast proliferation via multiple pathways [140] and exerts bactericidal effects by disrupting bacterial activity. The OH^- generated during degradation helps regulate the local microenvironment, creating favourable conditions for bone repair while enhancing corrosion resistance. With an ageing population and rising incidence of bone-related diseases (such as osteoporosis and bone defects) [141], there is an urgent need for efficient, safe, and multifunctional bone repair materials. Unlike other fracture types, fractures associated with osteoporosis are more difficult to stabilise due to bone loss, and patients are at a greater risk of secondary fractures and delayed healing. MgO demonstrates strong integration with bone tissue by promoting osteocyte adhesion and proliferation as well as angio-

Table 7. Application of MgO NPs as bone repair materials.

Application	Result	Mechanism	Ref.
Alloy	Incorporation of MgO into the alloy improves scaffold histocompatibility, promotes the growth of new bone tissue, and enhances antibacterial activity. The addition of MgO significantly increases the yield strength and ductility of the alloy.	Mg^{2+} released during degradation promote cell migration, proliferation, and angiogenesis. These ions can also penetrate bacterial cells, disrupting their function. The tightly bonded interface between MgO and the alloy enhances the mechanical properties of the composite.	[21,33,133]
Bone cement	The addition of MgO significantly reduces the exothermic reaction of bone cement, improves osteoblast adhesion, accelerates degradation, and decreases material brittleness.	MgO optimises the performance of bone cement through hydration reactions, reducing the peak heat release, refining surface characteristics, and inducing microscopic toughening, thereby improving clinical suitability.	[117,118,124]
Hydrogel	The sustained release of Mg^{2+} contributes to the differentiation of osteoblast precursor cells and the formation of Ca nodules, promotes osteoblast activity, and inhibits osteoclast activity.	MgO enables sustained Mg^{2+} release through its synergistic interaction with the hydrogel. The released Mg^{2+} promote the differentiation of osteoblast precursor cells and the formation of Ca nodules by activating osteogenesis-related signalling pathways and regulating the ionic environment, while simultaneously inhibiting osteoclast activity through modulation of the OPG/RANKL system.	[127,128,134]
Coating	Incorporation of MgO into the coatings effectively enhances the antibacterial and osteogenic properties of the material and improves mechanical properties.	Mg^{2+} released during degradation interact with bacteria, inhibiting their activity. MgO NPs refine surface morphology and enhance the overall structural and functional properties of the coating.	[131,132]

genesis, making it a promising candidate material for the next generation of orthopaedic implants. Through continued in-depth research and technological innovation, MgO-reinforced composites are expected to revolutionise treatment strategies in the fields of bone repair and regenerative medicine. Additionally, based on their fundamental surface properties, MgO-based materials are being extensively explored as inorganic drug carriers [142–144]. When used as carriers for acidic drugs, MgO improves drug-loading efficiency while avoiding harmful contamination and hypomagnesemia, thereby offering new possibilities for disease treatment [145].

Nevertheless, MgO NPs also present several challenges in practical applications. First, the immune response is a critical consideration in the application of bone repair implants. During MgO degradation, the effects of Mg^{2+} and OH^{-} on the immune system are bidirectional and concentration-dependent. An appropriate degradation rate provides an alkaline microenvironment and releases Mg^{2+}, which facilitates the conversion of macrophages from M1 to M2, thereby shortening the inflammatory period and promoting tissue repair. However, excessively high ion concentrations may induce cytotoxicity or inflammatory reactions [146,147]. Thus, the precise control of the MgO degradation rate is crucial for ensuring clinical safety and efficacy. Secondly, the degradation rate of MgO NPs *in vivo* is a key factor influencing the long-term stability of implants [43]. The typical time required for fracture healing is approximately two months, and bone defect repair may require even longer. Premature MgO degradation could result in an early loss of mechanical support from the implant material. Addressing this issue requires optimisation of particle size, surface modification and composite design. Furthermore, the development of intelligent release systems capable of adjusting the MgO NPs release rate in response to internal environment changes may allow precise control of degradation behaviour and improve therapeutic outcomes. Moreover, the distribution of MgO within composite materials considerably affects overall performance [148]. Uneven distribution of MgO can lead to particle agglomeration, causing non-uniform local stress concentrations and compromised material properties. Addressing this issue requires advancements in material fabrication techniques. Liu *et al.* [149] utilised friction stir processing to achieve uniform dispersion of MgO particles in Mg–Zn–Ca composites. This technique refined the grain

