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ASSESSMENT OF REMINERALIZING POTENTIAL OF BIOACTIVE RESTORATIVE MATERIALS ON DEMINERALIZED DENTIN: A SYSTEMATIC REVIEW

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Abstract

Background: Demineralization of dentin beneath restorations remains a major clinical challenge, compromising structural integrity, adhesion, and long-term restoration success. Bioactive restorative materials—such as calcium-silicate cements, bioactive glass composites, giomers, and ion-releasing resin-based systems—have emerged as promising alternatives due to their ability to release therapeutic ions and promote remineralization. Understanding the comparative remineralizing potential of these materials is essential for informed material selection in restorative dentistry.

Methods: A systematic review was conducted following PRISMA 2020 guidelines to evaluate the remineralizing performance of bioactive restorative materials on artificially demineralized dentin. Electronic searches of PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar (2000–2025) were performed. Inclusion criteria focused on laboratory studies that assessed remineralization through microhardness testing, Ca/P ratio analysis (EDX/EDS), Raman spectroscopy, FTIR, and SEM/FE-SEM evaluation of mineral deposition, tubule occlusion, or interface bridging. A total of 12 in-vitro studies met the eligibility criteria. Due to methodological heterogeneity, a qualitative synthesis was undertaken.

Results: Across the included studies, bioactive and ion-releasing materials consistently demonstrated measurable remineralization of demineralized dentin. ACTIVA BioACTIVE showed the highest microhardness recovery, with reported increases of up to **~82%**, and significantly improved Ca/P ratios. Calcium-silicate–based materials such as Biodentine exhibited superior structural remineralization, characterized by progressive mineral deposition and **distinct interface bridging**, surpassing conventional GICs and most resin-based systems. Bioactive glass–containing materials produced rapid tubule occlusion and surface apatite formation, while NACP-modified composites achieved elevated Ca/P ratios and enhanced mineral deposition. Raman spectroscopy findings supported strong phosphate peak recovery, particularly in ion-releasing resin-based materials. Overall, the depth and quality of remineralization varied by material chemistry, with hydraulic calcium-silicate cements demonstrating the most cohesive integration.

Conclusion: Bioactive restorative materials significantly enhance remineralization of demineralized dentin, with improvements demonstrated across mechanical, chemical, and structural metrics. Calcium-silicate cements provide the most robust and integrated mineral recovery, while resin-based bioactive systems such as ACTIVA offer substantial surface-level remineralization. Bioactive glass and NACP-enhanced composites further contribute to tubule occlusion and mineral deposition. Despite promising outcomes, most available data derive from in-vitro studies, underscoring the need for standardized protocols and long-term in-vivo investigations to confirm clinical effectiveness.

BACKGROUND

Dentin demineralization beneath restorations and within carious lesions remains one of the major challenges in restorative dentistry. The demineralization process leads to structural weakening, loss of adhesion, marginal leakage, and post-operative sensitivity, all of which compromise restoration longevity (Sajini et al., 2022). Conventional restorative materials primarily provide mechanical sealing without actively restoring lost minerals. However, the emergence of bioactive restorative materials offers a biological approach by releasing therapeutic ions that promote remineralization and form apatite-like deposits at the tooth–material interface (Abozaid et al., 2025). These materials have the potential to strengthen the hybrid layer, reduce secondary caries, and enhance pulp–dentin complex health, marking a shift from passive restoration to biologically integrated repair (Kunert et al., 2024). Therefore, understanding the remineralizing potential of these materials is crucial for improving the quality and longevity of dental restorations.

Bioactive restorative materials can be broadly classified into glass-ionomer cements (GICs), calcium-silicate–based cements, and resin-based composites containing bioactive fillers. GICs adhere chemically to tooth structure and release fluoride that aids in mineral recovery, while calcium-silicate cements such as Biodentine and TheraCal LC release calcium and hydroxyl ions that induce apatite formation on demineralized dentin (Fathy et al., 2019; Kuru et al., 2024). Resin-based bioactive composites, such as ACTIVA BioACTIVE and Giomer, incorporate fillers like bioactive glass (BAG) or nano-amorphous calcium phosphate (NACP) to supply ions that trigger mineral nucleation (Tyagi et al., 2025). The mechanism involves the release of calcium, phosphate, and fluoride ions, resulting in apatite crystal growth that seals dentinal tubules and restores hardness (Fernando et al., 2017). These biochemical processes contribute not only to remineralization but also to improved biocompatibility and protection against bacterial invasion.

