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INPLASY

Magnesium-Containing Biomaterials for Alveolar and Mandibular Bone Regeneration: Osteoimmune Responses and Translational Evidence—A Scoping Review Protocol

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 August 2026 and was last updated on 28 August 2026.

INTRODUCTION

Review question / Objective This scoping review aims to map the magnesium-containing biomaterials investigated for alveolar and mandibular bone regeneration; characterize the osteoimmune responses and underlying mechanisms evaluated; and determine the extent, characteristics, and translational maturity of the available in-vitro, animal, and human evidence. It will also identify methodological limitations, knowledge gaps, and priorities for future preclinical and clinical research.
PCC framework. Population
Humans with alveolar or mandibular bone defects; animal models of alveolar, mandibular, periodontal, or craniofacial bone regeneration; and relevant in-vitro cellular or tissue models. Calvarial studies will be considered supporting evidence only when the biomaterial is explicitly intended for craniofacial or jawbone regeneration.
Concept
Magnesium-containing biomaterials in which magnesium is an intentionally incorporated structural or bioactive component, including magnesium metals and alloys, membranes, scaffolds, ceramics, hydrogels, coatings, nanoparticles, composites, and fixation systems. The review will examine their osteoimmune and inflammatory effects and the relationship of these effects to angiogenesis, osteogenesis, degradation, and bone regeneration.
Context
Experimental, translational, and clinical research relevant to oral, periodontal, craniofacial, and maxillofacial bone regeneration, including in-vitro studies, preclinical animal studies, and human clinical studies conducted in any geographical or healthcare setting. Long-bone-only studies without explicit relevance to jaw or craniofacial regeneration will be excluded.

Background Alveolar and mandibular bone defects may result from tooth loss, trauma, infection, periodontal disease, tumour resection,

congenital abnormalities, or medication-related osteonecrosis. Reconstructing these defects remains challenging because successful regeneration requires coordinated inflammatory resolution, vascularisation, osteogenesis, and biomaterial degradation within the oral cavity's distinctive mechanical and microbiological environment.

Magnesium is an essential mineral involved in bone metabolism, cellular signaling, angiogenesis, and immune regulation. Magnesium-containing biomaterials—including biodegradable metals and alloys, membranes, scaffolds, ceramics, hydrogels, coatings, nanoparticles, composites, and fixation systems—have therefore gained attention as potential alternatives or adjuncts to conventional bone-regenerative materials. Through controlled degradation and magnesium-ion release, these materials may influence macrophage polarisation, cytokine production, oxidative stress, osteoclast activity, vascular development, and osteogenic differentiation. However, excessive or poorly controlled degradation may cause local alkalisation, gas formation, mechanical instability, or undesirable tissue reactions.

Evidence relevant to jawbone regeneration spans in vitro experiments, animal defect models, and a limited number of human investigations. The diversity of biomaterial platforms, anatomical models, immune measurements, and regenerative outcomes makes it difficult to determine which effects are directly demonstrated, which are inferred from general tissue responses, and how close individual technologies are to clinical translation.

Rationale Preliminary searches indicate that existing reviews have addressed magnesium-based materials in mandibular reconstruction, reconstructive oral and maxillofacial surgery, general bone immunomodulation, or magnesium membranes used for guided bone regeneration. However, no identified review has comprehensively mapped the full range of magnesium-containing biomaterials used specifically for alveolar and mandibular bone regeneration while simultaneously examining their osteoimmune mechanisms and translational maturity.

The available evidence is heterogeneous in biomaterial composition, magnesium incorporation, degradation behaviour, anatomical model, study design, immune assessment, and regenerative outcome. Some studies directly evaluate macrophage polarisation, cytokine expression, inflammatory signalling, oxidative stress, or osteoclast activity, whereas others report only indirect tissue-response or bone-regeneration outcomes. Consequently, the extent to which osteoimmunomodulation contributes to the reported regenerative effects remains unclear.

A scoping review is therefore appropriate to systematically identify and classify the available evidence rather than estimate a pooled treatment effect. The review will distinguish direct mechanistic immune evidence from indirect inflammatory or regenerative observations, map findings according to anatomical relevance and developmental stage, and identify under-investigated biomaterial platforms and pathways. This synthesis is expected to clarify the current evidence base, prevent duplication of research, and inform the design of future mechanistic studies, clinically relevant animal models, and human investigations of magnesium-containing biomaterials for jawbone regeneration.

