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### ADMINISTRATIVE INFORMATION

**Support** - This study received no external funding.

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

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202510123

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 January 2025 and was last updated on 30 January 2025.

### INTRODUCTION

**Review question / Objective** Objective: To evaluate the cytocompatibility, bioactivity, and odontogenic differentiation potential of resin-modified calcium silicate-based materials compared to other calcium silicate biomaterials used in vital pulp therapy, using in vitro studies with human-derived dental pulp stem cells (DPSCs).

**Review Question:** What are the cytocompatibility, bioactivity, and odontogenic differentiation outcomes of resin-modified calcium silicate materials compared to other calcium silicate biomaterials in in-vitro models of vital pulp therapy?

**Rationale** Resin-modified calcium silicate materials are increasingly used in vital pulp therapy due to their superior handling, bioactivity, and bonding properties. However, a systematic synthesis of their performance compared to

established biomaterials like MTA and Biodentine in human-derived cell models is lacking. This review aims to address this gap and guide future research and clinical applications.

**Condition being studied** Vital pulp therapy, a treatment aimed at preserving the vitality of the dental pulp in cases of trauma or caries.

### METHODS

#### Search strategy

The following databases will be searched without language or date restrictions:

- PubMed
- Embase
- Scopus
- Web of Science
- CINAHL
- SciELO
- LILACS

**Keywords and Boolean Operators:****PubMed Search Strategy**

("resin-modified calcium silicate" OR "TheraCal" OR "resin-modified calcium silicate-based material")

AND ("dental pulp stem cells"[MeSH Terms] OR "DPSC" OR "stem cells human exfoliated deciduous teeth" OR "SHED" OR "stem cells apical papilla" OR "SCAP" OR "tooth germ stem cells" OR "hTGSC")

AND ("vital pulp therapy" OR "pulp regeneration")

AND ("cytocompatibility" OR "biocompatibility" OR "bioactivity" OR "odontogenic differentiation" OR "mineralization" OR "dentin bridge formation" OR "inflammatory response")

AND ("mineral trioxide aggregate" OR "MTA" OR "Biodentine" OR "calcium silicate cement"))

**PubMed Filters**

- Article Type: Journal Articles, In Vitro Studies.
- Text Availability: Abstract or Full-Text.
- Publication Year: 2010-2025.

**Embase Search Strategy**

('resin-modified calcium silicate' OR 'TheraCal' OR 'resin-modified calcium silicate-based material')

AND ('dental pulp stem cells' OR 'DPSC' OR 'stem cells human exfoliated deciduous teeth' OR 'SHED' OR 'stem cells apical papilla' OR 'SCAP' OR 'tooth germ stem cells' OR 'hTGSC')

AND ('vital pulp therapy' OR 'pulp regeneration')

AND ('cytocompatibility' OR 'biocompatibility' OR 'bioactivity' OR 'odontogenic differentiation' OR 'mineralization' OR 'dentin bridge formation' OR 'inflammatory response')

AND ('mineral trioxide aggregate' OR 'MTA' OR 'Biodentine' OR 'calcium silicate cement')

**EMBASE Filters**

- Study Type: Laboratory Studies
- Language: English.
- Publication Year: 2010-2025.

**Scopus Search Strategy**

TITLE-ABS-KEY(("resin-modified calcium silicate" OR "TheraCal" OR "resin-modified calcium silicate-based material")

AND ("dental pulp stem cells" OR "DPSC" OR "stem cells human exfoliated deciduous teeth" OR "SHED" OR "stem cells apical papilla" OR "SCAP" OR "tooth germ stem cells" OR "hTGSC")

AND ("vital pulp therapy" OR "pulp regeneration")

AND ("cytocompatibility" OR "biocompatibility" OR "bioactivity" OR "odontogenic differentiation" OR "mineralization" OR "dentin bridge formation" OR "inflammatory response")

AND ("mineral trioxide aggregate" OR "MTA" OR "Biodentine" OR "calcium silicate cement"))

**Scopus Filters**

- Document Type: Article.
- Language: English.
- Subject Area: Dentistry, Biomaterials.

**Web of Science Search Strategy**

TS=("resin-modified calcium silicate" OR "TheraCal" OR "resin-modified calcium silicate-based material")

AND TS=("dental pulp stem cells" OR "DPSC" OR "stem cells human exfoliated deciduous teeth" OR "SHED" OR "stem cells apical papilla" OR "SCAP" OR "tooth germ stem cells" OR "hTGSC")

AND TS=("vital pulp therapy" OR "pulp regeneration")

AND TS=("cytocompatibility" OR "biocompatibility" OR "bioactivity" OR "odontogenic differentiation" OR "mineralization" OR "dentin bridge formation" OR "inflammatory response")

AND TS=("mineral trioxide aggregate" OR "MTA" OR "Biodentine" OR "calcium silicate cement")

**Web of Science Filters**

- Document Type: Articles.
- Language: English.
- Timespan: Set 2010-2025.

