Majalah Kedokteran Gigi Indonesia
Vol 11 No 2 – August 2025
ISSN 2460-0164 (print), ISSN 2442-2576 (online)
Available online at https://jurnal.ugm.ac.id/mkgi
DOI: http://doi.org/10.22146/majkedgiind.109296

SYSTEMATIC REVIEW

Exploring the potential of bromelain in orthodontic treatment

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Submitted: 16th July 2025; Revised: 25th July 2025; Accepted: 29th July 2025

ABSTRACT

Bromelain, a proteolytic enzyme derived from pineapple, has attracted significant attention in both medicine and dentistry due to its diverse therapeutic properties. It has been widely studied for its anti-inflammatory, digestive, and wound-healing effects. In dentistry, bromelain has been investigated for applications such as reducing postoperative pain, facilitating enamel deproteinization, aiding in caries removal, and serving as an endodontic irrigant. In orthodontics, its potential lies in deproteinizing enamel to improve the bond strength of orthodontic brackets during placement. Studies suggest that applying bromelain prior to acid etching can enhance bracket bond strength, providing a safer and more efficient alternative to sodium hypochlorite. It has also shown promise in reducing plaque accumulation and gingivitis, particularly in patients with fixed orthodontic appliances. Bromelain's antibacterial and anti-inflammatory properties support its role in maintaining oral hygiene and promoting healing. However, most existing evidence comes from in vitro or short-term clinical studies. Long-term clinical trials are needed to confirm its safety and efficacy in routine orthodontic practice.

Keywords: bromelain; enamel deproteinization; fixed orthodontic appliance; gingivitis; orthodontic; plaque accumulation

INTRODUCTION

Pineapple (Ananas comosus) is cultivated in several tropical and subtropical areas, including Thailand, the Philippines, China, Brazil, India, Nigeria, Costa Rica, Mexico, Indonesia, and Kenya.[1] Traditionally valued as a medicinal plant in various indigenous cultures, it continues to hold an important role in ethnopharmacology. Bromelain, a proteolytic enzyme extracted from different parts of the pineapple plant—including the stem, leaves, fruit, peel, core, and crown—has been chemically recognized since the 18th century and extensively studied for its medical and therapeutic potential.[2-4]

In 1891, proteolytic enzymes were first identified in pineapple juice, where they were noted for their ability to break down proteins into amino acids. By the early 20th century, researchers began isolating and characterizing these enzymes. Bromelain, a major sulfhydryl proteolytic enzyme derived from both the stems and fruits of the pineapple, has been investigated since the latter half of the 20th century.[5-6] Today, bromelain is widely available as a nutritional supplement and is incorporated into pharmaceuticals, cosmetics, and food processing. In the food industry, it functions as a natural protease, tenderizing meat by breaking down collagen and softening muscle proteins through its potent hydrolytic activity.[7]

Research has explored bromelain's potential as an anti-inflammatory agent, digestive aid, wound-healing compound, and adjunctive treatment for conditions such as osteoarthritis, sinusitis, and cancer.[5] Studies also indicate that bromelain exhibits antibacterial, antifungal, antiviral, and immunomodulatory properties.[6] More recently, it has demonstrated antioxidant potential, as evidenced by its ability to significantly reduce CCl_4-induced toxicity in rats, suggesting a role in mitigating oxidative stress and free radical production.[8]

Beyond its medical applications, bromelain has been investigated for various dental uses. Studies report its efficacy in reducing postoperative pain following third molar surgery, serving as an enamel deproteinizing agent to decrease microleakage in composite restorations after bleaching, functioning as a chemomechanical caries removal agent in primary dentition, acting as an active component in dentifrices for stain removal and whitening, and serving as an alternative endodontic irrigant to sodium hypochlorite.[9-14] Bromelain's role in reducing inflammation within dental pulp has also been examined. In lipopolysaccharide-induced human dental pulp cells (hDPCs), bromelain reduced inflammatory cytokine levels and enhanced mineralization, making it a promising candidate for regenerative endodontics.[15]

Additionally, bromelain's diverse applications in dental care include reducing postoperative edema and aiding in the management of periodontal disease, owing to its anti-inflammatory and antibacterial properties.[16] It can lower oral inflammatory markers and accelerate healing in ligature-induced periodontitis models, providing further evidence of its potential as an adjunctive agent in periodontics.[17] The potential benefits of bromelain in orthodontics are being explored primarily for its role as a deproteinizing agent. Research indicates that combining certain enzymes, including papain, can improve orthodontic bond strength.[3] Its antibacterial properties have also been examined for their ability to reduce plaque accumulation and gingivitis in patients undergoing fixed orthodontic treatment.[18-19]

