

Bioactive Glass Based Strategies for the Prevention and Remineralization of White Spot Lesions in Orthodontic Patients: Current Evidence and Emerging Applications

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ABSTRACT

White spot lesions are among the most prevalent adverse effects of fixed orthodontic treatment, resulting from plaque accumulation around orthodontic attachments. Their high incidence adversely affects esthetics, treatment outcomes, and the long term dental health of orthodontic patients. Bioactive glasses have attracted increasing interest as preventive and remineralizing biomaterials because of their ability to release calcium, phosphate, fluoride, sodium, and other therapeutic ions. Owing to their bioactive properties, various formulations of bioactive glasses are incorporated into a wide range of dental materials, topical and orthodontic delivery systems. Available evidence indicates that bioactive glass-based materials can promote enamel remineralization, enhance mineral recovery, provide acid neutralizing effects, and exert antibacterial activity. Bioactive glass containing dentifrices, mouthwashes, and orthodontic adhesives represent promising approaches to prevent orthodontic white spot lesions, but most remain supported predominantly by laboratory or early clinical evidence. Further, the evidence remains heterogeneous with substantial variation in composition, concentration, delivery systems, study protocols, and outcome measures. Well designed, adequately powered, randomized clinical trials are required to establish the role of bioactive glass based strategies in prevention of orthodontic white spot lesions.

Keywords: Bioactive glass; White spot lesions; Orthodontic treatment; Enamel demineralization; Orthodontic adhesives; Dentifrices; Antibacterial activity; Enamel remineralization; Fixed orthodontic appliances.

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INTRODUCTION

White spot lesions (WSLs) are the earliest detectable signs of enamel caries and represent one of the most common adverse effects of fixed orthodontic treatment. Clinically, they appear as opaque white areas caused by subsurface enamel demineralization.¹⁻⁵ WSLs remain a major global challenge in orthodontics, with a pooled prevalence of approximately 55% and an incidence of 34% among patients undergoing fixed orthodontic treatment, significantly compromising esthetic outcomes, prolonging posttreatment care, and affecting overall treatment success.⁶ The International Caries Detection and Assessment System (ICDAS) categorizes noncavitated enamel lesions encountered during orthodontic treatment as ICDAS Codes 1 and 2. Diagnostic techniques such as quantitative light induced fluorescence (QLF) and DIAGNOdent facilitate the early detection of WSLs by identifying enamel demineralization before it becomes clinically evident.⁷⁻⁹

Conventional and emerging strategies for the prevention and remineralization of WSLs in orthodontic patients encompass topical fluoride agents, fluoride

releasing materials, antimicrobial mouthrinses, calcium (Ca) and phosphate (PO₄) based remineralizing agents, nanomaterials, and protective nanocoatings. Established treatment approaches for existing lesions include remineralization therapy, resin infiltration, microabrasion, and restorative procedures in more severe cases to improve enamel appearance and integrity.^{10,11} Bioactive glasses (BAGs) are ceramic materials that interact with biological tissues through the controlled release of Ca, PO₄, sodium (Na), fluoride, and silicate ions.¹² Owing to their ion releasing properties, BAGs have been incorporated into a variety of dental materials, including toothpastes, mouthwashes, varnishes, sealants, orthodontic adhesives, orthodontic cements, and resin infiltrants, with the aim of preventing enamel demineralization and promoting remineralization.¹³ This narrative review summarizes the various types of BAGs and evaluates the current evidence on BAG based strategies for the prevention and remineralization of WSLs in orthodontic patients.

BIOACTIVE GLASS FOR DENTAL APPLICATION

Since Hench developed the first BAG in 1969, numerous formulations have been developed for dental applications.¹⁴ BAGs are classified based on their network-forming oxides, or their structural characteristics and porosity.¹⁵⁻¹⁹

SILICATE BIOACTIVE GLASSES

45S5 Bioglass

45S5 Bioglass is the original and most extensively investigated BAG formulation. It is a calcium phosphosilicate BAG with 45 wt% silicon dioxide (SiO_2) as the primary network former and 24.5 wt% sodium oxide (Na_2O). The calcium oxide (CaO) to phosphorus pentoxide (P_2O_5) ratio is approximately 5:1 in a 45S5 Bioglass formulation, contributing to its sustained bioactivity. It has been extensively investigated in restorative materials, orthodontic materials, remineralizing agents, and bone grafts.^{19,20} NovaMin® is a commercially available form of 45S5 Bioglass that is widely incorporated into desensitizing and remineralizing toothpastes, with demonstrated efficacy in managing dentin hypersensitivity and promoting remineralization of early enamel lesions.^{21,22}

BioMin F® is a fluoride containing calcium phosphosilicate glass that combines the remineralizing potential of conventional BAG with the anticaries benefits of fluoride, with a composition of 36–40 wt% SiO_2 , 28–30 wt% CaO , 22–24 wt% Na_2O , 4–6 wt% P_2O_5 , and 1.5–3.0 wt% calcium fluoride (CaF_2). It provides sustained fluoride release for up to 12 hours, which contributes to the antibacterial activity against cariogenic bacteria, fluorapatite (FA) formation, increased resistance to acid attack, and enamel remineralization.^{22,23} BioMin C® is a fluoride free chloride containing formulation that promotes chlorapatite (CA) formation, with potential for the short term management of dentin hypersensitivity. Unlike hydroxyapatite (HA) and FA, CA exhibits lower stability and greater susceptibility to dissolution, possibly due to the larger size of the chloride ion.^{24,25}

S53P4 Bioglass

It is a commercially available silicate BAG containing 53 wt% SiO_2 , 23 wt% Na_2O , 20 wt% CaO and 4 wt% P_2O_5 , uniquely recognized for its potent antimicrobial and bone regenerating properties. It is an FDA approved synthetic bone graft substitute highly valued in complex orthopaedic, cranial, and maxillofacial surgeries.²⁶

13-93 Bioactive Glass

13-93 BAG was developed as a modification of 45S5 BAG to improve its mechanical properties and processing characteristics. Its composition comprises 53 wt% SiO_2 , 20 wt% CaO , 6 wt% Na_2O , 12 wt% potassium oxide (K_2O), 5 wt% magnesium oxide (MgO), and 4 wt% P_2O_5 . The incorporation of MgO and K_2O improves the glass stability, mechanical strength, and sintering behaviour of 13-93 BAG, supporting its use in porous scaffolds and coatings for regenerative applications. The material exhibits slower degradation and more sustained ion release while retaining the ability to form a hydroxycarbonate apatite (HCA) layer upon contact with physiological fluids.²⁷

