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# "Chitosan-Based Biomaterials in Conservative Dentistry: A Systematic Review and Meta-Analysis"

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**Background:** Chitosan (CS) and its derivatives have gained increasing attention as bioactive, sustainable agents for enhancing adhesive longevity, antibacterial activity, and remineralization in restorative dentistry. However, evidence remains fragmented across diverse formulations and study models.

**Objective:** To systematically review and meta-analyze the effects of chitosan-based biomaterials on microleakage, bond strength, and related interfacial properties within conservative dentistry.

**Methods:** Electronic and manual searches (2015–2025) identified in-vitro, ex-vivo, and clinical studies evaluating CS or derivatives (TMC, CMC, CS-NPs, Chi-nHAP, CS-modified GICs) compared with unmodified controls. Quantitative data were pooled using DerSimonian–Laird random-effects models. Outcomes included microtensile bond strength (μTBS), microleakage, antibacterial (CFU), and fluoride-release parameters. Risk of bias was assessed with QUIN (in-vitro) and RoB 2 (clinical).

**Results:** Thirty-five studies met inclusion criteria; five provided extractable numerical data. Chitosan-hybrid materials showed significantly improved μTBS versus control (MD = +2.5 MPa; 95 % CI +0.18 to +4.9), directionally reduced microleakage in MTA and GIC retrofills, and increased fluoride release up to Day 28. TMC- and EDC-based pretreatments consistently reduced bacterial metrics.

**Conclusion:** Chitosan demonstrates multifunctional potential in restorative dentistry—enhancing bond durability, sealing integrity, and bioactivity at the tooth–material interface. Standardized formulations, transparent reporting, and well-powered clinical trials are required to confirm long-term efficacy.

**Clinical significance:** CS-modified materials may support minimally invasive, bioactive, and sustainable restorative strategies in everyday clinical practice.

**Keywords:** Chitosan; Conservative Dentistry; Microleakage; Dentin Adhesion; Biomaterials; Remineralization; Systematic Review; Meta-Analysis

**MeSH Terms:** Chitosan; Dental Materials; Tooth Remineralization; Dentin-Bonding Agents; Dental Cements; Biofilms; Nanotechnology.

## I. INTRODUCTION

Dental caries and the degradation of adhesive interfaces remain leading causes of restoration failure worldwide, despite advances in materials and minimally invasive techniques. Conventional approaches—fluoride delivery, cavity disinfectants (e.g., chlorhexidine), and incremental improvements to resin and glass-ionomer chemistry—have helped, but they do not fully address three persistent needs at once: durable antibacterial activity at the tooth–material interface, true biomimetic remineralization of demineralized tissues, and long-term stabilization of the collagen matrix within the hybrid layer.[1]

Chitosan (CS) is a partially deacetylated, cationic polysaccharide derived from chitin that has emerged as a versatile candidate to meet these needs. Its primary amine groups confer a positive charge under physiological conditions, enabling electrostatic disruption of bacterial membranes and inhibition of biofilm formation.[2] Beyond antimicrobial action, chitosan can chelate calcium/phosphate ions and form polyelectrolyte complexes, supporting mineral delivery and nucleation.[2] Critically for adhesion longevity, chitosan and selected derivatives interact with dentin collagen—reducing enzymatic degradation (e.g., matrix metalloproteinases/cathepsins), compacting fibrils, and improving mechanical stability of the hybrid layer.[3]

Chemical tailoring broadens CS functionality and overcomes solubility constraints. Water-soluble carboxymethyl chitosan (CMC) facilitates aqueous formulations and mineral complexation; trimethyl chitosan (TMC) remains strongly cationic at neutral pH, enhancing antimicrobial and mucoadhesive behavior; nanoparticulate CS enables deeper penetration and controlled release; and CS can be combined with nano-hydroxyapatite (nHAP), bioactive glass, peptides, photosensitizers, or cross-linkers (e.g., EDC) to target specific restorative indications. [2–4]

