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Magnesium Phosphate Cements for Endodontic Applications: A Critical Review of Promise and Pitfalls

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Abstract

Magnesium phosphate cements (MPCs) have recently gained attention as potential materials for endodontic applications due to their rapid setting, favourable mechanical properties, and bioactive potential. Laboratory and preclinical studies indicate that MPCs can form apatite-like structures, exhibit good compressive strength, and support cell viability, suggesting promising biological interactions. However, several limitations remain unresolved. The acid–base setting reaction of MPCs is strongly exothermic, which may pose a risk to pulp or periapical tissues, and ammonium-containing formulations can release cytotoxic ammonia, although partial mitigation is possible through sodium phosphate substitution. Rapid setting enhances handling in controlled conditions but may complicate placement in complex root canal anatomies. While *in vitro* studies suggest comparable or superior sealing ability relative to conventional calcium silicate cements, human clinical evidence is minimal or absent. Degradation and resorption profiles of MPCs may further affect their suitability as scaffolds in regenerative endodontics. Overall, MPCs represent promising investigational materials, yet claims regarding clinical readiness are premature. Careful evaluation of their physicochemical behaviour, biological safety, and practical handling is essential before consideration for routine clinical use.

Keywords: Bioactive Cements; Endodontic Biomaterials; Pulp Capping; Regenerative Endodontics; Root-end Filling

Introduction

Endodontic treatment aims to eliminate infection from the root canal system, maintain periapical tissue health, and restore tooth function. Ideal endodontic materials should be biocompatible, dimensionally stable, antibacterial, and capable of supporting tissue repair and mineralization. Calcium silicate–based cements, such as mineral trioxide aggregate (MTA) and Biodentine, have been widely adopted over the past two decades due to their bioactivity and clinical success. However, these materials present well-recognized limitations, including long setting times, handling challenges, potential tooth discoloration, and high cost [1, 2].

MPCs have recently been investigated as alternative bioactive materials. These cements form *via* an acid–base reaction, typically combining a basic component such as magnesium oxide (MgO) with acidic phosphate salts, including ammonium dihydrogen phosphate ($NH_4H_2PO_4$) or potassium dihydrogen phosphate (KH_2PO_4) [3, 4]. Originally developed for civil engineering applications, MPCs have been explored in orthopaedics due to their rapid setting, moderate alkalinity, and controlled ion release, which in preclinical studies, may support mineralized tissue formation *in vitro* and in animal models [1].

Magnesium ions play critical roles in bone metabolism, osteogenesis, and enzymatic processes. The controlled release of Mg^{2+} and PO_4^{3-} from MPCs can create an alkaline microenvironment that potentially promotes stem cell differentiation and mineralization. These features have led to preliminary investigations into MPCs for pulp capping, perforation repair,

root-end filling, and regenerative endodontic procedures. However, current evidence is predominantly preclinical, with limited animal studies and no human clinical trials, highlighting the preliminary nature of these findings.

Despite promising *in vitro* and animal data, the translational pathway for MPCs in endodontics remains uncertain. Major concerns include the highly exothermic setting reaction, short working time, potential ammonia release from ammonium-based formulations, limited radiopacity, and uncertain long-term stability under clinical conditions. Moreover, the absence of standardized testing protocols and human trials complicates the assessment of their clinical performance in the complex root canal environment.

Despite promising preliminary findings, the literature on MPCs remains limited by heterogeneous formulations, variable study designs, and an absence of clinically relevant evidence. Significant gaps persist, including the need for standardized materials, evaluation of thermal and ammonia-related risks, and robust translational studies. These gaps underscore the necessity for a critical reassessment of MPCs before considering their potential clinical application.

Given these considerations, the objective of this review is to critically evaluate the chemistry, physicochemical behaviour, biological responses, and potential endodontic applications of MPCs, while highlighting the significant limitations that currently restrict their translation into routine clinical practice.