58S Bioactive Glass

58S BAG is a Na free formulation containing 58 wt% SiO_2 , 33 wt% CaO , and 9 wt% P_2O_5 primarily produced by the sol-gel process, resulting in a highly porous structure and a large surface area. This enhances ion exchange, sustained ion release, rapid HA formation, and prolonged remineralization. Its high surface reactivity also contributes to enhanced bioactivity and antibacterial performance. Consequently, 58S BAG has been investigated for dental applications, including orthodontic adhesives, resin composites, implant coatings, and enamel remineralization.²⁸

Doped silicate glasses

Ion doping involves incorporating therapeutic ions such as strontium (Sr^{2+}), zinc (Zn^{2+}), copper (Cu^{2+}), magnesium (Mg^{2+}), silver (Ag^+), gallium (Ga^{3+}), cobalt (Co^{2+}) and lithium (Li^+) into the silicate BAG network. Ion doping can enhance antibacterial activity and osteogenic potential, modulate the degradation rate, facilitate sustained release of biologically active ions, promote hydroxycarbonate apatite (HCA) formation, and impart multifunctional and antioxidant properties, thereby enabling tailored therapeutic applications.^{29,30}

BOROSILICATE BIOACTIVE GLASS

Borosilicate BAGs are boron containing glasses in which a portion of the silica network is replaced by boron oxide (B_2O_3). Representative compositions include 13-93B1, in which approximately one third of the SiO_2 in 13-93 BAG is replaced by B_2O_3 ; 13-93B2, in which two thirds of SiO_2 is replaced by B_2O_3 ; and 13-93B3, in which the SiO_2 is completely replaced by B_2O_3 .³¹ Boron incorporation can enhance glass dissolution, thereby accelerating therapeutic ion release and HA formation, while potentially promoting angiogenesis, osteogenesis, and soft tissue healing. These properties have prompted investigation of borosilicate BAGs in bone and periodontal regeneration, implant coatings, antimicrobial restorative materials, and tissue-engineering applications.³¹

PHOSPHATE BASED BIOACTIVE GLASS

Phosphate based BAGs are a distinct class of BAGs in which P_2O_5 serves as the primary network former. Their composition can be tailored using network modifiers such as CaO , Na_2O and MgO to regulate degradation and ion release. CaO containing glasses exhibit good biocompatibility and can undergo substantial degradation under physiological conditions. Na_2O increases glass solubility, while MgO enables the sustained release of Mg^{2+} , which may support osteoblast proliferation and bone mineralization. These glasses have been investigated for bone regeneration, regenerative endodontics, and drug delivery applications; however, their commercial dental applications remain limited.³²

MICROPOROUS, MESOPOROUS, AND MACROPOROUS BIOACTIVE GLASSES

Based on their pore dimensions, BAGs can be classified into three categories. Mesoporous BAGs are typically silica

based materials synthesized by sol-gel processing with surfactant templating, which produces highly ordered pore structures measuring 2–50 nm and high surface areas. These characteristics facilitate ion exchange, therapeutic ion release, and HA formation, making them particularly attractive for biomedical and dental applications. Microporous BAGs have pore sizes of less than 2 nm, which facilitate controlled and gradual release of therapeutic ions. Macroporous BAGs have interconnected pores extending from >50 nm to several hundred micrometres, that facilitate cellular migration, proliferation, and tissue ingrowth. They are particularly suitable for tissue engineering scaffolds due to their larger pore architecture.³³⁻³⁵

EMERGING BIOACTIVE GLASS TECHNOLOGIES RELEVANT TO DENTAL AND ORTHODONTIC APPLICATIONS

Nanoscale BAG particles possess a larger surface area and greater surface reactivity than conventional particles, enabling accelerated ion release, enhanced bioactivity, and better penetration into subsurface enamel lesions for targeted remineralization.³⁶⁻³⁷ Combining BAG with hydrogels and electro spun nanofibers enables injectable and scaffold based systems that provide sustained ion release and support tissue regeneration. These materials show promise in enamel remineralization, pulp and periodontal regeneration, guided tissue regeneration, and wound healing.³⁸ Stimuli responsive BAGs are smart

materials that are capable of releasing therapeutic ions in response to environmental changes, particularly during episodes of demineralization.³⁹ BAGs can be incorporated into multifunctional systems by combining them with antimicrobial ions, biomimetic remineralizing agents, self assembling peptides, and polymeric carriers to provide synergistic effects.⁴⁰⁻⁴² Advances in additive manufacturing have enabled the incorporation of BAG into three dimensional printed scaffolds with customized architecture, porosity, and mechanical properties. These constructs may facilitate personalized preventive and restorative strategies, including customized biomaterials for patients at high risk of enamel demineralization.⁴³

MECHANISM OF PREVENTION AND REMINERALIZATION OF WSLs

When exposed to saliva or aqueous media, BAGs release Ca, PO₄, Na, and, in some formulations, fluoride or chloride ions. The release of sodium ions increases the local pH, helping to neutralize acids produced by cariogenic bacteria and thereby reducing further enamel demineralization. Simultaneously, Ca and PO₄ ions create a supersaturated environment that promotes the deposition of amorphous calcium phosphate (ACP), which subsequently transforms into crystalline HA, HCA, FA or CA. In addition, BAGs modified with Zn²⁺, Cu²⁺ or Ag⁺ exhibit antibacterial properties that may reduce biofilm formation around orthodontic appliances (Figure 1).⁴⁴⁻⁴⁹

