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ADMINISTRATIVE INFORMATION

Support - King Khalid University.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590054

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 September 2025 and was last updated on 14 September 2025.

INTRODUCTION

Review question / Objective To evaluate the efficacy of four bioactive molecule delivery platforms in enhancing outcomes for Regenerative Endodontic Therapy (RET).

Rationale Current clinical RET protocols lack controlled delivery of specific bioactive cues, often resulting in the regeneration of fibrous tissue.

Condition being studied Regenerative endodontic therapy for the treatment of necrotic teeth, immature permanent teeth with incomplete root development.

METHODS

Search strategy A comprehensive PICO-based search of PubMed/MEDLINE, Scopus and Web of Science databases.

Participant or population The review included in vitro studies, ex vivo models, animal models, and limited clinical case reports/series but no human clinical trials were found.

Intervention Use of advanced bioactive molecule delivery platforms, including hydrogels, nanogels, polymeric nanoparticles, liposomes, and mesoporous silica nanoparticles.

Comparator Standard RET techniques ; Control conditions.

Study designs to be included In vitro, ex vivo, animal studies, and clinical studies were considered for inclusion.

Eligibility criteria Studies were included if they involved RET and tested a defined delivery platform against a control; reviews, commentaries, and studies without a specific delivery system were excluded.

Information sources PubMed/MEDLINE, Scopus, Web of Science.

Main outcome(s) Delivery-system characterization, release kinetics, biocompatibility, and regenerative endpoints such as pulp-like tissue formation and dentin deposition.

Additional outcome(s) Secondary outcomes included antibacterial efficacy, cell viability, odontogenic differentiation markers.

Data management Data were extracted using a standardized form by two independent reviewers, with disagreements resolved by a third reviewer.

Quality assessment / Risk of bias analysis Risk of bias was assessed using a modified STROBE checklist for in vitro studies, the SYRCLE tool for animal studies.

Strategy of data synthesis Narrative synthesis grouped by platform type and model; limited meta-analysis performed only for sufficiently homogeneous outcomes.

Subgroup analysis Studies were grouped and synthesized by the type of delivery platform and further by model type.

Sensitivity analysis Not explicitly performed due to the narrative nature of the synthesis and heterogeneity of the included studies.

Language restriction Included only English-language publications.

Country(ies) involved Saudi Arabia, United States of America, India.

Other relevant information The review followed PRISMA 2020 guidelines.

Keywords Regenerative endodontics, tissue engineering, hydrogel scaffold, nanoparticle, controlled release, growth factors, nanocarriers, pulp regeneration.

Dissemination plans Peer-review publication and conference presentation as the primary dissemination routes.

Contributions of each author

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