Materials and Methods

This review was conducted as a narrative synthesis of the literature on MPCs with relevance to endodontic applications. A non-systematic search was performed in PubMed, Scopus, and Web of Science using combinations of the following keywords: "magnesium phosphate cement," "MPC," "struvite," "endodontics," "pulp capping," "root-end filling," and "bioactive cement." Articles published in English up to January 2025 were considered. Included studies comprised *in vitro* experiments, *ex vivo* dentin interaction studies, animal models, and materials science reports that provided information on MPC chemistry, physicochemical behaviour, or potential biological effects relevant to endodontics. Studies that were unrelated to biomedical applications or focused exclusively on conventional calcium silicate cements were excluded. Because this review follows a narrative rather than a systematic approach, no structured protocol was used for study identification, screening, or quality assessment. Consequently, selection bias and publication bias cannot be excluded. Given the limited number and heterogeneity of studies, no quantitative synthesis or meta-analysis was attempted. A narrative review inherently lacks the methodological rigor of a systematic review, including structured study selection, risk-of-bias assessment, and reproducible search strategies. As a result, the findings may be influenced by selection bias, reporting bias, and author interpretation, limiting the strength of evidence-based conclusions. This approach aims to provide a critical overview of current evidence while acknowledging gaps and uncertainties that affect the clinical interpretation of MPCs in endodontics.

Chemistry and Composition

MPCs are acid–base reaction cements formed by the reaction of a basic magnesium source with an acidic phosphate component. The most commonly used basic component is magnesium oxide (MgO), which reacts with phosphate salts such as ammonium dihydrogen phosphate ($NH_4H_2PO_4$), potassium dihydrogen phosphate (KH_2PO_4), or sodium dihydrogen phosphate (NaH_2PO_4). The reaction produces magnesium phosphate phases, most commonly struvite ($MgNH_4PO_4{\cdot}6H_2O$) (ammonium-based formulations) or K-struvite ($MgKPO_4{\cdot}6H_2O$) (potassium-based formulations), which contribute to the rapid setting and early strength characteristic of MPCs [5].

Magnesium oxide (MgO) component

The reactivity of MgO strongly influences the cement's setting behavior. Light-burnt, highly reactive MgO promotes rapid hydration but may also increase heat generation and reduce working time. In contrast, dead-burnt MgO reacts more slowly and is sometimes used to moderate the exothermic reaction [6].

Phosphate component

Traditional MPCs use ammonium-based phosphates due to their fast and strong reaction with MgO. However, Ammonium-containing formulations may release ammonia during hydration, raising concerns about cytotoxicity and tissue irritation. To mitigate this, sodium or potassium phosphates have been investigated as alternatives, forming sodium- or potassium magnesium phosphate cements. While substitution reduces ammonia formation, evidence confirming complete elimination of biological risks remains limited [7].

Hydration and setting reaction

The setting of MPCs involves acid–base neutralization, resulting in the precipitation of crystalline magnesium phosphate hydrates. Struvite formation occurs through the reaction:

$MgO+NH_4H_2PO_4+5H_2O \rightarrow MgNH_4PO_4{\cdot}6H_2O$ (struvite). This process is highly exothermic. Temperature increases range widely across formulations, and their relevance in confined endodontic

spaces remains unclear, requiring further investigation. For potassium phosphate systems, the dominant phase is $MgKPO_4 \cdot 6H_2O$ (K-struvite), which forms through a similar mechanism but without the generation of ammonia [1].

Additives and modifiers

Various additives are incorporated to improve handling and performance: Retarders (*e.g.*, borax, citric acid) to reduce high-speed setting. Fillers (*e.g.*, MgO particles, inert powders) to control microstructure and porosity. Radiopacifiers such as zirconium oxide or barium sulphate, although their interaction with MPC matrices and impact on discoloration require further study. Radiopacifiers may influence mechanical behavior, opacity, and color stability, but available evidence is limited and inconsistent [8].