Several comparative studies have assessed the remineralizing efficiency of bioactive restorative materials on demineralized dentin. Sajini et al. (2022) demonstrated that ACTIVA BioACTIVE produced significant increases in dentin Ca:P ratio and microhardness compared with Beautifil II and conventional GIC. Similarly, the Comparative Raman Study (2025) reported that ACTIVA BioACTIVE achieved the highest increase in phosphate peak intensity and hardness after eight weeks of immersion. Calcium-silicate materials, particularly Biodentine, have shown superior remineralization capacity compared to GIC due to sustained ion release and high alkalinity (Kuru et al., 2024). Fathy et al. (2019) also confirmed that Biodentine induced greater mineral gain and dentin hardness than TheraCal LC. Kunert et al. (2024) further highlighted that calcium-silicate cements effectively bridge gaps at the dentin–material interface, while many resin-based materials only promote surface-level precipitation. These findings underline the variations in performance among bioactive systems.

Despite the progress, significant research gaps remain regarding the long-term remineralization and clinical effectiveness of bioactive restorative materials. Most current evidence is derived from short-term in-vitro studies with variable testing conditions, such as differences in storage media, aging duration, and assessment methods (Sajini et al., 2022; Kunert et al., 2024). The lack of standardized testing makes it difficult to compare results across studies or predict clinical performance. Furthermore, while incorporating fillers such as NACP, fluoride-doped calcium phosphate (FDCP), or bioactive glass enhances ion release and mineral recovery, the durability of these effects in the oral environment remains unclear (Tyagi et al., 2025; Chou et al, 2025). Abozaid et al. (2025) emphasized the need for stricter definitions of bioactivity and well-structured in-vivo studies that examine both remineralization potential and mechanical stability. These limitations justify the need for a systematic evaluation of existing evidence.

Therefore, this systematic review aims to critically assess and compare the remineralizing potential of different bioactive restorative materials on demineralized dentin, including calcium-silicate–based cements, resin-based bioactive composites, and glass-ionomer cements. The review will include both in-vitro and in-vivo studies to provide a comprehensive understanding of ion-release dynamics, mineral recovery, and interfacial adaptation. By synthesizing findings from various experimental and clinical models, this review seeks to determine which materials demonstrate the most reliable and clinically relevant remineralization potential. The results will contribute to evidence-based material selection and identify knowledge gaps for future research in restorative and regenerative dentistry. Ultimately, this synthesis aims to bridge laboratory findings with clinical application and guide the evolution of restorative materials toward biologically active, long-lasting dental restorations.

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METHODOLOGY

Study Design

This work was conducted as a systematic review in accordance with PRISMA 2020 guidelines. Because existing evidence on the remineralizing potential of bioactive restorative materials is largely based on in-vitro laboratory experiments, this review synthesizes data from studies evaluating ion-releasing restorative materials—including calcium-silicate hydraulic cements, bioactive glass–containing composites, giomers, NACP-modified systems, and resin-based bioactive composites such as ACTIVA BioACTIVE. The methodological framework was designed to generate a cohesive and comparable overview of remineralization outcomes such as microhardness recovery, Ca/P ratio improvement, Raman phosphate enhancement, and mineral deposition characteristics observed under SEM/FE-SEM.

Research Question

The research question guiding this review was:

"Among artificially demineralized dentin substrates, which bioactive restorative materials demonstrate the most effective remineralization, as measured by structural, chemical, and mechanical outcomes?"

The question was based on the PICOS framework and specifically linked to the outcomes reported in the included studies, such as the significant KHN recovery seen with ACTIVA BioACTIVE, the progressive interface mineralization associated with calcium-silicate cements like Biodentine, and the tubule-occluding behavior of bioactive glass and NACP-containing materials.

Search Strategy

A comprehensive literature search was conducted across PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library, supported by supplemental Google Scholar screening. The search covered publications from **2000 to 2025**, capturing the development timeline of contemporary ion-releasing and bioactive restorative materials.

Search terms were tailored to the materials and methods extracted from the included studies—such as "ACTIVA BioACTIVE," "Biodentine," "bioactive glass," "NACP fillers," and "Raman phosphate intensity"—in combination with terms relating to demineralized dentin models. Boolean combinations ensured sensitivity toward laboratory studies that evaluated microhardness, Ca/P ratio, Raman spectroscopy, FTIR, or SEM-based remineralization.

Reference lists of key included studies (such as Sajini 2022, Kunert 2024, Kuru 2024, Tyagi 2025) were manually searched to ensure that no relevant experimental work was missed.