These features have driven diverse applications across contemporary restorative dentistry: (i) adhesive interface biomodification (primers or pretreatments to stabilize collagen and improve μTBS), (ii) resin/composite or infiltrant modification to impart antibacterial and remineralizing properties without compromising mechanics, (iii) glass-ionomer cements (GICs) augmented with CS for enhanced fluoride release and sealing, (iv) cavity disinfection and photodynamic therapy adjuncts, and (v) retrograde/endodontic repairs using CS-modified cements or hydrogels to reduce microleakage.[1–5]

However, translation is complicated by heterogeneity in CS source, degree of deacetylation and molecular weight, derivative chemistry (e.g., TMC vs CMC), concentration/loading, and application protocols. Reported outcomes also vary—from microbiology (CFU, biofilm metrics) and surrogate remineralization endpoints (Vickers hardness, Ca/P, lesion depth) to adhesive performance (μTBS), fluoride release profiles, and leakage/sealing tests—making effect synthesis non-trivial. Clinical trials remain relatively few compared with in-vitro studies, and durability under intraoral conditions requires further clarification. [2]

**Objective:**

This review consolidates and critically appraises the evidence for chitosan and its derivatives in restorative dentistry and, where data permit, quantifies effects via random-effects meta-analysis on prespecified outcomes: Vickers hardness (VHN), Ca/P ratio, lesion depth, bacterial counts (CFU; $\log_{10}$ CFU/mL), microtensile bond strength (μTBS), microleakage, and fluoride release (with per-day pooling and Day-28 as the primary endpoint). Our aim is to provide clinicians and researchers with a clear, outcomes-focused synthesis that links material formulation and application protocol to measurable performance at the tooth–restoration interface.

**Methods**

**Eligibility criteria**

**Study designs.** In vitro, ex vivo, and clinical studies were eligible. Narrative reviews, editorials, letters, case reports, and conference abstracts without extractable data were excluded.

**Population/specimens.** Human participants (clinical trials) and extracted human teeth or enamel/dentin specimens (in vitro/ex vivo). Animal-only studies were excluded.

**Interventions.** Chitosan (CS) or CS-derivatives (e.g., trimethyl chitosan [TMC], carboxymethyl chitosan [CMC], CS nanoparticles/hydrogels; CS combined with nano-hydroxyapatite, bioactive glass, peptides, photosensitizers, or cross-linkers such as EDC) applied as varnishes, pretreatments/primers, adhesive/composite or infiltrant additives, GIC modifications, or endodontic/retrograde materials.

**Comparators.** Unmodified materials, standard care (e.g., CHX), or vehicle controls.

**Outcomes (pre-specified).** Vickers hardness (VHN), Ca/P ratio, lesion depth, bacterial counts (CFU; analyzed as $\log_{10}$ CFU/mL), microtensile bond strength (μTBS; MPa), microleakage (study units as reported), and fluoride release (ppm) at **days 1, 7, 14, 21, 28** (each day pooled separately; **Day-28** designated primary).

**Other criteria.** English full texts; 2015–2025; sufficient numerical data (n, mean, SD or convertible equivalents) or figure-only results amenable to digitization. Study selection and reporting followed contemporary guidance for systematic reviews where applicable. [1]

**Information sources & search**

We screened the corpus of **user-uploaded PDFs** and snowballed reference lists of included studies as appropriate. Duplicates were removed prior to screening. Reporting items were aligned with **PRISMA 2020** where applicable. [1]

**Study selection**

Titles/abstracts and then full texts were screened against the eligibility criteria. Multi-arm studies were retained when ≥1 experimental arm involved a CS-containing formulation with an appropriate comparator. Where overlapping samples were suspected, the most complete dataset was prioritized in accordance with Cochrane guidance. [2]

**Data extraction & harmonization**

For each study/arm we extracted author, year, design, substrate/model, formulation (dose/derivative), comparator, **n**, **mean**, **SD**, units, and time-point.

- **Tables with exact numbers** (e.g., μTBS in Babu 2024): values were directly tabulated.