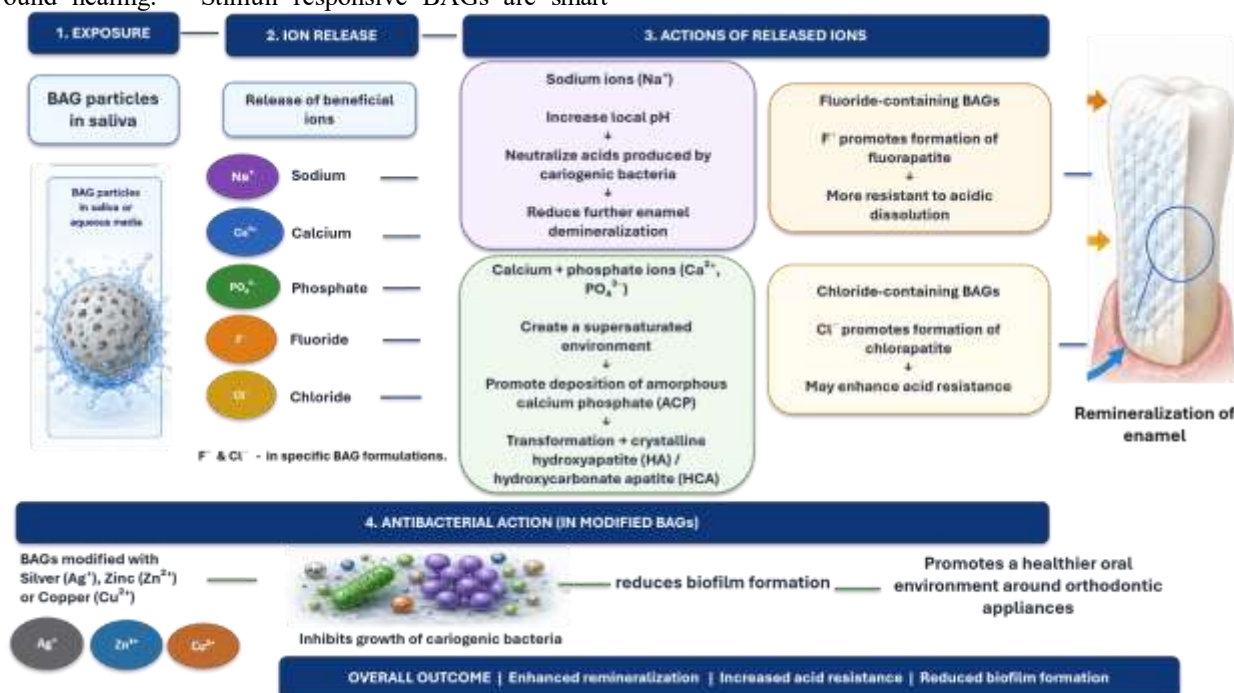


Figure 1: Mechanism of action of BAGs in the prevention and remineralization of WSLs

BIOACTIVE GLASS BASED STRATEGIES FOR PREVENTION AND REMINERALIZATION OF WSLs

The versatility of BAG has led to its incorporation into numerous preventive and restorative delivery systems,

including homecare products and professionally applied materials.

BAG containing Toothpastes

Commercial dentifrices commonly incorporate 45S5 BAG, NovaMin®, BioMin C®, or BioMin F®. Among BAG based approaches, dentifrices have been relatively well investigated for enamel remineralization, including in

patients undergoing orthodontic treatment. Their widespread use is facilitated by their ease of integration into routine oral hygiene practices and their potential to provide a sustained source of multiple therapeutic ions, which may support continued mineral deposition beyond the period of brushing.⁵⁰ BAG concentrations between 5 and 15 wt% have generally been associated with effective enamel remineralization and caries prevention, whereas lower concentrations are predominantly intended for the management of dentin hypersensitivity.⁵¹ The remineralization outcomes are comparable or, in certain experimental settings, superior to those achieved with fluoride, casein phosphopeptide–amorphous calcium phosphate (CPP-ACP) and nanohydroxyapatite (nHA) based formulations. Current clinical trials indicate that BAG containing dentifrices can promote remineralization of early enamel lesions during orthodontic treatment. However, their clinical effectiveness has not consistently been shown to exceed that of conventional fluoride toothpastes, with several studies reporting comparable remineralization outcomes.^{50,52-56}

BAG containing Mouthwashes

BAG containing mouthwashes have been proposed as a potential adjunctive approach for managing WSLs in orthodontic patients who are at increased risk of enamel demineralization. However, direct evidence evaluating BAG containing mouthwashes remains limited. At present, BAG containing mouthwashes are considered as an investigational approach rather than an established alternative to conventional preventive strategies.⁵⁷

BAG containing varnish and sealants

BAG containing varnishes provide a localized source of therapeutic ions and may be particularly useful for patients at high risk of developing WSLs. Applied before bracket placement, during active treatment, or after debonding, they may enhance enamel resistance to acid attack and facilitate the repair of early noncavitated lesions. Although studies have reported increased mineral deposition and enamel surface microhardness, with reduced mineral loss, the evidence remains limited and heterogeneous because of variations in material composition, application protocols, and outcome assessment.⁵⁸⁻⁶¹ Consequently, current clinical evidence is insufficient to establish superiority over conventional fluoride varnishes. Furthermore, the limited availability of commercially available BAG varnishes and the ongoing clinical evaluation of newer formulations currently restrict their widespread clinical adoption.

BAG containing luting cements

Bioactive orthodontic luting cements have demonstrated pull-off bond strength comparable with glass ionomer and zinc phosphate cements for molar band cementation.⁶² Resin based bioactive cements demonstrated less microleakage and comparable shear bond strength (SBS) to conventional resin luting agents under in vitro conditions. The BAG fillers allow ion exchange with saliva in response to pH changes, enhancing the marginal seal and resistance to demineralization.⁶³ Independent in vitro evidence has shown fluoride release and re-release following fluoride exposure from a bioactive luting cement, supporting its potential for sustained fluoride availability.⁶⁴ Clinical trials

demonstrated favourable retention and marginal integrity, with no secondary caries or visible marginal discolouration after one year of crown cementation.⁶⁵

BAG containing Orthodontic adhesives

BAG incorporation into bonding adhesives has gained considerable attention because it directly targets the bracket enamel interface, a site prone to plaque accumulation and WSL formation, without requiring additional patient compliance.⁶⁶ Most studies indicate that appropriate BAG concentrations maintain clinically acceptable SBS; however, excessive BAG incorporation may adversely affect polymerization and mechanical properties, highlighting the need to optimize the filler concentration.^{67,68} BAG particles retain their bioactivity even after incorporation into a polymeric matrix and maintain sustained ion release.⁶⁹ Incorporation of mesoporous BAG and zwitterionic material into adhesive orthodontic resin has demonstrated enhanced antimicrobial and remineralizing properties, supporting its potential as a multifunctional orthodontic adhesive.⁷⁰ Although systematic reviews of in vitro studies have identified BAG containing adhesives as a promising bioactive approach for preventing orthodontic WSLs, limitations related to formulation, mechanical performance, long term stability, biocompatibility, and translation from laboratory findings to clinical applications remain important challenges.^{71,72}