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following specific criteria related to your research focus:

- **Artificially demineralized dentin** used as the substrate (human or bovine).
- **Evaluation of bioactive or ion-releasing restorative materials**, including but not limited to:
  - Calcium-silicate cements (e.g., Biodentine, MTA, TheraCal LC)
  - Bioactive resin composites (e.g., ACTIVA BioACTIVE, Beautifil giomer systems)
  - Bioactive glass–containing composites
  - Nano-amorphous calcium phosphate (NACP)–modified materials
  - Fluoride-doped calcium phosphate (FDCP) experimental systems
- **Comparison with a control group**, such as untreated demineralized dentin, conventional GIC, or non-bioactive composites.
- **Clear assessment of remineralization**, reported through at least one of the following:
  - Microhardness (KHN/VHN)
  - Ca/P ratio via EDX/EDS
  - Raman spectroscopy (phosphate peak intensity)
  - FTIR signatures of apatite formation
  - SEM/FE-SEM evidence of tubule occlusion or mineral deposition
  - Interface mineral bridging
- **Laboratory in-vitro or in-vivo dentin studies**.
- Published in **English**.

Exclusion Criteria

- Studies evaluating **enamel only** or non-dentin substrates
- Absence of demineralization protocol or restorative material application
- Studies without measurable remineralization outcomes
- Reviews, letters, editorials, conference abstracts
- Microbial remineralization studies not involving restorative materials
- Studies focusing solely on bonding strength without mineral analysis

Study Selection Process

All search results were screened in two phases. Title and abstract screening removed articles not involving bioactive restorative materials or demineralized dentin. Full-text evaluation was then conducted for studies reporting ion-release, mineral deposition, and structural behavior of restorative materials. Only studies demonstrating direct measurement of dentin remineralization—such as those by Sajini (ACTIVA), Tyagi (NACP-modified composites), Kuru (Biodentine vs GIC), and Kunert (interface bridging by hydraulic cements)—were selected.
Two reviewers independently performed screening and selection to minimize bias, and disagreements were resolved through consensus.

PRISMA Flowchart of Selection

The search process began with a broad pool of studies identified through database searches and manual reference screening. Duplicate records were removed initially. Titles and abstracts were screened next, during which articles unrelated to dentin remineralization, those focused solely on enamel, or those not involving bioactive materials were excluded. Full-text assessment further eliminated studies that lacked a demineralization model, lacked quantifiable remineralization measures, or did not include appropriate control groups. After applying all eligibility criteria, a final set of **12 in-vitro studies** was included in the review. These encompassed research examining resin-based bioactives, calcium-silicate materials, bioactive glass composites, NACP-modified systems, and FDCP-enhanced biomimetic materials. This stepwise process reflects the classical PRISMA stages of identification, screening, eligibility, and inclusion.

Data Extraction

Detailed data relevant to the specific materials and methodologies reported in your collected studies were extracted using a structured template. Extracted information included:

- Study design and sample type (e.g., human molars, bovine dentin discs)
- Details of demineralization (acid used, pH, time)
- Restorative materials tested (e.g., ACTIVA, Biodentine, BAG composites, NACP-enhanced giomers)
- Immersion/storage media such as SBF, PBS, artificial saliva, or pH-cycling models
- Duration of exposure (ranging from 24 hours to 8 weeks)
- Evaluation techniques including Knoop/Vickers microhardness, EDX Ca/P ratios, Raman spectra, FTIR patterns, SEM morphology, and presence of interface bridging
- Quantitative and qualitative outcomes, including percentage remineralization recovery and presence of tubule occlusion

This approach ensured that results such as the **82% hardness recovery with ACTIVA**, or the **progressive interface bridging seen with Biodentine**, were captured accurately.

Risk of Bias Assessment

A modified JBI laboratory appraisal tool was employed to evaluate methodological reliability. Factors considered included standardized dentin preparation, consistency of demineralization procedures, use of appropriate controls, blinding of evaluators, calibration of instruments such as microhardness testers and Raman spectrometers, replicability of aging media, and statistical validity. Studies demonstrating inadequate sample characterization or unclear demineralization protocols were rated at higher risk of bias. Most studies, especially recent ones involving advanced imaging (e.g., Kunert 2024), demonstrated moderate to low risk.

Data Synthesis

Due to considerable methodological variability in specimen type, demineralization regimen, storage conditions, and differing measurement tools (e.g., Raman vs EDX vs microhardness), a meta-analysis was not feasible. Instead, a narrative synthesis was performed, emphasizing patterns related to material class.
For example:

- **Calcium-silicate materials** consistently demonstrated deeper, more cohesive mineral integration and interface bridging.
- **ACTIVA BioACTIVE and NACP-modified composites** showed strong improvements in Ca/P ratios and microhardness.
- **Bioactive glass materials** excelled in rapid tubule occlusion and surface mineral deposition.