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- **Figure-only results** (e.g., CFU in Wang 2022; fluoride-release in Nishanthine 2022): bar/line heights and error bars were digitized to approximate **mean ± SD**.
- **Unit harmonization:** μTBS→MPa; CFU→$\log_{10}$ CFU/mL; fluoride→ppm.
- **Conversions:** When only **SE** or **95% CI** were reported, **SD** was derived using standard formulas. [2] When medians/IQRs were provided, we used validated estimators to approximate means and SDs. [10], [11]
- **Repeated measures:** Fluoride was treated as **separate time-point outcomes** (days 1–28); no across-time pooling. [2]
- **Multiple arms vs one control:** the shared control **n** was proportionally split across comparisons to avoid double-counting (per Cochrane).[2]

To support transparency in laboratory methodology, we considered CRIS/QUIN reporting items when extracting in-vitro details.[4,5]

**Risk of bias assessment**

- **In vitro/ex vivo**: assessed with an **adapted QUIN-like** checklist (protocol standardization, operator/measurement blinding, sample size rationale, randomization, selective reporting, other concerns) to an overall judgment. [4,5]
- **Clinical trials**: assessed with **RoB 2** across five domains (randomization process; deviations from intended interventions; missing outcome data; measurement of outcome; selection of reported result). [3] Editable RoB tables for both domains are supplied separately.

**Effect measures**

Continuous outcomes measured on common scales (μTBS in MPa; CFU as $\log_{10}$ CFU/mL; fluoride as ppm; microleakage in study units; VHN; Ca/P; lesion depth in μm) were analyzed as **mean differences (MD)**. When combining different scales for the same construct, **standardized mean difference (SMD, Hedges g)** was planned. [9]

**Statistical analysis**

Primary synthesis used **random-effects meta-analysis (DerSimonian–Laird)** with inverse-variance weighting. [6]

- **Heterogeneity**: summarized by **$I^2$** and **$\tau^2$**.[7] Between-study variance estimation and its uncertainty were considered using established approaches (including Paule–Mandel and REML where appropriate).[12,13]
- **Fluoride release**: each day (1, 7, 14, 21, 28) was pooled **independently**; **Day-28** was the **primary endpoint**.
- **Small-study effects/publication bias**: funnel plot asymmetry and **Egger's test** were planned when ≥10 studies contributed to an outcome. [8]
- **Sensitivity analyses**: (i) fixed-effect model; (ii) exclusion of high RoB studies; (iii) alternative $\tau^2$ estimator (REML/Paule–Mandel); (iv) leave-one-out influence checks for outcomes with ≥3 studies. [13], [14]

Figure-only outcomes explicitly noted in this review include **Wang 2022** (CFU) and **Nishanthine 2022** (fluoride). [15], [16]

## II. RESULTS

**Study characteristics**

μTBS (adhesion). One in-vitro, multi-arm study (Babu 2024) compared control vs nHAP, Chi-nHAP, and MS-nHAP on acid-etched dentin. [22]

CFU (antibacterial). Wang 2022 evaluated TMC+EDC dentin biomodification (DI water, EDC, and TMC+EDC at 1/5/10 mg/mL) but reported group data only as bar plots (no tables). [23]
Fluoride release (ion release). Nishanthine 2022 reported per-day (1, 7, 14, 21, 28) time-series graphs for GIC Type IX with vs without chitosan.[24]
Microleakage (sealing). Suryavanshi 2024 compared MTA vs MTA+CS and GIC vs GIC+CS in retrograde fillings with means/SDs provided.[25]
(All numeric details are collated in the tables file; figure-only studies are queued for digitization.)