BAG coated orthodontic brackets and arch wires

Transforming orthodontic appliances into bioactive surfaces using BAG coatings represents an emerging strategy to reduce enamel demineralization during fixed appliance therapy. Electrophoretic deposition of BAG onto stainless steel (SS) orthodontic arch wires produced adherent coatings with favourable esthetic and surface characteristics. However, high friction and coating disruption at the bracket wire interface were observed under certain conditions, highlighting concerns regarding its clinical application.⁷³ Nano BAG (nBAG) coated orthodontic brackets have demonstrated uniform surface coverage and acceptable mechanical properties.⁷⁴ Long term studies are needed to establish coating durability, resistance to mechanical wear and frictional changes, and before routine clinical application can be recommended.

Bag based resin infiltration for post treatment enamel repair

Management of WSLs frequently extends beyond orthodontic treatment, as residual enamel opacities may persist after appliance removal. Conventional management options, including fluoride varnishes, CPP-ACP, resin infiltration and microabrasion, remain important therapeutic alternatives.⁷⁵ BAG has been investigated as a bioactive additive to resin infiltrants, with the potential to combine the conventional benefits of resin infiltration, including lesion masking and occlusion of enamel microporosities, with bioactive ion release and enhanced remineralization. Conventional resin infiltration penetrates the porous subsurface lesion and occludes diffusion pathways, while incorporation of BAG can potentially provide therapeutic ions that promote apatite formation and improve the mineral quality of the infiltrated enamel.^{75,76}

TRANSLATING EVIDENCE INTO CLINICAL PRACTICE

Studies evaluating BAG based strategies for the prevention and management of enamel demineralization, including in vitro studies, clinical trials, and systematic reviews, are summarized in Tables 1–7.^{51-56, 58, 59, 63, 65-71, 73, 74, 76-120} The available evidence is predominantly derived from in vitro studies, with BAG containing dentifrices, varnishes, orthodontic adhesives, coated orthodontic components, and resin infiltrants showing potential to enhance enamel remineralization, mineral recovery, ion release, and resistance to demineralization. However, outcomes vary with BAG composition, concentration, particle characteristics, delivery system, and experimental conditions.^{40, 41, 45, 48, 52, 53, 58, 59, 63, 66-70, 73-82, 87-95, 97-99, 103-109}

Clinical evidence provides more direct support for the prevention and management of WSLs during fixed orthodontic treatment, with NovaMin® and BioMin F® dentifrices showing potential to reduce WSL development or enhance remineralization.^{51, 54-56, 65, 75, 76, 96, 100, 101} However, clinical evidence for BAG containing adhesives and resin-infiltration approaches remains limited, and systematic reviews continue to emphasize methodological heterogeneity and insufficient clinical validation.^{71, 75, 76, 84-86, 110} BAG containing dentifrices have the most direct clinical evidence, whereas varnishes, orthodontic

adhesives, BAG coated brackets or arch wires, and BAG modified resin infiltrants remain promising but require further validation of mechanical performance, durability, long term effectiveness, and patient centered outcomes. Collectively, the evidence supports a multimodal strategy for patients undergoing fixed orthodontic treatment, in which conventional fluoride based preventive measures remain the foundation, while BAG containing dentifrices and other BAG based adjuncts may be considered to enhance remineralization and reduce demineralization risk.

CONCLUSION

BAG has emerged as a versatile biomaterial with potential applications in the prevention and management of orthodontic WSLs. However, despite encouraging laboratory and early clinical findings, evidence supporting many BAG based applications remains limited by methodological heterogeneity and a lack of long term randomized clinical trials. Future research should focus on optimizing material composition, standardizing evaluation protocols, and validating clinical performance under intraoral conditions. Such advances will be essential for translating BAG based technologies into routine orthodontic practice and establishing their role in evidence based management of WSLs.

Author (Year)	Intervention & control	Outcome measures	Main findings
Abbasoglu et al. (2019) ⁷⁷ In vitro study	sodium Fluoride (NaF), CPP-ACP, NovaMin™, NovaMin™ & NaF toothpastes	Remineralization potential: surface microhardness recovery of enamel	NovaMin™ demonstrated similar remineralization potential to NaF toothpaste
Ali et al. (2020) ⁷⁸ In vitro study	NovaMin® & BioMin F® toothpastes	Fluoride (F) release: ion selective electrode; Remineralization potential: microhardness recovery of enamel	BioMin F® demonstrated greater F availability & remineralization potential
Dhanya et al. (2021) ⁷⁹ In vitro study	NovaMin™ toothpaste (SHY-NM) & CPP-ACP (tooth mousse plus™)	Enamel remineralization: Scanning electron microscope (SEM) & DIAGNOdent®	NovaMin™ demonstrated remineralization potential similar to that of CPP-ACP
Farooq et al. (2021) ⁸⁰ In vitro study	BioMin F® toothpaste, Distilled water & Colgate™ F toothpaste	Microhardness, surface roughness (SR) of enamel: profilometry & volume loss/gain: micro CT	BioMin F® demonstrated smoother surface, greater hardness & greater volume gain
Dai et al. (2022) ⁵³ In vitro study	Strontium doped BAG containing toothpaste, F free toothpaste & deionized water	Surface morphology of enamel: SEM & Lesion depths & mineral loss of artificial WSLs: micro-CT	Strontium doped BAG containing toothpaste prevented artificial dentine caries formation
Eldeeb et al. (2024) ⁸¹ In vitro study	BioMin F® toothpaste with or without diode laser application for 30 s	Ca, P & F level of enamel: Energy Dispersive X-ray spectroscopy (EDX), surface morphology / mineral content: SEM	BioMin F® showed increased remineralization, laser application did not enhance the remineralizing effect.
Katkanchano et al. (2024) ⁵² In vitro study	BioMin F® toothpaste, deionized water, 1000 ppm & 1450 ppm NaF toothpaste	Mineral density & percentage of enamel remineralization at 0, 40, 80, 120 µm depth of artificial WSLs: micro CT	BioMin F® demonstrated significant remineralization of primary enamel lesions
Cetin et al. (2026) ⁸²	BAG, BAG + F, HA, HA + F, protein + calcium	Remineralization potential: microhardness recovery,	BAG, HA, & protein + calcium glycerophosphate & the