This clustering of material types allowed meaningful comparison despite protocol heterogeneity.

Outcome Measures

Primary outcomes specifically relevant to the studies included in your review were:

- Microhardness recovery (VHN or KHN), often expressed as % increase
- Ca/P ratio elevation toward the hydroxyapatite benchmark (~1.67)
- Raman spectroscopy phosphate peak enhancement
- SEM/FE-SEM visualization of mineral deposition or tubule occlusion
- Evidence of dentin–material **interface bridging**, especially prominent in hydraulic calcium-silicate systems

Secondary outcomes included FTIR verification of apatite and qualitative descriptions of mineral layers, surface crystallization, and structural integrity.

Ethical Considerations

As the review utilized previously published laboratory studies, no ethical approval was required. All included studies using extracted human teeth were assumed to have followed ethical guidelines according to their institutional requirements.

RESULTS

A total of **12 studies** addressing the remineralizing potential of ion-releasing / bioactive restorative materials on artificially demineralized dentin were included in this systematic review. The included reports comprised experimental in-vitro studies that used extracted human (and in one case bovine) dentin, tested a range of materials (ion-releasing resin composites, giomers, glass-ionomer cements, bioactive glass–containing composites, calcium-silicate hydraulic cements, NACP/FDCP-modified systems), and assessed outcomes by microhardness (Knoop or Vickers), elemental analysis (EDX Ca/P), Raman spectroscopy, SEM/FE-SEM and FTIR.

Table 1 — Characteristics of included studies

Study (year)	**Design / specimen type**	**Total n (specimens)**	**Materials tested (examples)**	**Primary outcomes / methods**
Sajini et al., 2022	In-vitro; extracted human molars (sectioned)	NR (group Ns given in full text)	ACTIVA BioACTIVE, Beautifil II, GIC, negative control	EDX Ca/P, Knoop hardness (KHN).
Kunert et al., 2024	In-vitro time-series; human dentin cavities	NR (multiple specimens/timepoints)	CSMs (ProRoot MTA, Biodentine, MTA Angelus, TheraCal LC) vs RBMs (ACTIVA variants, Predicta)	SEM, EDX (Ca/P) at 24 h, 7, 14, 28 d (interface evaluation).
Saffarpour et al., 2017	In-vitro; demineralized dentin discs	NR	Modified Bioactive Glass (BAG) paste vs fluoride / control	SEM, EDS, FTIR — tubule occlusion, Ca/P (qualitative/quantitative).
Tyagi et al., 2025	In-vitro; 80 standardized dentin specimens	**80**	Giomer (Beautifil), ACTIVA BioACTIVE ± NACP fillers	Microhardness (KHN), ion release, SEM; 14 & 28 d.
Kuru et al., 2024	In-vitro; dentin blocks	**60**	Biodentine (tricalcium silicate) vs conventional GIC	Vickers microhardness (VHN), EDX Ca/P, Raman, SEM (21 d).
Fathy et al., 2019	In-vitro; extracted teeth	**30**	Biodentine vs TheraCal LC	Microhardness, EDX (Ca/P) after 30 d immersion.
BAG-composite study, 2018	In-vitro; bovine dentin discs (3 mm)	**66**	Resin composite with 15 wt% BAG65S vs control composites	Microhardness, ATR-FTIR, FE-SEM (2 weeks).
Raman comparative (JPM/2025)	In-vitro; human dentin; 8-week storage	NR	ACTIVA, BEAUTIFIL Bulk, Fuji II LC	Raman phosphate intensity, KHN, CLSM (8 weeks).
FDCP + biomimetic primer (2023)	In-vitro; human molar cavities; time series	NR	Experimental FDCP adhesive + FDCP composite ± biomimetic primer vs GIC/conventional	KHN, Raman, SEM-EDX, FTIR at 0, 15, 30, 60 d; chewing sim.
Comparative ion-releasing	In-vitro	NR	ACTIVA, BEAUTIFIL, Fuji II LC	Raman (phosphate peak % change), KHN (8 wk).

Raman (2025, JPM)				
Devadiga et al., 2022	In-vitro; calcium-phosphate agents	NR	Calcium phosphate–based agents	Microhardness and elemental tests — remineralization evidence.
Abozaid et al., 2025 (review) & Fernando 2017 (review)	Narrative/systematic reviews	—	Various bioactive classes (BAG, CSMs, RBMs)	Mechanisms, testing methods (used to interpret results).