METHODS

Strategy of data synthesis A comprehensive literature search will be conducted in MEDLINE via PubMed, Scopus, the Cochrane Library, including CENTRAL and the Cochrane Database of Systematic Reviews, and Google Scholar, from database inception to the final search date. The search will combine controlled vocabulary, where available, and free-text terms covering three principal concepts: (1) magnesium, magnesium alloys, and magnesium-containing materials; (2) biomaterial platforms, including membranes, scaffolds, implants, ceramics, hydrogels, coatings, nanoparticles, composites, and fixation systems; and (3) alveolar, mandibular, periodontal, jaw, oral, maxillofacial, and craniofacial bone regeneration. Immune-related terms will be tested but will not be mandatory in every search combination because relevant studies may report immune or inflammatory findings without identifying them in their titles or abstracts.

For Google Scholar, the exact search strings, search dates, sorting method, and number of results screened will be documented. The first 200 results from each search, ranked by relevance, will be screened. The reference lists of relevant systematic reviews, scoping reviews, and other comprehensive reviews addressing magnesium biomaterials, guided bone regeneration, jaw reconstruction, or osteoimmunomodulation will be manually searched for eligible primary studies. Backward reference searching and forward citation tracking will also be conducted for included studies and key reviews. Records identified through supplementary searching will undergo the same deduplication, screening, and eligibility assessment as database records. Review articles will be used for study identification and contextual interpretation but will not contribute primary

outcome data or be double-counted in the synthesis.

The included evidence will be synthesised descriptively using structured tables, evidence maps, and narrative analysis. Studies will be grouped according to biomaterial platform, magnesium formulation and incorporation method, anatomical model, defect type, study design, degradation characteristics, measured biological outcomes, and translational stage. Evidence will be classified along two independent dimensions:

Anatomical relevance: direct alveolar or mandibular evidence, jaw-relevant in-vitro evidence, or supporting craniofacial evidence.

Osteoimmune evidence: direct mechanistic immune assessment, indirect inflammatory or tissue-response assessment, or no immune assessment.

Study characteristics and findings will be summarised using frequencies and proportions where appropriate. Mechanistic pathways connecting magnesium exposure or degradation with macrophage behaviour, cytokine regulation, oxidative stress, angiogenesis, osteogenesis, osteoclastogenesis, and bone regeneration will be narratively mapped. Evidence will also be organised across in-vitro, animal, and human stages to assess translational maturity and identify knowledge gaps. Meta-analysis is not planned because substantial heterogeneity in biomaterial composition, experimental models, outcome definitions, and measurement methods is anticipated. The review and study-selection process will be reported in accordance with PRISMA-ScR guidance.

Eligibility criteria Types of participants: Human participants of any age or sex with alveolar, mandibular, periodontal, peri-implant, or other jawbone defects requiring regeneration or reconstruction will be eligible. Relevant animal models of alveolar, mandibular, periodontal, maxillofacial, or craniofacial bone defects and in-vitro cellular, tissue, or co-culture models will also be included. Calvarial models will be considered supporting evidence only when the investigated material is explicitly intended for oral, jawbone, or craniofacial regeneration. Long-bone and other non-craniofacial models without explicit relevance to jawbone regeneration will be excluded.

Concept: The review will include biomaterials in which magnesium is an intentionally incorporated structural or bioactive component and its composition, incorporation, degradation, or release is adequately described. Eligible platforms may include magnesium metals and alloys, membranes, scaffolds, ceramics, bone substitutes, hydrogels, coatings, nanoparticles, composites, implants, and fixation systems. Studies must evaluate at least one outcome related to bone regeneration, osteogenic differentiation, mineralisation, angiogenesis, osteoclastogenesis, immune or inflammatory responses, material degradation, biocompatibility, or local tissue response. Studies without direct immune measurements may remain eligible if they evaluate regenerative or tissue-response outcomes, allowing gaps in osteoimmune assessment to be identified. Studies of systemic magnesium supplementation, incidental or uncharacterised trace magnesium, or purely mechanical, computational, corrosion, or material-characterisation outcomes without biological relevance will be excluded.

Context: Original primary research conducted in laboratory, preclinical, or clinical settings will be eligible, including in-vitro studies, animal studies, clinical trials, observational studies, case series, and clinically informative case reports. No restrictions will be applied according to publication date, geographical location, healthcare setting, comparator, or follow-up duration. Reviews will not contribute primary outcome data but will be searched to identify eligible studies. Protocols, editorials, commentaries, patents, and conference abstracts without sufficient original data will be excluded. Duplicate reports will be linked, and the most complete report will serve as the primary source.

Source of evidence screening and selection All records retrieved from PubMed, Scopus, the Cochrane Library, Google Scholar, and supplementary citation searching will be imported into reference-management software and deduplicated using automated and manual procedures. The deduplicated records will then be transferred to Rayyan for screening.