In vitro study	glycerophosphate, Sensodyne® repair & protect (NovaMin™ toothpastes), R.O.C.S. Sensitive (HA) & control	DIAGNOdent & FluoreCam of enamel	commercial pastes supported enamel remineralization. F enhanced the remineralizing effect
Hoffman et al. (2015) ⁵⁶ RCT	ReNew™ toothpaste (5% NovaMin®+ F) & Crest® toothpaste (0.15% fluoride)	Decalcification index (DI), gingival index (GI), plaque index (PI), & bacterial levels.	NovaMin® demonstrated similar potential to F toothpastes for reducing WSLs & gingivitis
Mollabashi et al. (2022) ⁵⁴ RCT	Sensodyne® Repair & Protect (F & NovaMin®), & Sensodyne® Rapid Relief (F)	DIAGNOdent measurements of WSLs at baseline, 1 month & 3 months;	NovaMin® demonstrated a synergistic effect with F in remineralization of WSLs
Salah et al. (2022) ⁸³ Double-blind RCT	BioMin F® slurry + toothpaste, NovaMin® slurry + toothpaste, & Recaldent (CPP-ACP)	Laser fluorescence, DIAGNOdent & Photographs	BioMin F® produced greater reduction in lesion size & esthetic improvement
Tiwari & Jain (2023) ⁵⁵ Prospective RCT	OEM (Probiotic), Sensodyne® (NovaMin®), & Colgate Total advanced (F) toothpastes	DIAGNOdent, laser fluorescence, incidence of WSLs	Probiotic was better than Novamin® & F toothpastes in reducing the incidence of WSLs.
Li et al. (2026) ⁵¹ Multicentric, RCT	Fluoride free toothpaste (7.5 wt% BAG) & Fluoride toothpaste (800 ppm F)	Caries increment: change in dmft & dmfs, & Caries incidence at 12 & 27 months.	BAG & F toothpaste demonstrated similar but limited effectiveness in caries prevention
Taha et al. (2017) ⁸⁴ Systematic review	Formulations of BAG compared with F, CPP-ACP & other remineralizing agents	In vitro evidence of enamel remineralization, using recognized laboratory techniques.	BAG showed increased enamel remineralization potential
Khijmatgar et al. (2020) ⁸⁵ Systematic review	NovaMin® containing products & Crest® - conventional fluoride toothpaste	DI & WSL remineralization	Evidence supported potential remineralizing effects of NovaMin® with limitations in available evidence were noted
Santhosh et al. (2025) ⁸⁶ Systematic review, meta-analysis	Various formulations of BAG compared with F, CPP-ACP & nHA,	In vitro evidence of enamel remineralization using recognized laboratory techniques	BAG showed increased remineralization potential compared to F, CPP-ACP & nHA for surface hardness & subsurface remineralization

Table 1. Evidence-based summary of BAG based toothpastes for the prevention & management of enamel demineralization

Author (Year)	Intervention & control	Outcome measures	Main findings
Kim et al. (2021) ⁵⁸ In vitro study	Nupro White varnish (F), tooth Mousse (CPP-ACP) , 30 wt% 63S BAG based experimental varnish, with & without desonation & control group	Microhardness: FE-SEM, elemental composition of enamel: EDX & X ray diffraction (XRD)	BAG varnish promoted recovery of enamel microhardness & HA precipitation
Durmuş et al. (2023) ⁵⁹ In vitro study	F, BAG & F + BAG varnish, eggshell powder, eggshell membrane protein + eggshell powder varnish, sodium trimetaphosphate -treated eggshell membrane protein + eggshell powder varnish	Elemental analysis: SEM, EDX, Cytotoxicity: MTT assay & real time cell analysis system	BAG varnishes showed remineralization comparable to that of F & eggshell powder & membrane protein varnish; cytotoxicity varied with formulation & dilution.
Sarialioglu Gungor et al. (2024) ⁸⁷ In vitro study	NaF varnish, experimental 58S5 BAG varnish + 37% phosphoric acid etching, enamel matrix derivative + EDTA etching, enamel matrix derivative + 37% phosphoric acid etching & untreated enamel	Surface microhardness: spectral domain optical coherence tomography, FluoreCam & DIAGNOdent	Remineralization & microhardness was comparable in 58S5 BAG & F varnish. Reduction in lesion depth was better in F varnish.
Cengiz et al. (2025) ⁸⁸	Metroberry, Imicryl (F varnish), BioViera, Imicryl (Na-tri-	SEM, attenuated total reflectance fourier	Protection against decalcification was similar for

In vitro study	metaphosphate treated eggshell and membrane powder) & Polimo, Imicryl (BAG varnish)	transform infrared spectroscopy & surface microhardness	BAG varnish, STMP treated eggshell/membrane powder varnish & F varnishes.
Sleem et al. (2025) ⁸⁹ In vitro study	Artificial saliva, F varnish, BAG varnish, F-BAG varnish, nAg-BAG varnish, nAg F varnish & nAg varnish	Surface hardness, elemental composition of enamel: EDX & SEM at baseline, after demineralization, & 2 weeks after varnish application	Remineralization potential of BAG varnish & F varnish was similar. F-BAG, nAg & nAg-BAG varnishes demonstrated greater remineralizing potential than F & BAG varnishes
Karawia et al. (2026) ⁹⁰ In vitro study	45S5 BAG nanoparticle varnish, 5% NAF varnish & untreated control	SR: profilometry, elemental composition of enamel: SEM /EDX & DIAGNodent	BAG varnish produced greater remineralization than F varnish, with lower DIAGNodent readings, higher Ca/P ratio & smoother enamel

Table 2. Evidence-based summary of BAG based dental varnishes for the prevention & management of enamel demineralization