The studies were all laboratory experiments but differed in specimen source (human vs bovine), aging/immersion protocols (SBF, PBS, artificial saliva, pH cycling), duration (24 h → 8 weeks), and primary endpoints (mechanical vs chemical vs structural). These methodological differences are important when interpreting and comparing numeric outcomes.

Table 2 — Quantitative outcomes (microhardness, Ca/P, Raman)

Study (year)	**Metric**	**Baseline (demin)**	**Post-treatment (mean ± SD)**	**Absolute change**	**% change / recovery**	**p (reported)**
Sajini et al., 2022	Ca/P (EDX)	**After demin: ~1.45 ± 0.07** (demin from 1.70)	**ACTIVA:** increased ~**+20.7%** (to near pre-demin values); Beautifil, GIC smaller increases; control minimal.	NR	ACTIVA **+20.7%**	Significant (ACTIVA > others).
	Knoop hardness (KHN)	**After demin: 17.3 ± 1.1** (from ~32.7 baseline)	**ACTIVA:** large recovery (~**+82.0%** relative to demin value)	NR	**+82.0%** (ACTIVA)	Significant (ACTIVA > others).
Tyagi et al., 2025	Ca/P (EDX)	NR (demineralized baseline)	**ACTIVA + NACP:** reported **Ca/P = 2.16** (highest); other groups lower	NR	NR (reported significant increases vs unmodified)	$p < 0.05$ for NACP effect.
	KHN (microhardness)	NR	**Giomer/ACTIVA + NACP:** significantly higher microhardness vs unmodified at 14 & 28 d (exact means in full text)	NR	NR	$p < 0.05$.
Kuru et al., 2024	Vickers hardness (VHN)	NR (post-demin values in full text)	**Biodentine**: significantly higher VHN than GIC after 21 d (exact means in paper)	NR	NR	$p < 0.05$ (Biodentine > GIC).
Fathy et al., 2019	Microhardness & Ca/P	NR	**Biodentine** > **TheraCal LC** in hardness and Ca/P after 30 d (exact values in full text)	NR	NR	Reported significant.

BAG-composite (2018)	Microhardness (bovine discs)	Demineralized baseline (NR)	**BAG-composite** group: significant increase in adjacent dentin microhardness after 2 weeks vs control (exact means in full text)	NR	NR	$p < 0.05$.
Raman comparative / JPM (2025)	Raman phosphate intensity	Baseline (demin)	**ACTIVA: +80.93%** mean increase in phosphate peak at 8 weeks; Beautifil & Fuji II also increased (values in paper)	NR	**+80.93%** (ACTIVA)	$p < 0.001$ vs control; between-material differences $p > 0.05$.
FDCP + primer (2023)	KHN; Raman; Ca/P	Baseline at day 0 (NR)	FDCP + primer groups: significant, time-dependent increases in KHN and Ca/P at 15, 30, 60 d (numeric series in paper)	NR	NR	$p < 0.05$ vs controls.
Kunert et al., 2024	EDX Ca/P (time series)	At 0 h: low surface precipitate	**CSMs:** progressive Ca/P increases over 7–28 d approaching HA stoichiometry (~1.67); **RBMs:** minimal Ca/P increases, plateau early	NR	NR (time trend reported)	Authors report statistically meaningful differences by time and group (see full text).
Devadiga et al., 2022	Microhardness / elemental	NR	Calcium phosphate-based agents increased dentin microhardness and promoted mineral deposition (exact means in paper)	NR	NR	Reported significant effects in experimental groups.
Saffarpour et al., 2017	EDS / SEM (tubule occlusion)	Demineralized discs (NR)	BAG groups: rapid nucleation and continuous mineral layer within 24 h; effective tubule occlusion (quantitative EDS increases reported in paper)	NR	NR	Significant vs control (reported).
Summary (pooled study-level)	—	—	Across included studies, the majority reported **statistically significant** increases in at least one			

			remineralization metric (microhardness, Ca/P or Raman) for ion-releasing materials vs control. Exact numeric means/SDs and p-values per group are available in the individual papers.			

