

**BROMELAIN: A NATURAL APPROACH TO WHITENING TEETH
EFFECTIVELY**

An Undergraduate Research Scholars Thesis

by

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ABSTRACT

Bromelain: A Natural Approach to Whitening Teeth Effectively

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Teeth whitening using peroxide is a popular cosmetic dental procedure. While peroxide whitening is time efficient and a relatively low-cost procedure, the goal of a whiter smile may come at a greater cost. Peroxide whitening may be contraindicated for some patients due to the varying side effects. Side effects can include hypersensitivity due to effected tooth structure. Bromelain, an enzyme found in the stems of pineapples, has emerged as a new whitening alternative with greater patient acceptance. The enzyme has been shown to have positive attributes which aid in systemic health and protection of the oral cavity. Extended whitening applications with hydrogen peroxide have shown to affect the enamel matrix, the microhardness

of enamel, and the cell viability of the tooth. Bromelain, with similar whitening applications, has shown to produce similar results as peroxide whitening gel without affecting the tooth structure. Peroxide whiteners may lead to dentinal hypersensitivity during the degradation of the enamel by hydrogen peroxide while tooth bleaching, damaging the fibroblasts. Due to the altered tooth structure, hydrogen peroxide moves through the exposed dentinal tubules to the pulp chamber causing a sensitive nerve impulse to the patient's oral cavity. When used for bleaching, Bromelain has shown to degrade the tooth stain on the enamel surface allowing light to reflect off of the enamel surface giving the appearance of a whiter smile visible to the naked eye. During this process the structure of the tooth is not altered itself leaving the fibroblasts untouched.

DEDICATION

To our friends, families, instructors, and peers who supported us throughout the research process.

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INTRODUCTION

When making a first impression, a smile is often the first detail a person will notice. In today's society, the outward appearance of a person may affect their self-esteem. In recent years, teeth whitening has become an increasingly popular cosmetic dental procedure. This treatment is influenced further across a variety of outlets, such as celebrities, social media, advertisements, and even by word of mouth. Peroxide whitening is commonly used in modern dentistry, but it may not be an inclusive treatment for all patients due to the varying side effects that patients may experience with its use. Not only should the side effects be considered but the patient's personal decision as well. Patients demand for natural alternatives to healthcare has increased significantly. Hence, this research is to find a new therapy with a natural approach to teeth whitening as effective as peroxide whitening without the side effects. The intent of this narrative review is to inform about the natural compound Bromelain. To evaluate the time and effectiveness of hydrogen peroxide whitening, analyze the effects on enamel structure by hydrogen peroxide, understand the oral and systemic effects of Bromelain, and to analyze the comparisons between Bromelain and hydrogen peroxide on external bleaching.

1. EVALUATE TIME AND EFFECTIVENESS OF HYDROGEN PEROXIDE WHITENING

Hydrogen peroxide whitening is one of the most popular means of teeth whitening, but beyond removing exogenous and endogenous stains, the method of teeth bleaching using peroxide oxidizers is not completely understood. It had been speculated that peroxide whiteners were effective by altering the chromophores in the enamel. The result would be a molecule with a greater capacity to reflect less light.¹

In 2012, Eimar et al. identified that peroxide whiteners oxidized enamel structures via free radicals, peroxide anion, and reactive oxygen molecules.¹ They conducted an ex vivo study in which they analyzed 60 adult sound maxillary incisors and canines which had been recently extracted.¹ The team utilized a Scanning Electron Microscope Energy Dispersive Spectroscopy and Easy shade spectrophotometer to analyze each tooth's crystallinity index and shade before and after receiving treatments.¹ The group tested four solutions including a 1 M sodium hydroxide deproteinizing solution, a 0.5 M ethylenediaminetetraacetic acid demineralizing solution, a 30% hydrogen peroxide oxidizing solution, and a deionized distilled water to act as a control solution.¹ It was found that the deproteinizing solution produced a minor enhancement in the tooth shade and chroma but the demineralizing solution had negative effects in regard to the overall shade.¹ However, the hydrogen peroxide solution offered an increase in the enamel opacity, increasing the tooth's lightness and chroma.¹ It was concluded that while hydrogen peroxide oxidizes the organic enamel matrix of a tooth, it does not alter the organic or inorganic structure of the dental enamel.¹ The researchers speculated that younger patients may see better

results from hydrogen peroxide bleaching because the organic component of the enamel matrix, which is utilized in this type of whitening, has not undergone extensive remineralization.¹