Author (Year)	Intervention & control	Outcome measures	Main findings
Yang et al. (2016) ⁹¹	Varying percentages of 45S5 BAG & silanized glass (SG) in Bis-GMA/TEGDMA 50/50 (wt%). [0% BAG + 50.0% SG, 12.5% BAG + 37.5% SG, 25.0% BAG + 25.0% SG, 37.5% BAG + 12.5% SG, & 50.0% 45S5 BAG + 0% SG] in pit & fissure (P&F) sealant	Microhardness, SR: profilometry & SEM at 15, 30 & 45 days.	Increasing BAG % significantly reduced SR & increased hardness. 50% BAG group enamel surface was similar to those of control group even after prolonged storage in acid.
Safwat et al. (2023) ⁹² In vitro study	Experimental Bis-GMA-based P & F sealant containing 0 wt%, 5 wt%, 15 wt% and 25 wt% of $\text{Ca}_5(\text{PO}_4)_3\text{F}$ in CaSiO_3 / Na_2SiO_3 , i-SEAL LC & Composan glass.	Microhardness, compressive strength, flow, depth of cure, pH changes & ion release after immersion in artificial saliva for different time intervals	15 wt% $\text{Ca}_5(\text{PO}_4)_3\text{F}$ containing sealant demonstrated HA forming ability & prolonged Ca/P ion release for 90 days with acceptable mechanical properties
Choi et al. (2024) ⁹³ In vitro study	P & F sealant with varying percentages of 45S5 BAG & SG (0% BAG + 50 wt% SGs, 12.5% BAG + 37.5 wt% SG, 25 wt% BAG & 25 wt% SG, 37.5% BAG & 12.5 wt% SG)	Ca & PO_4 ion release, pH variation, Raman spectroscopy, SEM-EDX	BAG containing sealants demonstrated enhanced ion release & apatite formation
Khan et al. (2024) ⁹⁴ In vitro study	P & F sealants with 70% resin matrix (Bis-GMA/TEGDMA), 20 wt% (BioMin F® or BioMin C® or S53P4) + 10 wt% silica, Seal-Rite	SR, water contact angle, nanohardness, elastic modulus, water sorption & solubility.	BioMin F® & BioMin C® reduced the SR, all BAG groups reported improved wettability.
Al-Mutairi et al. (2025) ⁹⁵ In vitro study	P & F sealants; 70 wt% Bis-GMA/TEGDMA resin, 20 wt% (S53P4, BioMin C®, or BioMin F®) + 10 wt% silica filler, Seal-Rite (commercial sealant)	FTIR; XRD; SEM; flowability; depth of cure; compressive, tensile, diametral tensile & flexural strength (FS)	BioMin C® exhibited higher flowability. BioMin F® demonstrated higher compressive strength.
Kouzmina et al. (2009) ⁹⁶ Prospective clinical study	Esterfill® Ca & F P & F sealant containing BAG	Sealant retention, marginal adaptation, fissure caries development, SR & colour change around the sealant using adapted Ryge/ADA criteria.	BAG containing sealant demonstrated good retention & favourable clinical performance over 1 year

Table 3. Evidence-based summary of BAG based pit & fissure sealants for the prevention & management of enamel demineralization

Author (Year)	Intervention & control	Outcome measures	Main findings
Engstrand et al. (2012) ⁹⁷ In vitro study	Ceramir Crown & Bridge (BAG containing glass ionomer luting cement)	Grazing incidence (XRD), SEM, & X-ray photoelectron spectroscopy (XPS)	The bioactive cement demonstrated HA formation following exposure to human saliva
Jefferies et al. (2013) ⁹⁸ In vitro study	Ceramir Crown & Bridge luting cement, Conventional luting (RelyX Luting, Fuji Plus & RelyX Unicem)	Compressive strength, film thickness, net setting time, vickers hardness & dimensionaol expansion properties	Ceramir C&B showed physical & mechanical properties suitable for use as a dental luting cement
Vohra et al. (2020) ⁶³ In vitro study	ACTIVA (BAG containing luting cement), Ketac Cem (glass ionomer cement), Nexus 3 (resin luting cement)	Microleakage: micro-CT & SBS: universal testing machine.	BAG cement exhibited less microleakage & comparable SBS to resin luting agents
da Costa Lima Assad et al. (2021) ⁹⁹ In vitro study	RelyX ARC 3M ESPE (resin luting cement) + 0%,10% or 20% 45S5 BAG or HA	Three-point FS, microhardness, SR, film thickness, contact angle, colour, & MG63 cell viability: MTT assay	HA & 45S5 BAG modified resin cement exhibited reduced FS, appropriate film thickness except for 20% HA & constant CA except for 10% 45S5 group. Cell viability remained above 50% for all groups.
Jefferies et al. (2009) ⁶⁵ Prospective clinical study	Ceramir Crown & Bridge luting cement,	working/setting time & ease of cement removal, retention, tooth sensitivity, gingival inflammation, marginal integrity & discoloration, secondary caries,	Bioactive luting cement demonstrated satisfactory one year clinical performance with acceptable postoperative sensitivity
Jefferies et al. (2012) ¹⁰⁰ Prospective clinical study (2-year follow-up)	Ceramir C&B (formerly XeraCem) bioactive dental luting cement & bioactive calcium-aluminate/glass ionomer cement	Retention, marginal integrity, marginal discolouration, secondary caries, gingival inflammation & tooth sensitivity	Bioactive luting cement demonstrated satisfactory clinical performance at two years
Jefferies et al. (2013) ¹⁰¹ Clinical follow-up study	Ceramir C&B (Doxa Dental AB) bioactive dental luting cement	Retentive properties; clinical performance	Bioactive luting cement demonstrated favourable retention & clinical performance at three years

Table 4. Evidence-based summary of BAG based luting cements for the prevention & management of enamel demineralization