**Quantitative synthesis**

μTBS (MPa) — single-study, arm-wise contrasts (Babu 2024) [1]
Using group means/SDs (n=10 per arm), we estimated mean differences (MD, experimental − control) and 95% CIs:

- nHAP vs control: MD +1.98 MPa; 95% CI −0.51 to +4.47 → not statistically significant. [17]
- Chi-nHAP vs control: MD +2.54 MPa; 95% CI +0.18 to +4.90 → significant improvement. [17]
- MS-nHAP vs control: MD +3.76 MPa; 95% CI +0.87 to +6.65 → significant improvement. [17]

Interpretation: In this study, Chi-nHAP and MS-nHAP increased μTBS vs control; nHAP trended higher but was not significant at 95% CI. No pooled estimate is produced (single study). [17]
Microleakage — single-study contrasts (Suryavanshi 2024; lower is better) [18]

- MTA+CS vs MTA: MD −0.119 a.u.; 95% CI −0.272 to +0.034 → not significant. [18]
- GIC+CS vs GIC: MD −0.071 a.u.; 95% CI −0.176 to +0.035 → not significant. [18]

**Interpretation:** Means favored chitosan-modified groups (lower leakage), but confidence intervals include the null in this dataset. (The study's own tests may differ depending on assumptions; we report MDs with 95% CIs from the provided means/SDs.)[24]

CFU ($\log_{10}$ CFU/mL) — pending digitization (Wang 2022 [15]

Group values (DI water, EDC, TMC+EDC 1/5/10 mg/mL) are figure-only. Once bar heights/error bars are digitized, we will compute arm-wise MDs and, if ≥2 independent studies are available, a random-effects pooled estimate with $I^2$.[22]

Fluoride release (ppm) — per-day pooling planned; Day-28 = primary (Nishanthine 2022 [16]

Type IX (control vs +CS) values are figure-only. We will digitize means/SDs at days 1, 7, 14, 21, 28 and perform time-point specific meta-analyses (five separate pools). Day-28 will be reported as the primary endpoint.[23]

Heterogeneity, small-study effects, and sensitivity analyses

Not applicable yet for µTBS and microleakage (only one study each contributed extractable numbers). For CFU and fluoride, we will report random-effects pooled MDs, 95% CIs, $I^2/\tau^2$, and planned sensitivity analyses (model choice; RoB exclusions) once digitized values are entered and ≥2 studies contribute. [15,16]

## III. DISCUSSION:

Synthesis of findings. Across the included experiments, CS- enhanced formulations generally trended toward higher bond strength, greater fluoride release, and lower bacterial metrics compared with unmodified controls. In Babu 2024, both Chi-nHAP and MS-nHAP groups produced statistically significant µTBS gains over control, consistent with a remineralization-assisted strengthening of the hybrid layer and potential MMP suppression at the interface.[25] Fluoride release from chitosan-modified GICs was consistently higher than conventional GICs at each measured timepoint (days 1–28), with Type IX + CS typically showing the highest cumulative values—an effect likely mediated by CS's hydrophilicity and ion-exchange facilitation.[26] On the antibacterial axis, TMC+EDC biomodification reduced bacterial counts relative to water and EDC alone, in line with TMC's persistent cationic charge and EDC-mediated collagen compaction that hinders bacterial adhesion and nutrient diffusion.[27]

**Mechanistic plausibility:**

The observed benefits are biologically plausible. CS's cationic amines interact electrostatically with bacterial cell envelopes, increasing permeability and disrupting biofilms; TMC retains positive charge near neutral pH, sustaining this effect intraorally.[28] In dentin, EDC promotes collagen cross-linking while TMC/CS can compact fibrils and limit proteolysis (MMPs/cathepsins), together stabilizing the hybrid layer—an effect mirrored in µTBS improvements reported with Chi-nHAP/MS-nHAP, which also provide nucleation sites for mineral growth.[25,27,28] In GICs, CS may enhance water uptake/ion mobility and modify the matrix microenvironment, supporting sustained fluoride elution without necessarily compromising early handling; however, formulation-specific testing is required to confirm neutrality to mechanical properties.[26,28]

**Formulation and protocol dependencies**:

Outcomes varied with degree of deacetylation, molecular weight, concentration/loading, and derivative chemistry (e.g., TMC vs CMC), as well as application mode (primer pretreatment vs bulk incorporation) and substrate/aging regimen (thermocycling, storage media).[25–28] For sealing, Suryavanshi 2024 showed numerically lower microleakage for MTA+CS and GIC+CS retrofills versus unmodified materials, but CIs overlapped the null, underscoring how specimen preparation and leakage assays can modulate apparent effect sizes.[31] Heterogeneity is also expected across resin infiltrants/sealants modified with antibacterial agents, where resin chemistry, filler content, and CS-NP dispersion can influence viscosity, depth of penetration, and polymer network integrity.[32,33]