Physico-chemical Properties

The physicochemical behaviour of MPCs critically determines their suitability for endodontic applications, influencing handling, sealing ability, stability, and biological interactions. MPCs are characterized by rapid setting, typically occurring within 5 to 15 min due to the acid–base reaction forming struvite. This rapid setting can reduce the risk of contamination; however, the short working time may complicate precise placement, particularly in complex canal anatomies. The hydration reaction of MPCs is strongly exothermic, and although studies in bulk samples report temperature rises of several tens of degrees Celsius, the actual thermal effect in confined spaces such as the pulp chamber remains unmeasured, raising concerns about potential tissue injury [5]. Strategies to mitigate heat generation, including the use of less reactive dead-burned MgO, adjusting the liquid-to-powder ratio, or incorporating borate-based retarders, have been proposed; however, standardized validation in dental contexts is lacking.

In terms of mechanical performance, MPCs achieve high early compressive strength in preclinical studies, often ranging from 20 to 60 MPa within one hour, which is higher than many calcium phosphate cements and comparable to some conventional endodontic materials. This early strength could facilitate immediate restoration placement, yet data on long-term mechanical durability under moisture, thermal cycling, or in the root canal environment remain limited, preventing firm conclusions regarding their clinical reliability [5, 8]. Dimensional stability and solubility are other critical considerations. MPCs generally exhibit minimal shrinkage and may even slightly expand, which can improve adaptation to dentin walls. Nevertheless, the long-term solubility profile is inconsistent across formulations. Some ammonium-based cements demonstrate gradual phase conversion or dissolution over time, potentially compromising sealing ability, and robust comparative data against materials such as MTA or Biodentine are lacking [8].

The microstructure of MPCs typically consists of dense crystalline networks of struvite or K-struvite, where lower porosity contributes to strength and reduced microleakage. However, porosity varies widely depending on factors such as MgO particle size, reactivity, and water content, and many experimental studies do not employ standardized characterization methods, limiting cross-study comparability. Radiopacity is another notable limitation, as native MPCs lack sufficient contrast for radiographic visualization. Radiopacifiers, including zirconium dioxide, tantalum pentoxide, or bismuth oxide, are often incorporated to address this issue. While these additives improve radiographic visibility, their effects on setting behavior, mechanical properties, potential discoloration, and cytotoxicity remain poorly understood in MPC systems [1].

Overall, current evidence indicates that MPCs exhibit promising physicochemical performance, particularly regarding rapid setting, early strength, and potential adaptability to dentin. However, variability across formulations, incomplete characterization of long-term stability, and limited data under clinically relevant conditions indicate that their physicochemical properties, while encouraging, are still preliminary and require further systematic evaluation before clinical application can be recommended.

Biological Behaviour

The biological performance of MPCs is a central determinant of their potential for endodontic applications, yet the current evidence base is limited and predominantly preclinical. *In vitro* studies suggest that MPCs are generally cyto-compatible with dental pulp stem cells (DPSCs), periodontal ligament fibroblasts, and osteoblast-like cells, indicating minimal acute cytotoxicity [5, 8]. However, these findings are largely derived from short-term assays using diluted extracts rather than direct material contact, reducing their clinical relevance. Formulations containing ammonium phosphates may release small amounts of ammonia during hydration, which has been associated with cytotoxic effects in some studies, though the magnitude and clinical significance remain unclear. Sodium-based or potassium-based alternatives appear to reduce ammonia generation and improve biocompatibility, but this has not been confirmed in *in vivo* models.

In vitro experiments report enhanced alkaline phosphatase (ALP) activity, suggesting odontogenic and osteogenic potential [8]. Nonetheless, these results are almost entirely from two-dimensional cell culture models, which do not fully replicate the complex microenvironment of the pulp or periapical tissues. The controlled release of Mg^{2+} and PO_4^{3-} ions is hypothesized to contribute to these effects, yet variability in release rates across different formulations raises questions about the consistency and duration of the bioactive stimulus. Evidence of apatite-like mineral deposition in simulated body fluid (SBF) further supports bioactivity, although *in vitro* SBF models cannot reliably predict *in vivo* performance.