Author (Year)	Intervention & control	Outcome measures	Main findings
Lee et al. (2017) ⁴⁰ In vitro study	Transbond XT™ Primer & Transbond XT™ Primer + 0.2% or 1% BAG or Ag or Zn doped BAG	Microhardness, cell viability, antibacterial assay against <i>S. mutans</i> : turbidimetric assay, SBS, & remineralization after pH cycling: micro CT	BAG increased the microhardness, antibacterial activity, remineralization & SBS. Cytotoxicity was within permissible limits. 1% Ag-doped BAG formulation demonstrated the highest remineralization.
Al-Eesa et al. (2017) ⁶⁶ In vitro study	Resin + 80%, 60%, 50%, 40%, 20%, or 0% BAG	pH change, F, Ca & PO ₄ ion release at ten time points between 6 hrs & 6 months	The rise in pH & the release of Ca & F was directly related to the BAG loading & the time of immersion.
Kim et al. (2018) ⁴¹ In vitro study	Transbond XT™, Charmfil™ Flow, & Charmfil™ Flow + 10%	Ion release at 1, 6, 24, 72, 168, & 840 hours, microhardness, SBS & cytotoxicity,	Ag- or Zn-doped BAG demonstrated stronger antibacterial and

	& 15% Ag, Zn or Ag and Zn doped BAG	antibacterial & remineralization potential	remineralization effects than conventional orthodontic adhesives
Lee et al. (2018) ¹⁰² In vitro study	Transbond XT™ & Transbond XT™ + 1 wt%, 3 wt% & 5 wt% BAG & graphene oxide (GO)	SEM, XRD, microhardness, cell viability, antibacterial activity against <i>S. mutans</i> , SBS, ARI & remineralization potential.	The addition of 3 or 5 wt% BAG and GO resulted in increased microhardness, antibacterial activity, and resistance to demineralization.
Nam et al. (2019) ⁴⁸ In vitro study	CharmFill Flow & CharmFill flow + 1 wt%, 3 wt% or 5 wt% BAG + 2.5% fluorinated graphite (FGt)	Microhardness, SBS, MTT assay, antibacterial activity against <i>S. mutans</i> , F dissolution, & remineralization effect	Addition of FGt & BAG did not alter the microhardness, SBS, ARI, & cytotoxicity. FGt & BAG increased F release, antibacterial activity & remineralization.
Song et al. (2019) ¹⁰³ In vitro study	CharmFill Flow & CharmFill Flow + 1%, 3% or 5 wt% & Ga-doped mesoporous BAG nanoparticles (GaMBN)	Ion release at 1, 7, and 14 days, microhardness, SBS, ARI, MTT assay, antibacterial activity against <i>S. mutans</i> & anti demineralization activity	Microhardness, ion release, antibacterial effect, & anti demineralization effect increased with GaMBN concentration, whereas SBS, ARI, & cell viability remained unchanged.
Firzok et al. (2019) ¹⁰⁴ In vitro study	Transbond XT™ & Transbond XT™ + fluoridated or nonfluoridated BAG nanoparticles	FTIR, SEM, morphological analysis & enamel remineralization following 14-day pH cycling	Fluoridated BAG adhesives showed greater remineralization potential; calcium nitrate derived formulations performed better than calcium hydroxide derived formulations
Choi et al. (2021) ¹⁰⁵ In vitro study	Ortho Connect Flow (OCF), OCF + 1%, 3% or 5 wt% nano mesoporous BAG particles (nMBAG)	Microhardness, DC, SBS, ARI, antibacterial activity against <i>S. mutans</i> & <i>P. gingivalis</i> , & anti demineralization after pH cycling	nMBAG increased microhardness, anti demineralization, SBS & antibacterial activity in a concentration-dependent manner; while DC & ARI were not significantly affected
Par et al. (2022) ⁶⁹ In vitro study	Experimental adhesive with 0%, 10% or 20 wt% of 45S5 BAG or low-Na F-containing BAG	Ca, PO ₄ & F release, pH, SEM & FTIR analysis of surface apatite after 4, 8, 12, 16, 20, 24, 28, and 32 days.	Adding BAG resulted in multiple-ion release & pH elevation under acidic conditions, while promoting ion uptake & apatite precipitation on the composite surface in artificial saliva
Choi et al. (2022) ⁷⁰ In vitro study	OCF, OCF + 3% or 5% 2 metha cryloyloxyethyl phosphorylcholine (MPC), & OCF + 3% or 5% MPC + 1% or 3% nMBAG	SBS, microhardness, adhesive remnant index (ARI), ion dissolution, DC, & antibacterial properties	Addition of nMBAG & zwitterionic material (MPC) demonstrated enhanced antimicrobial & remineralizing properties. MPC alone decreased the SBS, adding nMBAG improved the SBS.
Nethivalavan et al. (2024) ¹⁰⁶ In vitro study	Transbond XT™, & Transbond XT™ + nMBAG prepared by sol-gel process (12 different surfactant to oil ratio)	SBS, & ARI after 6-month pH cycling	MBG enhanced bonding resin demonstrated clinically acceptable initial bond strength and maintained mechanical properties after six months of pH cyclin
Parihar et al. (2024) ¹⁰⁷ In vitro study	BAG-Bond (nMBAG in primer), Transbond XT primer & BAG bond + Transbond XT primer	SBS, ARI & SEM evaluation of enamel demineralization after 6-month simulated salivary aging	BAG-Bond demonstrated higher initial & 6-month SBS than Transbond XT & reduced enamel demineralization around the brackets
Seifi et al. (2024) ¹⁰⁸ In vitro study	Orthodontic adhesive with 0%, 1%, 3% or 5 wt % nAg containing BAG & GC Ortho Connect	SBS, microhardness, SEM/EDX remineralization, antibacterial activity against <i>S. mutans</i> , MIC/MBC & MTT cytotoxicity	Nano Ag containing BAG improved antibacterial & remineralizing properties while maintaining acceptable mechanical characteristics
Sheikhi et al. (2024) ⁶⁷ In vitro study	Ambar FGM orthodontic adhesive with 5 wt%, 10 wt%, 15	SBS & ARI	5–15% BAG did not significantly affect SBS whereas 20% BAG significantly increased SBS. ARI