Despite bromelain's well-established uses in medicine and general dentistry, its specific applications in orthodontics remain underexplored. Preliminary findings suggest potential advantages, such as increased orthodontic bond strength through enamel deproteinization and antibacterial effects that may help reduce plaque accumulation and gingival inflammation in patients with fixed appliances.[3,18,19,20] However, existing evidence is scattered, often limited to in vitro studies or short-

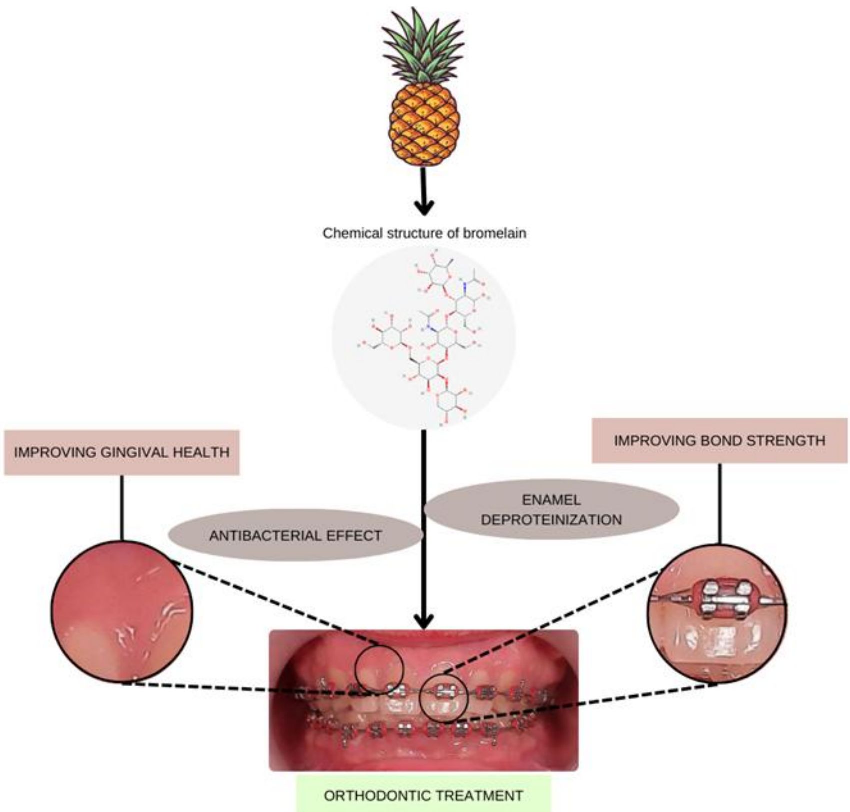

Figure 1. Bromelain applications and its role in orthodontic treatment (Parts of this figure were obtained from https://pubchem.ncbi.nlm.nih.gov/compound/Bromelain; accessed on 22 April 2025)

term clinical observations, with no comprehensive synthesis available to guide clinical practice or future research. With the growing interest in natural bioactive agents for orthodontic care, investigating bromelain's application represents a timely and novel research area. Therefore, this scoping review aims to systematically map the current literature, assess the scope and nature of research on bromelain in orthodontics, and identify knowledge gaps to inform future studies and potential clinical applications.

MATERIALS AND METHODS

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines, adapted for narrative synthesis. The guiding research question was: "What are the potential applications and effects of bromelain in orthodontic treatment?"

A comprehensive literature search was conducted in two electronic databases, PubMed and Google Scholar, in April 2025. The search strategy for PubMed was:

("bromelain" OR "pineapple" OR "ananas comosus") AND ("orthodontic" OR "orthodontics" OR "orthodontic treatment"). The search strategy for Google Scholar used the same keywords and Boolean operators. Reference lists of all included articles were screened to identify additional relevant studies.

Studies were included if they were original in vitro, in vivo, or clinical research investigating bromelain derived from pineapple in orthodontic-related procedures, reported outcomes related to enamel deproteinization, orthodontic bond strength, plaque accumulation, or gingival health, and were published in English between the last five years. Articles were excluded if they were reviews, case reports, editorials, or letters without primary data, if bromelain was not the primary intervention, or if they were published in languages other than English.