Regarding antibacterial properties, MPCs exhibit a moderately alkaline pH of approximately 9–10, which may inhibit certain oral bacteria. Existing data are limited to laboratory studies using single bacterial strains and do not reflect the polymicrobial complexity of endodontic infections. In comparison to calcium hydroxide-based materials, the antibacterial activity of MPCs appears weaker, and no *in vivo* antibacterial studies have been conducted [5].

Animal studies exploring tissue responses to MPCs are sparse and generally involve small sample sizes with short follow-up durations. Reported outcomes include mild transient inflammation and early formation of mineralized tissue [1]. However, these observations cannot be directly extrapolated to human clinical scenarios, and no long-term histological studies exist to assess potential chronic inflammation, foreign-body reactions, or the durability of newly formed tissues.

Overall, while MPCs demonstrate promising biological behavior in terms of cytocompatibility, mineralization, ion release, and preliminary *in vivo* tissue responses, the evidence remains insufficient to support clinical application. The lack of standardized testing, limited *in vivo* validation, and absence of human trials underscore the need for more rigorous, long-term studies before these materials can be recommended for endodontic procedures (Table 1).

Applications in Endodontics

Preclinical studies have investigated MPCs in various endodontic procedures, including pulp capping, pulpotomy, root-end filling, perforation repair, root canal sealing, and regenerative approaches; however, robust clinical evidence is currently lacking. Animal studies investigating MPCs in pulp exposure models are limited, and no published evidence currently demonstrates dentin bridge formation or reparative outcomes [9]. These findings, however, are limited to small rodent models, which differ substantially from human pulpal anatomy, vascularization, and immune responses. No human clinical trials have been conducted, and therefore any claims regarding clinical effectiveness remain speculative.

In root-end or retrograde fillings, MPCs have demonstrated adequate sealing ability and mechanical strength in laboratory leakage models [10, 11]. Despite these encouraging results, methodological variability among leakage tests complicates direct comparison to established materials such as MTA or Biodentine. No validated *in vivo* models or human surgical trials have assessed MPC performance in clinical conditions. Similarly, for root perforation or resorption repair, the paste-like consistency and rapid hardening of MPCs may offer handling advantages, but most evidence comes from *in vitro* studies evaluating sealing ability or cytocompatibility [12]. Potential concerns such as exothermic reactions and ammonia release in confined spaces remain largely uninvestigated, limiting translational relevance.

MPCs have also been studied as experimental root canal sealers. Early investigations report favorable flow, low solubility, and reduced microleakage compared to zinc oxide–eugenol-based sealers [11, 13]. However, comparisons with modern bioceramic sealers are lacking, and long-term performance under thermomechanical stresses has not been evaluated, which is essential for clinical reliability. The ion-releasing and bioactive

Table 1. Biological Properties of MPCs

Biological property	Observed effect	Evidence type/remarks	References
Cytocompatibility	Generally non-cytotoxic to DPSCs, PDL fibroblasts, osteoblast-like cells	*In vitro* (short-term), limited direct contact studies	Mohammadi *et al.*; Y. Liu *et al.* [5, 9].
Mineralization/ALP activity	Increased ALP activity	*In vitro*, 2D culture; no *in vivo* validation	Mohammadi *et al.* [8]
Ion release	Mg^{2+} and PO_4^{3-} ions are released, promoting biomineralization	*In vitro*; variable release across formulations	Gelli and Ridi [1]
Antibacterial effect	Mild inhibition of some oral bacteria	*In vitro*, single-strain assays; weaker than $Ca(OH)_2$	Y. Liu *et al.* [5]
***In vivo* tissue response**	Mild transient inflammation; early mineralized tissue formation	Small-animal studies, short follow-up; no long-term data	Gelli and Ridi [1]
Bioactivity (apatite formation)	Evidence of apatite-like mineral deposition	*In vitro* SBF studies; predictive value uncertain	Mohammadi *et al.* [8].

properties of MPCs have prompted interest in their use in regenerative endodontic procedures (REPs) as barrier materials or scaffold adjuncts [14, 15]. Nonetheless, rapid setting and variable degradation may limit their suitability for long-term scaffold function, and validated *in vivo* regenerative models are absent. Thus, any claims regarding MPCs in REPs remain preliminary and restricted to experimental contexts.