size by 42%, and produced composites with excellent corrosion resistance and mechanical strength. Similarly, Yu *et al*. [150] prepared Mg–3Zn–0.7CaO composites using high-shear melt technology, wherein CaO reacted with Mg to form uniformly distributed MgO, significantly improving tensile strength and corrosion resistance. Furthermore, the incorporation of MgO NPs can influence the mechanical properties of composite materials, including strength and toughness [151]. Therefore, optimisation of particle dispersion and interface bonding is essential to ensure adequate mechanical integrity and performance. Recently, increasing attention has been directed towards carbon nanotubes as a reinforcing materials for Mg matrices. Saberi *et al*. [152] incorporated 0.5 wt.% carbon nanotubes into Mg-3Zn materials and reported that compressive strength increased from 122 ± 6 to 185 ± 9 MPa, while the hardness increased from 59 ± 2.3 to 79 ± 3.1. Although no studies have yet explored the incorporation of carbon nanotubes into MgO, the significant improvements in compressive strength and hardness achieved with carbon nanotube reinforcement in other Mg-based materials provide valuable insight into potential strategies for addressing the mechanical limitations of MgO composites. Long-term *in vivo* experiments are required to evaluate the safety and biodegradability of MgO NPs and their metabolic products. At present, most research on MgO remains confined to *in vitro* and animal experiments, primarily involving small-animal models such as rabbits and mice. Differences in stress distribution and patterns between small-animal models and humans inevitably led to discrepancies between experimental and clinical mechanical outcomes. Currently, the clinical use of MgO is largely limited to oral treatments for gastrointestinal disorders and as an anticonvulsant agent. Although MgO has not yet achieved full recognition in orthopaedic applications, its established biosafety provides a strong foundation for further research. With continued progress in material design and clinical evaluation, the widespread application of MgO in bone repair materials appears imminent.

Conclusions

This review systematically summarises current research on MgO NP-containing composites in the field of orthopaedic implants and highlights their potential to overcome the limitations of traditional orthopaedic materials through multi-mechanism synergy. MgO NPs enhance the mechanical properties and corrosion resistance of composites by refining grains and filling surface defects. By releasing Mg^{2+}, they regulate the local microenvironment and activate signalling pathways such as PI3K/Akt and P_{38}/Osx/Runx2, thereby promoting both osteogenic activity and antibacterial function simultaneously. Furthermore, MgO demonstrates broad adaptability across various orthopaedic implant systems—including alloys, bone cements, hydrogels, and coatings—providing strong theoretical support for the design of a next-generation degradable and multifunctional bone repair material. However, the limited clinical data currently available underscore the need for further studies to validate the universal application of MgO in clinical treatment and long-term orthopaedic use.

List of abbreviations

Mg, Magnesium; MgO, Magnesium oxide; NPs, Nanoparticles; ROS, Reactive oxygen species; CSF, Compressive strain at fracture; EIS, Electrochemical impedance spectroscopy; 3D, Three-dimensional; BMSCs, Bone marrow-derived mesenchymal stem cells; HAp, Hydroxyapatite; SF, Shape memory fibre cellulose; BMP-2, Bone morphogenetic protein-2; MIC_{50}, The half minimum inhibitory concentration; PC3, Prostate cancer cells; PDSC, Periosteum-derived stem cell; PMMA, Polymethyl methacrylate; CS, Chitosan; ALN, Alendronate; CPC, Calcium phosphate cement; CSMP, Water-soluble phosphocreatine-functionalised CS; MgYREZr, Magnesium–yttrium–rare earth–zirconium.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding authors on reasonable request. All data generated or analyzed during this study are included in this published article. The manuscript, includ ing related data, and figures have not been previously pub lished and are not under consideration elsewhere.

Author Contributions

HDX, DWZ and WDW contributed to the design of this work. JHY, PW and TWZ contributed to the interpretation of data. XY and SBH analyzed the data. HDX, WDW, WWZ and XYC drafted the work. JLL, DWZ revised critically for important intellectual content. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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