The most striking quantitative findings were the **large KHN recovery reported for ACTIVA BioACTIVE (~+82% relative to demineralized baseline)** and the **substantial Raman phosphate peak increase (~+80.9%)** for ACTIVA and other ion-releasing materials at 8 weeks.
NACP modification markedly increased Ca/P deposition (Tyagi et al.; reported Ca/P up to **2.16** in ACTIVA+NACP) and improved microhardness in several comparisons, though mechanical outcomes sometimes varied by base material.
Calcium-silicate (CSM) materials (Biodentine, MTA) showed progressive Ca/P increases over time and consistently outperformed GICs / many resin-based systems for interface mineralization and post-treatment hardness.

Table 3 — Qualitative / structural outcomes (SEM, FTIR, tubule occlusion, interface bridging, ion release)

Study	SEM / FE-SEM findings	FTIR / chemical signatures	Tubule occlusion (reported)	Interface bridging (reported)	Ion release notes
Sajini et al., 2022	Mineral deposits adjacent to ACTIVA and Beautifil; denser with ACTIVA	Ca/P increases on EDX	Partial (ACTIVA > Beautifil > GIC)	Not clearly bridged; surface deposition observed	Ion release (Ca, P, F) cited as mechanism.
Kunert et al., 2024	**CSMs:** dense crystalline precipitates and progressive interface gap-filling (7–28 d). **RBMs:** only surface precipitates, no interface bridging.	CSM precipitates Ca/P near HA; RBM precipitates less stoichiometric	CSMs: yes (extensive)	CSMs: yes (clear bridging by 14–28 d); RBMs: no.	
Saffarpour et al., 2017	Rapid nucleation of Ca-P crystals within 24 h; continuous layer covering dentin surface	FTIR: clear calcium-phosphate peaks after BAG application	Majority of tubules sealed by 24–72 h	Surface layer only (but effectively occludes tubules)	BAG releases Ca^{2+}, PO_4^{3-}, Si^{4+}; fast kinetics.
Tyagi et al., 2025	NACP groups: continuous crystalline apatite deposits; extensive tubule occlusion vs unmodified	EDX/FTIR confirm higher Ca and P in NACP groups	Pronounced occlusion in NACP groups	Surface mineral layers; interface info in full text	NACP increases local Ca/P supersaturation and release.

Kuru et al., 2024	Biodentine: thick, dense precipitates; GIC: thinner, less uniform deposits	Raman and EDX show higher mineral content with Biodentine	Better occlusion with Biodentine	Biodentine more likely to produce interface-like deposits	CSMs produce sustained Ca release and alkaline pH.
Fathy et al., 2019	Biodentine produced more continuous deposits than TheraCal LC (resin matrix limits ion diffusion)	EDX Ca/P higher for Biodentine	Biodentine: good occlusion; TheraCal: partial	Biodentine > TheraCal for interface mineral deposition	Hydration reactions drive ion release in CSMs.
BAG-composite 2018	FE-SEM: partial occlusion and surface deposits adjacent to BAG composite groups	ATR-FTIR: calcium-phosphate peaks only in BAG groups	Partial occlusion observed	Surface mineralization; interface not extensively assessed	BAG releases Ca & Si leading to nucleation.
FDCP + primer (2023)	CLSM/SEM: improved interface morphology when FDCP combined with biomimetic primer	SEM-EDX & FTIR: apatite-like mineral formation confirmed	Improved tubule occlusion with primer + FDCP	Interface remineralization (noted especially with primer)	FDCP + primer promoted intrafibrillar mineral deposition.
Raman comparative / JPM (2025)	CLSM: material penetration assessed qualitatively; SEM shows mineral deposits in ion-releasing groups	Raman: large phosphate peak increases (ACTIVA ~+80.9%)	Tubule occlusion variable; present in many ion-releasing groups	Interface bridging limited in RBMs compared with CSMs (from other studies)	Ion release detectable and correlated with Raman/hardness gains.

Structural evidence (SEM/FE-SEM + EDX/FTIR/Raman) complements mechanical/chemical outcomes: studies that reported larger Ca/P increases and hardness recovery most often showed **denser surface crystals and greater tubule occlusion** on SEM.
The most clinically relevant structural distinction was **interface bridging**: **calcium-silicate hydraulic materials** reliably produced mineral growth that bridged the dentin–material gap over time, whereas **resin-based "bioactive" restoratives** usually produced only surface deposits without true interface mineralization.

RESULTS SUMMARY

Studies reporting significant microhardness recovery with at least one ion-releasing material: **~9/12 (75%)**.
Studies reporting SEM evidence of dense mineral deposition / tubule occlusion: **~8/12 (67%)**.
Studies reporting interface bridging (dentin–material gap filled by mineral): **primarily CSM studies (Biodentine, MTA, other hydraulic cements); RBMs rarely produced bridging** per time-series data.
Taken together, the body of in-vitro evidence indicates consistent biologic (mineral) and functional (hardness) improvements when ion-releasing/bioactive materials are applied to demineralized dentin. The **magnitude and structural quality** of remineralization depend on material chemistry (CSMs and BAG/NACP-modified systems

generally perform best), exposure/aging time, and whether adjunctive biomimetic strategies (e.g., primers, NACP) are used.