RESULTS

The initial search retrieved 84 records. After removing duplicates, 78 records remained. Title and abstract screening excluded 47 records that did not meet the inclusion criteria. Full-text review of the remaining 37 articles resulted in the exclusion of 31 for reasons such as unrelated outcomes, absence of bromelain intervention, or incomplete data. Finally, 6 studies met the eligibility criteria and were included in this review.

DISCUSSION

Bromelain as an enamel deproteinizing agent to enhance orthodontic bond strength

The development of materials capable of achieving optimal orthodontic bond strength is a critical aspect of contemporary dentistry. Regardless of the bonding technique employed, adequate enamel surface preparation is essential for creating a durable bond.[21] Enamel conditioning involves preparing the surface for adhesion by generating surface irregularities and removing the enamel pellicle.[22] Standard practice involves etching with 37% phosphoric acid for 15 seconds, producing rough surface microporosities that facilitate micromechanical retention.[23]

Recent studies, however, indicate that etching for 15 seconds with 37% phosphoric acid gel does not consistently remove the outer aprismatic enamel layer.[24] This incomplete removal may result in inadequate mineral loss from certain teeth or surface areas, leading to potential failures in orthodontic bracket adhesion. To address this limitation, researchers have proposed supplementary enamel surface treatments. Enamel deproteinization—removing organic material from the enamel surface—can enhance the effect of acid etching, improving bracket bond strength and resistance to orthodontic traction by producing a more defined etching pattern.[3]

Bromelain, a proteolytic enzyme, functions as a deproteinizing agent by breaking down organic components—particularly proteins—on the enamel surface. It has been studied alongside papain gel, derived from papaya, as an alternative or adjunct to sodium hypochlorite, a conventional deproteinizing agent. Bromelain has been shown to produce a more favorable etching pattern and to

Majalah Kedokteran Gigi Indonesia. Agustus 2025; 11(2): 91-99
ISSN 2460-0164 (print)
ISSN 2442-2576 (online)

enhance the bond strength of composite resin. Its ability to break down IgG protein bonds results in effects similar to those of sodium hypochlorite.[25-26]

The incorporation of a deproteinizing step prior to acid etching is particularly recommended in pediatric patients to enhance enamel bond strength. Bromelain, a natural deproteinizing agent, has been proposed as an alternative to sodium hypochlorite in this population without compromising bond strength efficacy. Unlike sodium hypochlorite, a potent oxidizing agent associated with drawbacks such as unpleasant taste, odor, and adverse soft-tissue reactions,[25] bromelain is considered safer and more biocompatible.

When using self-etch adhesives, pretreatment with bromelain enzyme solution can increase bond strength to enamel and dentin by partially dissolving the organic phase of the smear layer. This effect is comparable to that achieved with hypochlorous acid (HOCl) solution.[27] Bond strength improvements may result from protein dissolution and compositional changes that enhance monomer diffusion by increasing tooth permeability.[18]

Bromelain's ability to deproteinize enamel without adverse effects makes it a valuable tool for improving bond strength in orthodontic procedures. Several studies have demonstrated its efficacy as an enamel deproteinizing agent and its role in enhancing the bond strength of composite resins. However, these findings are largely based on in vitro studies. Further clinical research is needed to confirm bromelain's potential under in vivo conditions, considering factors such as the oral environment and the influence of saliva.

Bromelain as an adjunct for managing dental plaque in orthodontic therapy

Dental biofilm formation begins with the adhesion of pioneer bacteria, such as *Streptococcus* species, to the acquired pellicle—a naturally formed protein film on the enamel surface. These early colonizers secrete extracellular polysaccharides and DNA, forming a matrix that facilitates further bacterial attachment and biofilm maturation. Over time, additional species integrate into the biofilm, resulting in a complex, structured community known as dental plaque. This biofilm matrix stabilizes the plaque, protects resident bacteria, and retains nutrients, making it resistant to mechanical removal and antimicrobial agents. Such resistance can compromise the success of orthodontic treatment.[28-29]

Plaque control requires both mechanical (e.g., toothbrushing and flossing) and chemical (e.g., mouthwash) interventions.[30] Patients with fixed orthodontic appliances face additional challenges in plaque removal, as brackets, wires, and interproximal spaces hinder toothbrush access.[31]