Before formal screening, two reviewers will independently pilot the eligibility criteria on a sample of records. Any differences in interpretation will be discussed, and the eligibility guidance will be refined before screening proceeds. Formal selection will occur in two stages. First, two reviewers will independently screen all titles and abstracts against the predefined eligibility criteria. Records considered potentially eligible by either reviewer will advance to full-text assessment. Second, the same reviewers will independently assess the full texts of potentially eligible sources.

At both stages, reviewers will make decisions independently and remain blinded to each other's decisions until screening is completed. Disagreements will initially be resolved through discussion and reference to the protocol. If consensus cannot be achieved, a third reviewer will adjudicate. Reasons for exclusion will be

recorded for every source excluded during full-text assessment.

Multiple publications arising from the same experiment, animal sample, or clinical population will be identified and linked. The most complete report will be treated as the primary source, while companion publications will be used only to obtain supplementary information and will not be counted as separate studies.

Potentially eligible records identified from reference-list searching or forward citation tracking will undergo the same deduplication and independent screening procedures. The complete selection process—including records identified, duplicates removed, records screened, full texts assessed, exclusions with reasons, and final included sources—will be documented using a PRISMA-ScR flow diagram. A final list of included studies will be verified by both reviewers before data charting begins.

Data management Search results will be exported in their original database formats and stored in a dedicated project folder. Records will be imported into Zotero for citation management and duplicate identification and then transferred to Rayyan for title, abstract, and full-text screening. Each record will be assigned a unique study identifier. Duplicate reports and multiple publications arising from the same experiment or participant population will be linked under a common study-family identifier to prevent double-counting.

Data will be charted using a standardised and piloted Microsoft Excel form. The form will capture bibliographic information, country, study design, experimental or clinical population, anatomical site, defect model, biomaterial platform, magnesium composition and incorporation method, degradation and magnesium-release characteristics, comparator, follow-up duration, immune and inflammatory outcomes, angiogenic and osteogenic outcomes, adverse tissue responses, principal findings, funding sources, conflicts of interest, anatomical relevance, strength of osteoimmune evidence, and translational stage.

One reviewer will extract the data, and a second reviewer will independently verify all entries against the full-text source. Discrepancies will be resolved through discussion; unresolved disagreements will be adjudicated by a third reviewer. The charting form may be refined iteratively if additional relevant variables emerge, with all modifications documented and applied consistently to previously charted studies.

Separate files will be maintained for the original search results, deduplicated records, screening decisions, full-text exclusion reasons, extracted data, and the final verified dataset. Version-controlled copies will be stored in secure, access-restricted cloud storage available to the review team, with regular backups retained. Because the review will use published literature, no identifiable participant-level information will be collected. The final extraction framework and supporting dataset will be made publicly available through a suitable repository, where permitted, following publication of the review.

Reporting results / Analysis of the evidence The study-selection process will be reported using a PRISMA-ScR flow diagram, showing the numbers of records identified, duplicates removed, records screened, full texts assessed, exclusions with reasons, and sources included. The characteristics of the included studies will be presented in structured evidence tables and summarised descriptively using counts, frequencies, and proportions where appropriate.

Evidence will be analysed according to the following domains:

Study design and translational stage: in-vitro, animal, or human evidence.

Anatomical site and defect model.

Biomaterial platform and magnesium formulation.

Method of magnesium incorporation, degradation, and ion release.

Direct immune and inflammatory measurements.

Osteogenic, angiogenic, osteoclastic, regenerative, and adverse tissue outcomes.

Proposed molecular or cellular mechanisms.

Clinical applicability and remaining translational gaps.

Each study will be classified independently according to two dimensions:

Anatomical relevance: direct alveolar or mandibular evidence, jaw-relevant in-vitro evidence, or supporting craniofacial evidence.

Osteoimmune evidence: direct mechanistic immune assessment, indirect inflammatory or tissue-response assessment, or no immune assessment.

The findings will be presented as a narrative synthesis supported by summary tables, evidence matrices, and graphical maps showing relationships among magnesium biomaterial platforms, immune pathways, regenerative outcomes, anatomical relevance, and translational stage. Particular attention will be given to macrophage polarisation, cytokine and inflammatory signalling, oxidative stress, angiogenesis, osteogenic differentiation, osteoclastogenesis, material degradation, and bone formation.

Evidence gaps will be identified by examining biomaterial platforms, anatomical models, immune

outcomes, and translational stages for which evidence is absent, limited, inconsistent, or based only on indirect measurements. No meta-analysis or pooled effect estimation is planned because substantial heterogeneity is expected. Formal risk-of-bias assessment is not planned because the purpose of the review is to map the nature and extent of the evidence rather than determine comparative effectiveness. Accordingly, conclusions concerning effectiveness or clinical superiority will not be drawn solely from the number or direction of reported findings.