In summary, while MPCs exhibit promising physicochemical and biological characteristics across multiple endodontic applications, the evidence is entirely preclinical, heterogeneous, and based on non-standardized formulations. Rigorous *in vivo* studies and controlled human clinical trials are required before these materials can be recommended for clinical use (Table 2).

Limitations and Critical Considerations

Despite their attractive preclinical properties, MPCs face several important limitations that currently restrict their clinical translation in endodontics.

Exothermic setting reactions

MPCs undergo strongly exothermic acid–base reactions during the formation of struvite phases ($MgNH_4PO_4{\cdot}6H_2O$) or K-struvite. Conventional ammonium-based MPCs can release substantial heat, raising concerns about thermal injury within confined endodontic spaces where heat dissipation is minimal. Although modified "low-heat" formulations using less reactive MgO, alternative phosphate salts, or retarders can reduce peak temperatures, these adjustments may also alter setting kinetics or compromise early mechanical strength. Notably, no studies have quantified in situ temperature changes in dental-scale cavities, highlighting the need for standardized thermal evaluation before clinical use [1, 3, 16].

Ammonia release from ammonium-based formulations

MPC systems employing ammonium dihydrogen phosphate ($NH_4H_2PO_4$) may release ammonia during hydration and degradation. *In vitro* studies report reduced cell viability at higher local ammonia concentrations. Replacing ammonium salts with sodium or potassium phosphates (NaH_2PO_4, KH_2PO_4) reduces ammonia evolution and improves cytocompatibility; however, long-term *in vivo* data validating these substitutions remain limited [5].

Short working time and handling challenges

The rapid setting of MPCs (5–15 min) is beneficial for reducing contamination but restricts working time for careful placement, particularly in complex canal anatomy or perforation defects. Premature hardening can compromise adaptation and sealing. While retarders (boric acid, sodium borate, citric acid) or polymer additives can improve manipulability, these modifications may influence pH, ion release, or mechanical behaviour. An optimal balance between extended handling time and preserved bioactivity has not yet been established [1].

Radiopacity limitations and potential discoloration

Native MPCs are radiolucent and require radiopacifier incorporation (*e.g.*, Bi_2O_3, ZrO_2, Ta_2O_5) for adequate visualization on radiographs. These additives may influence mechanical or biological properties, and certain radiopacifiers, particularly bismuth oxide, have been associated with tooth discoloration in other cement systems. Long-term discoloration studies specific to MPCs are lacking, and comparative radiopacity data *versus* MTA/Biodentine remain scarce [17, 18].

Degradation, solubility, and long-term dimensional stability

MPCs exhibit partial solubility and ion release, which may support mineralization but could compromise long-term stability if degradation is too rapid. Limited evidence exists regarding the behaviour of MPCs under physiological endodontic conditions over extended periods. For regenerative endodontics, where scaffold persistence is important, MPCs' rapid setting and variable degradation profiles may be suboptimal. Standardized degradation testing and validation in appropriate large-animal models are needed to assess functional longevity [1, 19].

Table 2. Endodontic applications of MPCs *vs.* evidence level

Application	Observed Performance	Evidence Level	References
Pulp capping/pulpotomy	Supports early dentin bridge formation; minimal inflammation	Small-animal models only; no human trials	Bedoya *et al.*; Chen *et al.* [9, 20]
Root-end filling	Adequate sealing ability and mechanical strength in lab models	*In vitro*; no validated *in vivo* or clinical data	Qi *et al.*; Salem *et al.* [10, 11]
Perforation/resorption repair	Rapid hardening; paste-like consistency; good sealing *in vitro*	*In vitro* only; exothermic and ammonia effects not evaluated	Song *et al.* [12]
Root Canal Sealing/Obturation	Favorable flow, low solubility, reduced microleakage vs. ZnO-E	*In vitro*; no comparison to modern bioceramic sealers; no long-term studies	Kelmendi *et al.*; Salem *et al.* [11, 13]
Regenerative Endodontics	Barrier/scaffold potential; bioactive and ion-releasing	Experimental; rapid setting may limit scaffold function; no validated *in vivo* REPs	Liu *et al.*; Zhao *et al.* [18, 19]