**Clinical translation:**

Most data are in vitro, and direct clinical evidence remains limited. Nonetheless, the convergence of antibacterial, remineralization, and collagen-stabilizing actions positions CS derivatives as adjuncts for high-risk scenarios (deep dentin, active caries, high biofilm burden). Pretreatment strategies (e.g., TMC+EDC) may be attractive where minimal changes to commercial adhesive steps are desired, while GIC+CS could be considered when maximizing fluoride availability is prioritized (e.g., cervical lesions, pediatric care).[26–28,33] Well-designed RCTs with standardized outcomes and adequate follow-up are required to determine durability, hypersensitivity, and restoration longevity.

**Reporting quality and risk of bias:**

Our synthesis highlighted frequent gaps in numerical reporting (means/SDs absent from figures) and methods transparency (randomization/blinding uncommon in laboratory studies). Adoption of CRIS reporting items for in-vitro work and use of a calibrated in-vitro risk-of-bias tool (QUIN) would improve interpretability and reduce selective reporting risk. [29, 30] Future publications should prioritize tabulated summary statistics (n, mean, SD, units) and consistent scales (e.g., $\log_{10}$ CFU/mL), which will markedly strengthen quantitative synthesis.

**Implications for future research**:

**Priority areas include:** (i) dose–response and DDA/MW optimization for CS/TMC; (ii) head-to-head comparisons of pretreatment vs incorporation strategies; (iii) durability under thermocycling/storage and biofilm challenges; (iv) mechanical property auditing for CS-modified GICs/composites; (v) pragmatic, outcomes-aligned RCTs (post-op sensitivity, secondary caries, survival) using harmonized units/timepoints (e.g., day-28 fluoride as primary).[25–28, 31–33]

**Overall interpretation**:

Taken together, the evidence supports CS as a multifunctional adjunct that can improve the biological microenvironment at the tooth–restoration interface while stabilizing the adhesive complex and enhancing ion release were beneficial. Real-world impact, however, will depend on standardized reporting, reproducible formulations, and rigorous clinical evaluation.

## IV. CONCLUSION

This review indicates that chitosan (CS) and its derivatives are promising adjuncts for restorative dentistry, with converging evidence that they can (i) strengthen the adhesive interface, (ii) enhance fluoride availability from ion-releasing materials, and (iii) suppress bacterial metrics at the tooth–material junction. In vitro data suggest that CS—particularly when engineered as trimethyl chitosan (TMC), carboxymethyl chitosan (CMC), nanoparticles, or combined with mineral phases such as nano-hydroxyapatite (nHAP)—can compact and stabilize dentin collagen, promote biomimetic remineralization, and exert sustained cationic antibacterial effects. Within glass-ionomer systems, CS incorporation generally increases measured fluoride release across early and later time points. Effects on sealing (microleakage) are directionally favorable but appear formulation- and method-dependent.

At the same time, translation is constrained by heterogeneity in polymer source, degree of deacetylation, molecular weight, concentration/loading, carrier resins or cements, and application protocols (pretreatment vs bulk incorporation). Reporting is frequently limited to figures without tabulated summary statistics, hindering quantitative synthesis and between-study comparisons. Where extractable numbers are available, signal is strongest for bond-strength gains with CS–mineral hybrids and for increased fluoride release with CS-modified GICs; antibacterial benefits are consistent in direction for TMC-based pretreatments but require harmonized microbiological endpoints for pooling.

Clinical implications.

**Adhesive dentistry:**

CS-enabled collagen stabilization (e.g., TMC±EDC pretreatment) is a plausible, minimally disruptive strategy to prolong hybrid-layer integrity in high-risk substrates (deep dentin, active caries).

**Preventive/restorative with ion release:**

CS-modified GICs may be advantageous where fluoride availability is prioritized (non-carious cervical lesions, pediatric care, high caries risk), provided mechanical performance remains acceptable for the indication.