Presentation of the results Results will be presented through a combination of narrative summaries, structured tables, and graphical evidence maps. The planned presentation will include:
PRISMA-ScR flow diagram: numbers of records identified, deduplicated, screened, assessed in full text, excluded with reasons, and included.
Study-characteristics table: author, year, country, study design, experimental or clinical population, anatomical site, defect model, comparator, sample size, and follow-up.
Biomaterial-characteristics table: biomaterial platform, magnesium formulation, method of incorporation, magnesium concentration, degradation behaviour, ion-release characteristics, and intended clinical application.
Osteoimmune and regenerative-outcomes table: immune cells and markers assessed, macrophage phenotype, cytokines, signalling pathways, inflammatory and oxidative-stress outcomes, angiogenesis, osteogenesis, osteoclastogenesis, bone formation, adverse responses, and principal conclusions.
Two-dimensional evidence matrix: studies will be mapped according to anatomical relevance—direct alveolar or mandibular, jaw-relevant in-vitro, or supporting craniofacial evidence—and strength of osteoimmune evidence—direct mechanistic, indirect tissue-response, or no immune assessment.
Translational evidence map: biomaterial platforms will be displayed across in-vitro, animal, and human stages to demonstrate the maturity of each technology and identify where translation has stalled.
Mechanistic pathway figure: proposed relationships among magnesium degradation or ion release, immune and inflammatory regulation, macrophage behaviour, angiogenesis, osteogenesis, osteoclastogenesis, and bone regeneration.
Research-gap table: missing immune outcomes, under-investigated anatomical models, insufficiently characterised materials, methodological limitations, and priorities for future preclinical and clinical research.
Where appropriate, categorical findings will be summarised using frequencies and proportions. Graphical presentations may include heat maps, bubble plots, and bar charts; however, their final format will depend on the quantity and characteristics of the included evidence. All figures and tables will distinguish direct experimental findings from author interpretations or indirectly inferred mechanisms.

Language restriction No language restrictions will be imposed during the search or study-selection process. Studies published in languages other than English will be assessed using translated titles and abstracts, followed by full-text.

Country(ies) involved Iraq.

Other relevant information The review will be conducted in accordance with the Joanna Briggs Institute methodology for scoping reviews and reported using the PRISMA Extension for Scoping Reviews (PRISMA-ScR). A final search update will be performed shortly before manuscript submission to identify newly published eligible studies.
Any amendments to the registered protocol, including changes to the research question, eligibility criteria, search sources, classification framework, or synthesis plan, will be documented with the date, description, and justification for the change. Material amendments will be updated in the INPLASY record and transparently reported in the final publication.
Directly measured immune outcomes will be distinguished from indirect tissue-response findings and mechanisms inferred solely by the original authors. Anatomical relevance and osteoimmune evidence will be classified independently to avoid treating craniofacial-supporting evidence as equivalent to direct alveolar or mandibular evidence. Because the review will use publicly available published evidence and will not collect individual participant data, research ethics approval is not required. The final search strategies, data-charting framework, and supporting dataset will be made publicly accessible, where permitted, following publication.

Keywords Magnesium-containing biomaterials; biodegradable magnesium; jawbone regeneration; alveolar bone regeneration; mandibular reconstruction; osteoimmunomodulation; macrophage polarisation; guided bone regeneration; bone tissue engineering;.

Dissemination plans The completed scoping review will be submitted for publication in a peer-reviewed journal specialising in biomaterials, oral and maxillofacial surgery, bone regeneration, or dental research. Findings may also be presented at relevant national or international conferences and academic research meetings. The INPLASY record will be updated with the review status and final publication details.

Where permitted, the complete search strategies, study-selection information, data-charting form, evidence classifications, and final dataset will be deposited in an openly accessible repository. The results will also be communicated to researchers and clinicians in oral surgery, periodontology, implant dentistry, tissue engineering, and biomaterials science to support future mechanistic studies, clinically relevant animal models, and human translational research.

Contributions of each author

Author 1 - Hani Radhi - Conceived the review, developed the research question and methodology, designed the search strategy and eligibility criteria, and will participate in study screening, data charting, evidence synthesis, and interpretation. Author 1 will draft the manuscript, coordinate revisions, manage the project, and act as guarantor of the review.
Email: hani.h.radhi@uomustansiriyah.edu.iq
Author 2 - Ahmad Hassan - Contribution will be to the review methodology and refinement of the eligibility criteria and search strategy. Will independently screen records, verify data charting, contribute to evidence synthesis and interpretation, critically revise the manuscript, and approve the final version.
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