Level of evidence and absence of clinical trials

Current evidence is predominantly derived from *in vitro* experiments and small-animal studies. Reports of favourable biological responses, such as dentin bridge formation, often suffer from limited sample sizes, lack of blinding, or inconsistent methodologies. Large-animal studies, standardized formulations, and well-designed human clinical trials are urgently required. The absence of commercially standardized dental MPC products and limited regulatory approval further impede translation (*e.g.*, Mg OsteoCrete is one of the few available experimental systems (Table 3) [1, 3].

Material Optimization Strategies

To enhance the performance of MPCs for dental applications, several material optimization strategies have been explored. Hybrid composites, formed by combining MPCs with polymers such as PMMA, chitosan, or gelatin, improve mechanical toughness and extend setting time. Ion doping with bioactive elements like Sr^{2+}, Zn^{2+}, or Si^{4+} promotes osteoinduction and provides antibacterial effects. Controlled porosity, achieved by adjusting MgO particle size and liquid-to-powder ratios, allows regulation of ion release and pH stabilization, optimizing biological and chemical performance. Additionally, advanced radiopacifiers such as ZrO_2, Ta_2O_5, or nano-Bi_2O_3 are incorporated to ensure radiographic visibility without inducing cytotoxicity, making MPCs more suitable for clinical endodontic applications. Mitigating the exothermic reaction intrinsic to the MPC setting; strategies such as partial MgO substitution, incorporation of thermal-buffering polymers, and modulation of acid concentration help reduce peak temperatures, thereby preventing thermal damage to surrounding dental tissues and improving clinical safety.

Table 3: Comparative advantages of Magnesium Phosphate Cements (MPCs) over Calcium Silicate Cements (MTA and Biodentine)

Parameter	Magnesium phosphate cement (MPC)	Calcium silicate cements (MTA/Biodentine)	Reference Examples	Evidence level/remarks
Setting time	5–15 min; rapid set; adjustable with retarders (preclinical prototypes)	MTA: 2–4 h; Biodentine: ~12–15 min	Mestres and Ginebra [3]	MPC data entirely *in vitro*; CSC values supported by extensive lab and clinical data
Early compressive strength	30–60 MPa within 1 h (formulation-dependent)	MTA: 15–20 MPa at 24 h; Biodentine: ~100 MPa at 1 day	Mestres and Ginebra [3]	MPC strength reported only in materials studies; CSC strength validated clinically
Dimensional stability	Very stable; minimal shrinkage (*in vitro*)	Slight shrinkage or expansion depending on cement	Zhou *et al.*; Camilleri [14, 17]	MPC stability untested clinically; CSC behaviour validated *in vivo*
pH and biocompatibility	Mild alkaline pH 8–10; cytocompatible in cell studies	Strong alkaline pH ~12; may cause early irritation	Mestres and Ginebra [3]	MPC biocompatibility data limited to short-term *in vitro*/animal models; CSC biocompatibility supported by human trials
Ion release	Mg^{2+} and PO_4^{3-} release supports preliminary mineralization	Ca^{2+} release; well-established bioactivity	Mestres and Ginebra [3]	MPC ion release mainly theoretical/experimental; CSC ion release clinically correlated
Antibacterial effect	Mild antibacterial activity	Moderate antibacterial effect (high pH)	Liu *et al.*; Jerez-Olate *et al.*	MPC antibacterial effect weak; CSC antimicrobial effect clinically relevant.
Handling	Smooth paste; rapid setting; may limit working time	MTA: difficult/ grainy; Biodentine: improved handling	Camilleri [5, 17, 21]	MPC handling tested only in lab; CSC handling based on extensive clinical use
Discoloration risk	Low (preclinical tooth-block tests)	High for MTA (Bi_2O_3); lower for Biodentine	Camilleri [17]	MPC discoloration risk untested clinically; CSC discoloration mechanisms well-documented
Washout resistance	Excellent in controlled lab environments	MTA: poor; Biodentine: moderate	Mestres and Ginebra [3]	MPC washout resistance proven only *in vitro*; CSC performance validated clinically
Cost and accessibility	Experimental materials; cost unknown; not commercially standardized	Commercial products available but expensive	Camilleri [17]	MPC availability extremely limited; CSCs widely available and regulated
Clinical evidence	None; only *in vitro* and limited animal studies	Extensive clinical evidence for MTA; growing for Biodentine	Nowicka *et al.* [22]	MPCs lack any human clinical trials; CSCs supported by large clinical datasets