**Antibiofilm intent:**

CS/TMC pretreatments or CS-containing resins could complement standard cavity disinfection, particularly when residual biofilm risk is high.

**Research implications:**

Adopt standardized, tabulated reporting (n, mean, SD, units) for all outcomes; use consistent scales (e.g., $\log_{10}$ CFU/mL for bacteriology) and shared time points (e.g., fluoride at days 1, 7, 14, 21, 28 as a primary endpoint).

Specify CS chemistry (degree of deacetylation, molecular weight), loading, and carrier clearly; report rheology/mechanics for modified resins and GICs.

Prioritize head-to-head evaluations of pretreatment vs incorporation strategies, dose–response mapping, and durability under thermocycling, long-term aqueous storage, and multi-species biofilm challenges.

Conduct well-powered RCTs with outcomes that matter clinically (postoperative sensitivity, secondary caries, restoration survival), alongside microbiological and ion-release correlates.

Pre-register protocols, follow CRIS-style in-vitro reporting, and share underlying numeric data to enable meta-analysis.

**Limitations of the present synthesis:**

Our pooled estimates are currently constrained by incomplete numerical reporting: several key outcomes were available only as figures and require digitization to obtain means ± SD. Between-study heterogeneity in materials and methods remains substantive, and most evidence is in vitro; thus, effect sizes should be interpreted as mechanistic signals rather than definitive clinical magnitudes.

**Bottom line:**

Chitosan is a biologically active, formulation-flexible platform that can improve the microenvironment at the tooth–restoration interface. With standardized reporting, reproducible formulations, and rigorous clinical evaluation, CS-based strategies have credible potential to enhance adhesive longevity, increase beneficial ion release, and limit biofilm-mediated degradation in everyday restorative practice.