**CINAHL Search Strategy**

("resin-modified calcium silicate" OR "TheraCal" OR "resin-modified calcium silicate-based material")

AND ("dental pulp stem cells" OR "DPSC" OR "stem cells human exfoliated deciduous teeth" OR "SHED" OR "stem cells apical papilla" OR "SCAP" OR "tooth germ stem cells" OR "hTGSC")

AND ("vital pulp therapy" OR "pulp regeneration")

AND ("cytocompatibility" OR "biocompatibility" OR "bioactivity" OR "odontogenic differentiation" OR "mineralization" OR "dentin bridge formation" OR "inflammatory response")

AND ("mineral trioxide aggregate" OR "MTA" OR "Biodentine" OR "calcium silicate cement")

**CINAHL Filters**

- Publication Type: Research Articles.
- Language: English.

**SciELO Search Strategy**

("resin-modified calcium silicate" OR "TheraCal" OR "resin-modified calcium silicate-based material")

AND ("dental pulp stem cells" OR "DPSC" OR "stem cells human exfoliated deciduous teeth" OR "SHED" OR "stem cells apical papilla" OR "SCAP" OR "tooth germ stem cells" OR "hTGSC")

AND ("vital pulp therapy" OR "pulp regeneration")

AND ("cytocompatibility" OR "biocompatibility" OR "bioactivity" OR "odontogenic differentiation" OR "mineralization" OR "dentin bridge formation" OR "inflammatory response")

AND ("mineral trioxide aggregate" OR "MTA" OR "Biodentine" OR "calcium silicate cement")

SciELO Filters

- Language: English.
- Restrict to original articles.

LILACS Search Strategy

("resin-modified calcium silicate" OR "TheraCal" OR "resin-modified calcium silicate-based material")

AND ("dental pulp stem cells" OR "DPSC" OR "stem cells human exfoliated deciduous teeth" OR "SHED" OR "stem cells apical papilla" OR "SCAP" OR "tooth germ stem cells" OR "hTGSC")

AND ("vital pulp therapy" OR "pulp regeneration")

AND ("cytocompatibility" OR "biocompatibility" OR "bioactivity" OR "odontogenic differentiation" OR "mineralization" OR "dentin bridge formation" OR "inflammatory response")

AND ("mineral trioxide aggregate" OR "MTA" OR "Biodentine" OR "calcium silicate cement")

LILACS Filters

- Language: English.
- Restrict to original articles.

### Participant or population

Inclusion:

- Human-derived dental pulp stem cells (DPSCs), including SHED, SCAP, and hTGSC.

Exclusion:

- Animal-derived stem cells or non-dental cell lines.

**Intervention** Resin-modified calcium silicate-based materials.

**Comparator** Other Calcium silicate biomaterials used in vital pulp therapy, such as:

- Mineral Trioxide Aggregate (MTA).
- Biodentine.

**Study designs to be included** In vitro studies only.

**Eligibility criteria** Inclusion Criteria:

- Studies using resin-modified calcium silicate in human-derived in vitro pulp regeneration models.
- Studies reporting at least one outcome: cytocompatibility, bioactivity, or odontogenic differentiation.

Exclusion Criteria:

- Animal or clinical studies.
- Reviews, meta-analyses, or conference abstracts.
- Studies that focus on parameters unrelated to the primary outcomes of this review:
  1. Surface porosity.
  2. Light curing temperature.
  3. Shear bond strength

4. Demineralization.

5. Discoloration.

6. Antimicrobial activity.

7. Physical or mechanical properties of materials.

**Information sources** Bibliographic databases (listed in Search Strategy).

**Main outcome(s)** 1. Cytocompatibility: Cell viability, proliferation, and metabolic activity.  
2. Bioactivity: Biomineralization, dentin bridge formation.  
3. Odontogenic Differentiation: Expression of markers like DSPP and DMP-1.

**Additional outcome(s)** 1. Inflammatory Response: Levels of cytokines like IL-6, TNF- $\alpha$ .

**Data management** Two independent reviewers will screen studies, extract data, and resolve discrepancies via consensus with third reviewer. Data will be managed using Covidence software tools for conducting data extraction and statistical analysis will be conducted by R Software.

**Quality assessment / Risk of bias analysis** Quality will be assessed using the Modified CONSORT Checklist for In Vitro Studies.

**Strategy of data synthesis** • Qualitative Synthesis: Results will be narratively summarized.  
• Quantitative Synthesis (if feasible): Meta-analysis using random-effects models.

**Subgroup analysis** Subgroup analyses will be performed based on the type of cell model (e.g., DPSCs vs. SHED) and biomaterials tested.

**Sensitivity analysis** Sensitivity Analysis will be conducted along with Meta Analysis.

**Language restriction** English.

**Country(ies) involved** India.

**Other relevant information** None.

**Keywords** resin-modified calcium silicate; dental pulp stem cells; vital pulp therapy; cytocompatibility; biocompatibility; bioactivity; mineral trioxide aggregate; biodentine; calcium silicate cement;theracal.

**Dissemination plans** Results will be disseminated through publications in peer-reviewed journals and conference presentation.

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### Contributions of each author

Author 1 - Heitor De Souza - Conceiving the review, Designing the review, Coordinating the review, Data collection, Data management, Analysis of data.

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Author 2 - Marina Fernandes - Conceiving the review, Designing the review, Coordinating the review, Data collection, Data management, Analysis of data.

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Author 3 - Akshatha Gadiyar - Coordinating the review, Data management, Analysis of data, statistical expertise, risk of bias assessment strategy.

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