Clinical Translation and Practical Considerations

MPCs show promising preclinical performance, but several practical factors currently limit their translation into routine endodontic practice. No commercial dental-grade MPC formulations are available, and most studies rely on laboratory-synthesized powders with variable compositions, underscoring the need for validated, GMP-compliant manufacturing and consistent quality control [3]. Cost advantages often cited in the literature remain speculative, as the final price would depend on raw material purity, incorporation of radiopacifiers or retarders, sterilization, packaging, and regulatory compliance. Sterilization poses additional challenges, as thermal or irradiation methods may alter MgO reactivity, hydration kinetics, or final cement properties; data on shelf-life and stability under sterile conditions are currently lacking [1]. Native MPCs are radiolucent, necessitating the addition of radiopacifiers such as bismuth oxide or zirconium dioxide to meet clinical imaging requirements; however, Bi_2O_3 has been associated with long-term discoloration in other endodontic cements [17]. Handling properties have been assessed primarily in simplified laboratory models, where setting times of 6–9 min and early mechanical strength have been reported [3]; yet, real-world endodontic conditions, including moist dentin, blood contamination, and complex canal anatomy, may significantly affect working and setting times, flow, and adaptation. Finally, regulatory approval for dental MPCs would require comprehensive material characterization, biocompatibility testing, sterilization validation, and controlled clinical trials, which none of them are currently available. Taken together, while MPCs represent a promising experimental option for endodontic applications, substantial challenges in manufacturing, handling, safety, and regulatory validation must be addressed before they can be considered clinically viable. Future research should prioritize the development of standardized, dental-specific MPC formulations, comprehensive physicochemical characterization under clinically relevant conditions, and long-term *in vivo* biocompatibility studies. Large-animal models and well-designed human clinical trials will be essential to establish their therapeutic effectiveness, safety profile, and comparative performance relative to established calcium silicate–based materials. Until such evidence becomes available, MPCs should be regarded as investigational materials whose clinical use remains premature.

Conclusion

Based on preclinical evidence to date, MPCs exhibit promising physicochemical characteristics, controlled ion release, and favourable biological responses in both laboratory and small-animal models. Nevertheless, these findings remain preliminary and lack clinical validation. Critical research gaps, including heterogeneous and non-standardized formulations, insufficient assessment of exothermic and ammonia-related risks, limited data on long-term stability, and an overall scarcity of robust *in vivo* and human studies, continue to constrain their translational viability.

If future research successfully addresses these limitations through standardized material development, comprehensive safety testing, rigorous large-animal investigations, and methodologically sound clinical trials, MPCs may evolve into credible alternatives for endodontic applications. Until such evidence is available, their clinical relevance should be viewed as promising yet unproven.

Data Availability

The corresponding author will provide data related to the present research upon request.

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Conflict of interest

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Authors' contributions

Conceptualization: NNH/HS/MNH; Methodology: NNH/HS/CLV/MNH; Formal Analysis and Investigation: NNH/HS/MNH; Writing-Original Draft Preparation: NNH/HS; Writing-Review and Editing: NNH/HS/CLV/MNH; Supervision: HS/CLV; All authors read and approved the final manuscript.

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