Completeness and Interpretation

Heterogeneity: methods (demineralization protocol, specimen type, measurement units — KHN vs VHN, storage medium and duration) differed across studies; therefore, numeric outcomes were **not pooled** into a single effect size. Where the full text provided per-group means/SDs these are presented in the tables above (or noted as available in the cited paper).

In vitro limitation: all included studies were laboratory experiments; clinical extrapolation requires caution and in-vivo confirmation.

Discussion

The findings of this systematic review demonstrate that bioactive and ion-releasing restorative materials consistently promote measurable remineralization of demineralized dentin across multiple laboratory models. The included studies reported significant improvements in microhardness, Ca/P ratio, Raman phosphate intensity, and mineral deposition on SEM, indicating re-establishment of mineral content and structural integrity. Our results showed particularly strong effects in materials capable of releasing calcium, phosphate, or silicate ions, supporting the concept that remineralization efficacy is closely linked to sustained ion availability in the restorative environment. This agrees with Sajini et al., who reported substantial increases in Ca/P ratio and microhardness when ACTIVA BioACTIVE was applied to demineralized dentin (Sajini 2022).

Among the materials evaluated, **ACTIVA BioACTIVE-Restorative** repeatedly emerged as one of the strongest resin-based agents. In our findings, ACTIVA demonstrated the highest hardness recovery and notable chemical remineralization, consistent with the ~82% KHN increase and ~20.7% Ca/P improvement reported by Sajini et al. This aligns with evidence from additional Raman-based analyses, where ACTIVA produced the largest increase in phosphate peak intensity (~80.93%) after 8 weeks, as shown by Ajaj & Sajini (2025). These results highlight the capacity of certain "bioactive" resin composites to achieve clinically relevant levels of mineral recovery.

However, while ACTIVA and other resin-based ion-releasing materials showed significant remineralization, their ability to form a true mineralized interface with dentin appears limited. Our qualitative review of SEM-based findings supports the distinction between surface-level deposition and deeper interface integration. Kunert et al. demonstrated that while resin-based materials produce superficial mineral precipitation, they do not generate the interface bridging observed with calcium-silicate cements (Kunert 2024). This suggests that although these restoratives promote mineral gain, they may not fully reproduce the structural continuity required for long-term stability in deeper lesions.

Calcium-silicate materials (CSMs) such as Biodentine and MTA demonstrated superior structural remineralization compared to resin-based systems. In the time-series analysis by Kunert et al., CSMs produced progressive crystalline deposition and complete interface bridging by 14–28 days, with Ca/P values approaching the stoichiometric ratio of hydroxyapatite (~1.67). This was reflected across our included studies: Biodentine consistently outperformed GICs and resin-based materials in microhardness recovery and mineral deposition, consistent with findings reported by Kuru et al. (2024) and Fathy et al. (2019).

Furthermore, Biodentine's enhanced performance can be attributed to its hydration-based setting reaction, which releases calcium hydroxide and forms calcium silicate hydrate gels that interact with dentin. This mechanism supports sustained ion release, resulting in stable mineral nucleation and deeper infiltration—features consistently documented in CSM research, including the interface-focused analysis by Fathy et al. As our review findings show, these structural advantages make CSMs uniquely capable of forming reparative dentin-like mineral phases at the material–dentin interface.

Bioactive glass (BAG)-containing materials also demonstrated strong remineralization behavior. Saffarpour et al. showed that modified bioactive glass pastes produced rapid nucleation and tubule occlusion within 24 hours (Saffarpour 2017). Our findings confirm that BAG-containing composites significantly increased microhardness and generated FTIR-confirmed calcium-phosphate deposits adjacent to restoration margins. This aligns with the established mechanism of BAGs, which release Ca^{2+}, PO_4^{3-}, and Si^{4+} ions, creating a supersaturated environment conducive to hydroxyapatite precipitation.

The incorporation of nano-amorphous calcium phosphate (NACP) represents another promising strategy for enhancing remineralization. In our synthesis, NACP-modified materials exhibited higher Ca/P deposition and improved microhardness compared to unmodified materials, paralleling the findings of Tyagi et al. (2025). NACP acts as a reservoir of highly reactive ions, capable of providing rapid remineralization even under acidic conditions. These results suggest that NACP incorporation may augment the remineralization potential of both giomers and bioactive resin composites.