Bromelain has been shown to inhibit biofilm development by preventing bacterial adhesion to the enamel surface and to other bacteria.[19] Studies suggest that using bromelain as a pre-rinse alongside toothbrushing and flossing may be beneficial as an adjunctive therapy in orthodontic patients. Bromelain mouth rinses

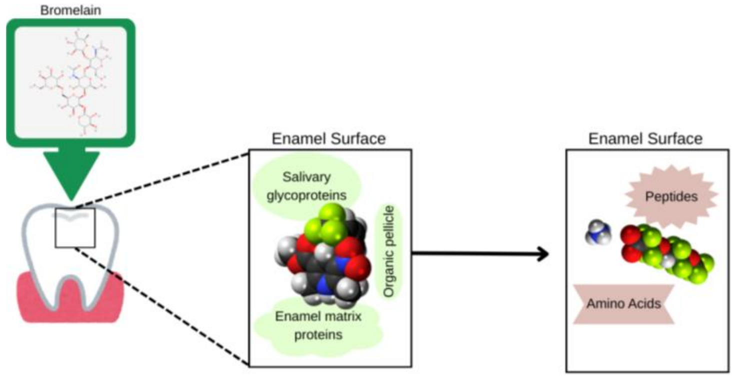

Figure 2. Bromelain as an enamel deproteinizing agent

Table 1. Characteristics of included studies

Bromelain dose and formulation	Methodology	Result	Reference
60% of indigenously prepared bromelain gel	The study evaluated SBS of pit and fissure sealant with and without deproteinization using: 5% NaOCl, papain gel, and bromelain gel, and tested samples after 24 hours.	Bromelain gel group had the highest mean SBS, followed by the papain gel group, 5% NaOCl group, and control group.	Thankachan et al[25]
10% bromelain enzyme solution (Bromelain 020-04262, FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan)	Pretreatments were applied to Class V cavities (bromelain, papain, HOCl-solution and none), followed by Scotchbond Uiversal (SU) or Clearfil Universal Bond Quick (UQ), and filling resin composite. Interfacial gap lengths, micro-shear bond strength, and morphological investigation on enamel and dentin were performed.	Bromelain and HOCl-solutions significantly increased SU's µSBS to enamel and dentin, improving enamel-marginal and internal adaptations, but not UQ's. Papain treatment slightly thinned the dentin smear layer.	Alshahni et al[27]
6% Bromelain gel (bromelain powder 250 mg mixed with other solution and distilled water)	Sodium hypochlorite, papain gel, and bromelain gel were used as deproteinizing agents and their impact on the microleakage and SBS of pit and fissure sealants was assessed.	Bromelain group had the lowest microleakage scores, highest shear bond strength, and superior results for SBS and microleakage after deproteinization before acid etching.	Bhatt et al[33]
Pineapple peel extract 6.24% mouthwash	45 orthodontic patients divided into three groups: those given banana peel extract, pineapple peel extract, and a control group. Plaque index was measured before and after mouthwashing.	Pineapple peel extract and banana peel extract mouthwashes effectively inhibited the formation of plaque in fixed orthodontic patients.	Beumaputra et al[31]
1 gram of bromelain enzyme powder was mixed with 15 mL of warm pineapple juice	43 orthodontic subjects, randomly received bromelain enzyme or placebo pre-rinse, followed by manual tooth brushing and use of a Waterpik. Residual plaque accumulations were recorded at each treatment step.	Bromelain group showed significantly lower plaque scores after brushing compared to placebo. Bromelain may be beneficial as an adjunct in managing dental plaque when combined with traditional oral hygiene methods.	Rose et al[19]
0.05 g of Bromelain powder added to 50 ml of distilled water	This study evaluated the effectiveness of a bromelain mouth rinse in reducing gingival inflammation and bacterial plaque in adolescents; gingival index (GI) and plaque index (PI) were measured at baseline and after 30 days.	Significant difference in mean GI and PI scores at one month, suggesting bromelain mouthwash improves gingival status without adverse effects.	Patel and Kumaresan[20]

have been reported to significantly reduce plaque and gingivitis, improve gingival health, and lower plaque scores without adverse effects.[20] Gargling with a 6.24% pineapple peel extract mouthwash containing bromelain has been shown to inhibit plaque formation in patients with fixed orthodontic appliances more effectively than an Aquadest control.[31] Moreover, its efficacy as a mouthwash in limiting plaque and gingivitis suggests that bromelain could be a potentially beneficial adjunctive agent when combined with traditional oral hygiene measures and clinical therapy in orthodontic patients.[19]