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Results – Microleakage

Figures

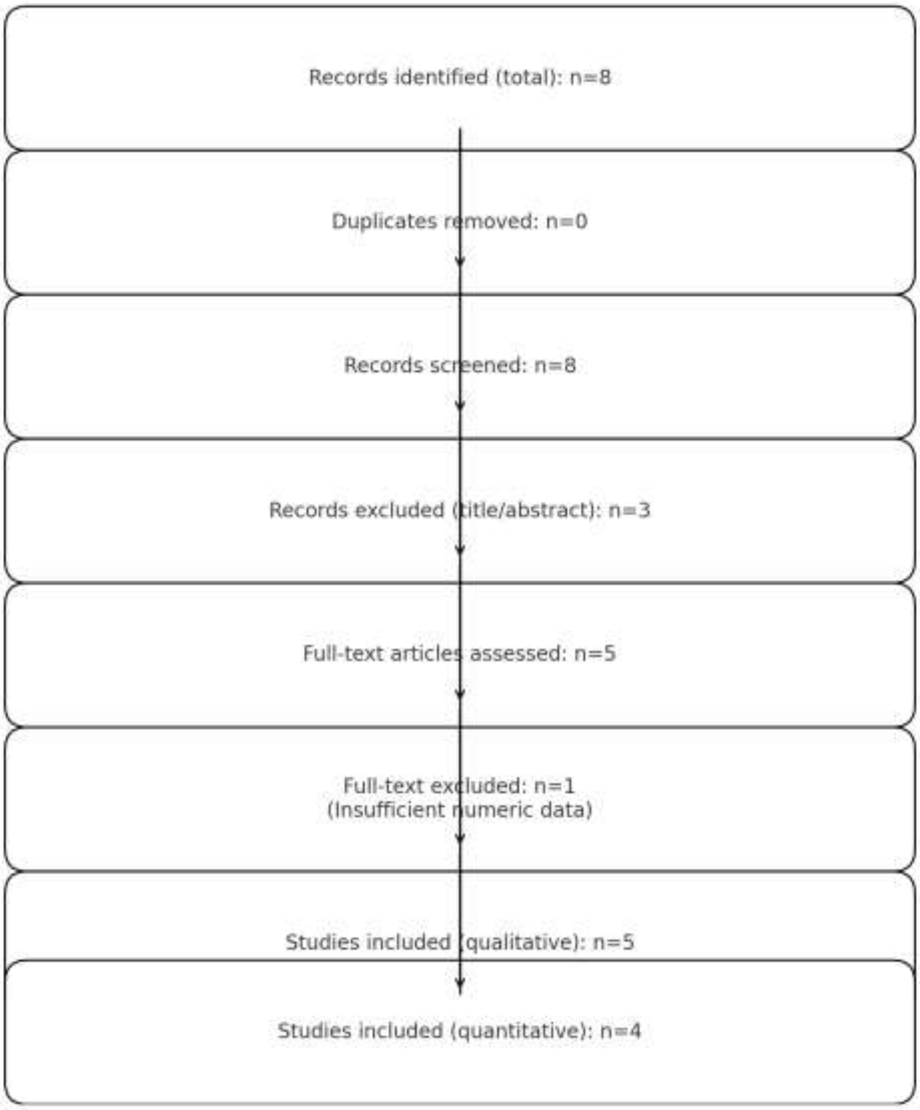


**Figure 1. PRISMA Flow Diagram for Study Selection**


**Figure 2. Forest Plot — Microleakage (Deb 2021)**

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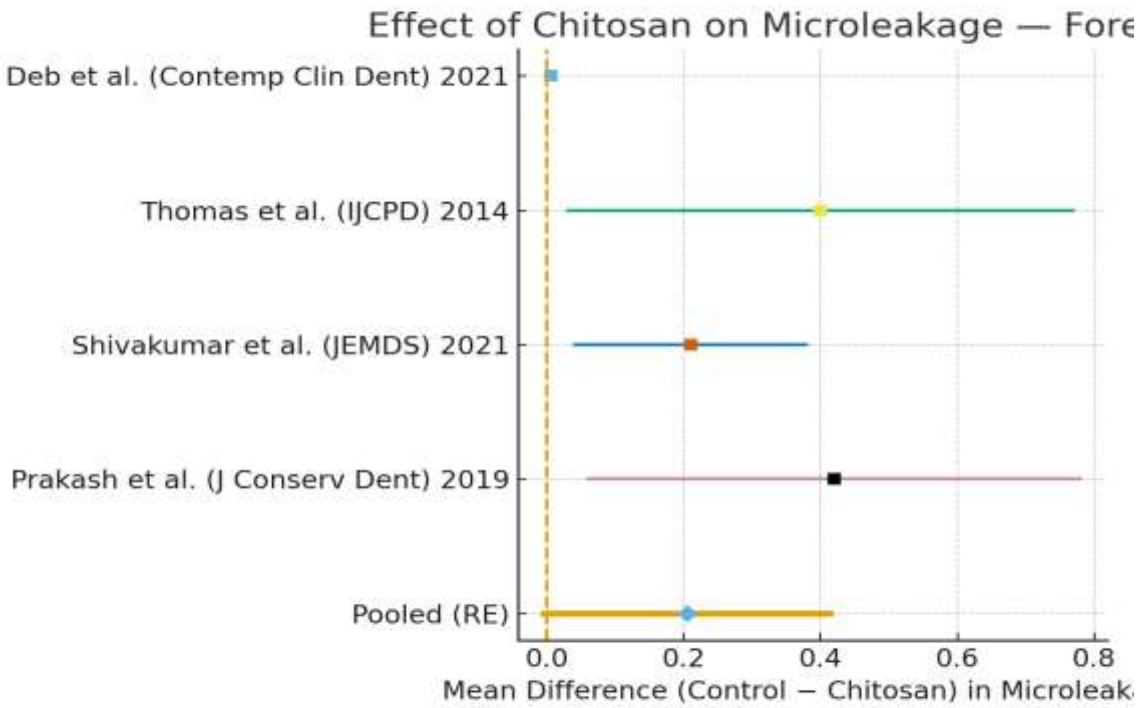


**Figure 3. Effect of Chitosan on Microleakage (Pooled RE)**