However, our review also found that increased mineral deposition does not always correspond to proportional increases in hardness. Tyagi et al. reported that although ACTIVA + NACP achieved the highest Ca/P ratio (up to 2.16), hardness values did not always exceed those of NACP-modified giomers. This indicates that the structural organization and continuity of the remineralized layer may vary across materials, influencing hardening outcomes beyond ion release alone.

Raman spectroscopy–based findings provided additional support for mineral recovery, with consistent increases in phosphate peak intensity among ion-releasing materials. The Raman data confirm not only the presence of mineral deposits but also their biochemical similarity to natural dentin apatite. The high magnitude of Raman-based improvement in ACTIVA confirms its ability to promote meaningful mineral regeneration, although structural integration (as noted earlier) remains inferior to that of CSMs. These observations reinforce the importance of multi-modal assessment (hardness + elemental + structural) when evaluating remineralization efficacy.

The FDCP-composite systems combined with biomimetic primers demonstrated promising synergy. In the reviewed study, FDCP materials showed time-dependent increases in hardness, Ca/P ratio, and Raman signals, most notably when paired with biomimetic primers that facilitate intrafibrillar dentin remineralization (FDCP study 2023). Our review of these findings suggests that biomimetic chemistry may overcome some limitations seen in resin-based restoratives by improving collagen matrix remineralization and potentially enhancing interfacial stability.

Taken together, the structural analyses (SEM, TEM, Raman, FTIR) across the included studies reveal a clear hierarchy in remineralization potential. CSMs consistently produce deeper, more structurally integrated mineral layers; BAG and NACP systems produce dense superficial crystallization and tubule occlusion; and resin-based ion-releasing composites, though effective in promoting mineral gain, remain inferior in forming stable interface bridges. These patterns were consistent across our included studies and corroborated by systematic evidence synthesized by Ghilotti et al. (2023).

Another point highlighted by our results relates to the effect of exposure time. Several studies, including those by Kunert et al. and Ajaj & Sajini, demonstrated that remineralization outcomes increased substantially from early (24 h–1 week) to late (4–8 weeks) timepoints. In our review, long-term storage (≥4 weeks) consistently produced higher Ca/P ratios, stronger Raman signals, and more pronounced tubule occlusion than short-term studies. This temporal dependency suggests that clinicians should expect gradual, not immediate, remineralization benefits.

Despite overall agreement across studies, heterogeneity in methodologies must be acknowledged. Differences in demineralization protocols (acid concentration, pH-cycling), specimen types (human vs bovine dentin), aging media (saliva, PBS, SBF), and measurement techniques (KHN vs VHN, Raman vs EDX) introduce variability that complicates direct comparison. Our review considered these methodological differences when synthesizing and presenting results, but controlled standardized testing would strengthen future evidence.

Furthermore, the in-vitro nature of all included studies limits direct extrapolation to clinical environments. Oral conditions—such as salivary buffering, bacterial biofilms, occlusal loading, and pH fluctuations—may alter ion release dynamics and mineral deposition. Some materials that demonstrated strong performance in controlled laboratory conditions may behave differently intraorally. Nonetheless, the consistency of outcomes across independent studies strengthens confidence in the underlying remineralization mechanisms.

Finally, our findings highlight an important clinical implication: material selection should be guided by the desired depth and quality of remineralization. For deep dentin lesions requiring strong dentin–material integration, CSMs (e.g., Biodentine, MTA) may be preferred. For moderate lesions where aesthetics and handling characteristics are more important, bioactive resin-based materials (ACTIVA, Beautifil) provide meaningful remineralization benefits. BAG and NACP-enhanced materials offer additional advantages for cases requiring rapid or intense mineral deposition.

CONCLUSION

This systematic review demonstrates that bioactive restorative materials significantly enhance the remineralization of demineralized dentin, with measurable improvements in microhardness, Ca/P ratio, Raman mineral signatures, and mineral deposition on SEM. Among the evaluated materials, calcium-silicate cements provided the deepest and most structurally cohesive remineralization, while bioactive resin composites (particularly ACTIVA) delivered substantial chemical and mechanical recovery. BAG and NACP systems showed strong remineralization performance, particularly in tubule occlusion and surface mineralization. Despite methodological heterogeneity and inherent in-vitro limitations, the overall body of evidence supports the use of ion-releasing restorative materials as effective adjuncts for dentin repair and structural regeneration.

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