	wt% or 20 wt% 45S5 BAG		showed no significant differences among groups.
Mafetano et al. (2025) ⁶⁸ In vitro study	Transbond XT + 0 wt%, 20 wt%, 30 wt% or 50 wt% 45S5 BAG (Vitryxx®) & FL BOND II with S-PRG	SBS, ARI, DC, calcium release & SEM particle-size analysis	BAG incorporation increased Ca release and DC without affecting SBS. 50 wt% BAG demonstrated the highest Ca release.
Mohammed et al. (2025) ¹⁰⁹ In vitro study	Selfcure orthodontic resin (SAR) & SAR+ 0.5% grape seed extract (GSE), SAR+ 0.5% GSE +1% 45S5 BAG, SAR+ 0.5% GSE + 0.5% SrF ₂	SBS, ARI, enamel damage index & microhardness after water storage, acid challenge & thermocycling	The 1% BAG + 0.5% GSE formulation yielded clinically satisfactory SBS, minimal adhesive residue, minimal enamel damage, and highest microhardness
Alamri et al. (2020) ⁷¹ Systematic review	Anti demineralizing potential of BAG enhanced orthodontic resins	Enamel anti demineralization effect with micro CT, Polarized light microscopy and hardness	Studies demonstrated superior concentration dependent anti demineralization with BAG containing adhesives
Hamdi et al. (2024) ¹¹⁰ Systematic review	Remineralizing & anti demineralizing potential of orthodontic adhesives	Subsurface & surface remineralization, elemental analysis, surface morphology & ion release	Included studies support the effectiveness of incorporation of remineralizing agents into orthodontic adhesives despite methodological heterogeneity

Table 5. Evidence-based summary of BAG based adhesives for the prevention & management of enamel demineralization

Author (Year)	Intervention & control	Outcome measures	Main findings
Kawaguchi et al. (2017) ¹¹¹ In vitro study	Noncoated SS disks & BAG coated SS disks. Coated by electrophoretic deposition (EPD) using direct current or alternating current at 10 V or 15 V	Frictional resistance, acid neutralization, enamel remineralization, & cytotoxicity	BAG coated specimens demonstrated enamel remineralization & acid-neutralizing potential
Kawaguchi et al. (2020) ⁷³ In vitro study	Noncoated orthodontic SS wires & wires coated with 45S5 BAG by EPD with DC or AC at 10 V or 15 V	Spectrophotometry, SR, SEM, 3D laser scanning microscopy (LSM), hardness and elastic modulus: nanoindentation, & frictional resistance	Higher-voltage BAG coatings showed improved optical properties, lower SR, higher coating hardness, & E modulus. Most BAG coated wires demonstrated frictional forces comparable to noncoated wires.
Khan et al. (2025) ⁷⁴ In vitro study	Noncoated orthodontic SS brackets, nHA & nBAG coated SS orthodontic brackets (coated by spin coating)	SBS, ARI, optical microscopy & SEM at 1, 7, 14, & 30 days of demineralization & remineralization cycling	nBAG coated brackets demonstrated improved mechanical & morphological characteristics during simulated treatment conditions.

Table 6. Evidence-based summary of BAG coated orthodontic wires & brackets for the prevention & management of enamel demineralization

Author (Year)	Intervention & control	Outcome measures	Main findings
Bagheri et al. (2020) ¹¹² In vitro study	RI & RI with 2 wt% or 5 wt% BAG or nano-Fluoro HA (n-FHA)	Spectrophotometric assessment at baseline, after demineralization & 14 days after RI	n-FHA + RI demonstrated superior masking of WSLs, whereas BAG + RI did not demonstrate equivalent efficacy.
Ashraf (2022) ¹¹³ In vitro study	ICON RI & ICON RI with 10 wt% nano BAG,	Vickers microhardness, colour stability after	Addition of 10% nano-BAG did not significantly alter enamel hardness, penetration ability or colour stability

		staining & penetration ability	
Souza et al. (2023) ¹¹⁴ In vitro study	Experimental RI (ERI), RI with 5 wt% or 10 wt% Biosilicate BAG, RI + 10 wt% nHA & ICON RI	SEM, EDX, ATR-FTIR, DC, sorption, solubility, FS, elastic modulus, CA & resin penetration	Biosilicate BAG or nHA compromised the physicochemical properties, increased the bioactivity of the RI without affecting the resin penetration.
Meng et al. (2024) ¹¹⁵ In vitro study	RI & RI followed by BAG or CPP-ACPF	SEM, EDX, XRD, atomic force microscopy (AFM), SR & Vickers microhardness	BAG or CPP-ACPF application followed by RI reduced SR, increased Ca/P ratio & HA formation
Ahmed et al. (2024) ¹¹⁶ In vitro study	ERI, ERI + 2.5 wt% 45S5 BAG, boron containing BAG or F-BAG & ICON RI,	Vickers microhardness, SR, & surface morphology	BAG doped RIs produced greater microhardness, reduced roughness, & improved surface morphology of the enamel
Wang et al. (2025) ¹¹⁷ In vitro study	ICON resin infiltrant & ERI + high Phosphorus BAG (Bioactive RI or BRI)	DC, cytotoxicity, water sorption, Ca/P release, microhardness, elastic modulus, colour change, penetration depth & remineralization	BRI showed physicochemical properties comparable to ICON, favourable infiltration depth, esthetic properties, & improved enamel microhardness with remineralization potential.
Shen et al. (2026) ¹¹⁸ In vitro study	45S5 BAG slurry (10% w/v) RI, BAG slurry + RI & untreated control.	SR, microhardness, Ca ion release, and laser scanning confocal microscopy	BAG slurry & RI exhibited superior remineralization efficacy and resistance to secondary demineralization
Albashaireh et al. (2025) ¹¹⁹ Randomized clinical trial	BAG adhesive (Hi-Bond Universal) & ICON resin infiltrant	Lesion area, deepest point & fluorescence loss using Quantitative light induced fluorescence	Both Hi-Bond & ICON effectively promoted the esthetic recovery of ICLs for over the one-month follow-up period.
Albashaireh et al. (2026) ¹²⁰ Randomized clinical trial	BAG adhesive (Hi-Bond Universal) & ICON resin infiltrant	Patient & clinician satisfaction on esthetic improvement using 100-mm visual analogue scale.	Both Hi-Bond & ICON achieved favourable esthetic outcomes at one month follow-up
Aldarisi et al. (2025) ⁷⁶ Systematic & critical review	Studies evaluating RIs containing HA, BAG, ACP or Tricalcium phosphate	microhardness, roughness, DC & colour stability	BAG containing infiltrants demonstrated favourable effects on enamel surface properties & remineralization.

Table 7. Evidence-based summary of BAG incorporated resin infiltrants for management of enamel demineralization

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