Bromelain disrupts dental plaque by degrading the protein components of the plaque biomatrix, interfering with the adhesion of the dental

Majalah Kedokteran Gigi Indonesia. Agustus 2025; 11(2): 91-99
ISSN 2460-0164 (print)
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pellicle to the tooth surface through hydrolysis of protein linkages. The dental pellicle, composed primarily of glycoproteins, may fail to adhere effectively when such protein bonds are broken. Bromelain and other enzymes can also hydrolyze extracellular glucans, thereby preventing bacterial adhesion and subsequent plaque formation.[19]

In addition, other studies have shown that bromelain exhibits antibacterial activity by targeting bacterial cell walls. It functions by denaturing the structural proteins of the bacterial cell wall, leading to cell wall deterioration, inhibition of bacterial growth, and eventual cell death over time.[30] The use of bromelain as a mouth rinse may therefore be beneficial as an adjunct antimicrobial therapy in orthodontic treatment. However, further investigation is warranted, as a single plant source may not provide all the desired pharmacological properties. Combining bromelain with other plant extracts is recommended for developing innovative oral care products.[32]

Safety considerations for bromelain use

Extensive research has validated the safe application of bromelain, highlighting its minimal side effects and notable therapeutic benefits. Bromelain is listed as a direct food substance affirmed as *Generally Recognized as Safe* (GRAS) by the U.S. Food and Drug Administration (FDA). Studies indicate that its use for enamel deproteinization prior to orthodontic bracket bonding can enhance bond strength while preserving enamel integrity. Similarly, gargling with a 6.24% pineapple peel extract mouthwash has been shown to reduce plaque index scores in patients with fixed orthodontic appliances without significant adverse effects.[3,31]

In addition to being non-toxic, bromelain is generally considered safe and is associated with only minimal adverse reactions. Its efficacy has also been evaluated following mandibular third molar surgery. Bhoobalakrishnan et al reported that bromelain performed comparably to diclofenac in controlling postoperative edema, pain, and trismus. However, bromelain can cause IgE-mediated respiratory allergic reactions in individuals allergic to pineapple, which may manifest as breathing difficulties, sinus congestion, angioedema, wheezing, and coughing.[34] As with any supplement, caution is advised, and further research is needed to assess the safety of bromelain for prolonged use in orthodontic care.

Research on the sustained application of bromelain during prolonged orthodontic care remains scarce, despite its efficacy in reducing inflammation and improving bracket adhesion. Current use is predominantly short-term—for example, as a mouthwash for one week to reduce dental plaque, or in combination with papain during the initial stages of bracket bonding.[3,31] Its known effects are largely limited to short-term application, and it is unclear whether extended use over the course of orthodontic treatment—often lasting months to years—offers additional benefits or poses risks.

Despite the promising results, certain limitations should be acknowledged. The majority of bonding studies were conducted in vitro, limiting their direct applicability to the clinical environment where factors such as saliva, intraoral temperature, and mechanical forces can influence outcomes. Additionally, the included clinical studies varied in bromelain concentration, formulation, and application protocols, making it difficult to establish a standardized regimen. Long-term studies assessing the sustained use of bromelain in orthodontic patients are scarce, and the potential effects of extended exposure remain unclear.

Overall, bromelain appears safe for short-term use with minimal side effects; however, long-term safety and efficacy data for continuous use in orthodontics are lacking. Until such evidence is available, bromelain use should be limited to targeted, short-term needs in orthodontic treatment. Data from other medical fields indicate that bromelain is generally safe when used appropriately, with reported adverse effects including mild diarrhea, minor gastric disturbances, and occasional allergic reactions.[35] Future well-designed clinical trials are needed to confirm its efficacy under real-world conditions, determine optimal concentrations and delivery methods, and evaluate its long-term safety in diverse patient populations.

CONCLUSION

Bromelain's proteolytic properties allow it to remove organic material from enamel surfaces, thereby facilitating acid etching and improving the bond strength between orthodontic brackets and teeth. As a naturally derived enzyme, it represents a safer alternative to sodium hypochlorite, particularly in pediatric patients, due to its lower incidence of side effects. Its antibacterial and anti-inflammatory properties also support its role in reducing plaque accumulation and gingivitis among patients with fixed orthodontic appliances.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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