In 2017 an in vitro study was conducted by Vekaash et. Al. which analyzed the combined effects of hydrogen peroxide and pineapple extract.² The study examined 60 incisors which were first divided up into three groups which were to be treated with hydrogen peroxide of varying strengths of 30%, 20%, and 10%.² A horizontal cut at the cementoenamel junction was made on each tooth to remove the root leaving just the crown of the tooth to be tested.² Each tooth was then cut again sectioning the tooth mesio-distally providing two identical halves for the researches to test.² One half of the tooth was treated solely with the predetermined percentage of hydrogen peroxide solution and the other half of the tooth was treated with a combination of the matching hydrogen peroxide concentration and extracted pineapple enzymes.² To create the mixed solution the researchers used 1mL of pineapple extract, 1mL of phosphate buffered solution, and 28mL of the previously specified concentration hydrogen peroxide.² The solutions were then left on half of the teeth for 10 minutes and the other half for 20 minutes.² The teeth were analyzed by a reflectance spectrophotometer, which records color variables in accordance to the CIEL*a*b color system.² In conclusion the researchers found statically significant results (5%) when comparing the whitening result from the combined solutions to the hydrogen peroxide alone.² The research team found they could achieve the same result of the 30% hydrogen peroxide when they used a lower concentration of 10% hydrogen peroxide combined with the pineapple enzymes.² It was also noted that the color change obtained after 20 minutes of exposure to the solutions were significantly greater than the teeth that were only exposed for 10 minutes.² The researchers noted that the bromelain, an oxidizing enzyme present in pineapple extract, was one of the essential agents that played a significant role in the examined bleaching

process.² They noted that the bromelain acts as an oxidizing agent which helps form a complex with the hydrogen peroxide and improves the efficacy of the bleaching process and helps reduce enamel defects.² The bleaching result occurs from the bromelain reducing the activation energy of the hydrogen peroxide while increasing the efficacy of the rate of the chemical reaction.²

2. ANALYZE THE EFFECTS OF HYDROGEN PEROXIDE ON ENAMEL STRUCTURE

Though hydrogen peroxide whitening is one of the most sought out cosmetic dental treatments, this product may permanently alter tooth structure.³ The chemical components of the hydrogen peroxide are meant to slightly degrade the enamel's surface stain in order to achieve a whiter smile.⁴ This occurs when reactive oxygen species from hydrogen peroxide interact with the organic chromophores (the part of a molecule responsible for color) by oxidation.⁵ Without careful and proper use these side effects (enamel surface alteration) can occur.⁴ The altering of tooth structure is generally followed by hypersensitivity.

Studies have examined enamel hardness and surface texture following bleaching with peroxide whitening agents. In 2019, Vilhena et al. evaluated the effectiveness of peroxide-based whiteners using bovine teeth (n=116).³ The sample teeth were randomly allocated into four groups.³ Group one was the negative control group placed in water-soluble gel, group two was the positive control group placed under the manufacturer's recommended application time. While group three represented the manufacturer's recommendations prolonged by 50% and group four exceeded the manufacturer's time by 100%.³ The study conducted a longitudinal design, with a twenty-eight-day time span. Once the twenty-eight-day time span was complete, the results appeared to be clinically significant on a microscopic level and statistically significant.³ The study found a substantial decrease in the microhardness of the enamel when the peroxide acted on the enamel organic matrix. This led to the decrease of the microhardness value of the tooth.³ A very fragile enamel was the result of the degraded organic matrix.³ The

researchers determined the chemical composition of the teeth presented significant modification.³

Another study conducted in Brazil by Guilherme et al. demonstrated clinical significance when it was determined 3% hydrogen peroxide can illustrate a negative effect to the enamel's surface structure and hardness.⁶ The experiment used 6 human molars (n=6).⁶ The study resulted in significant reduction of enamel microhardness ($p < .0001$).⁶ There were also areas of erosion present on the teeth after bleaching 3 hours a day for 2 weeks.⁶ In another study conducted by Lilaj et al, researchers evaluated cell viability after placing tooth fibroblasts and dental pulp cells in different amounts of hydrogen peroxide whitening agents.⁷ The in-vitro study demonstrated decreased cell viability, meaning the cells became damaged and unhealthy in the presence of increasing amounts of hydrogen peroxide.⁷

A common consequence of the enamel degradation and alteration of the tooth structure, is dentinal hypersensitivity.⁴ When the top layer of enamel is removed, the fluid is able to flow through the dentinal tubules that are now exposed and reach the pulpal chamber, where the nerve is located, creating a jolting shock for the patient.⁴ Dentinal hypersensitivity presents as a quick, sharp pain that can affect a patient's everyday life. In 2020, Ribeiro et al. found that nearly 85% (n=30) of whitening patients developed sensitivity.⁴ The chemical components in the hydrogen peroxide degrade the enamel so that the dentinal tubules become exposed.⁴ It is believed that dental bleaching leading to dentinal sensitivity is in correlation with reactive oxygen species (ROS) from the degradation of hydrogen peroxide moving into the pulp chamber by the now exposed dentinal tubules.⁴ This creates the release of IL-1 β and RANK-L9,10, which are the inflammatory mediators.⁴ Dentinal hypersensitivity is a common side effect of hydrogen

peroxide bleaching due to the dentinal tubules becoming exposed and the alteration of tooth structure.⁴

3. UNDERSTAND THE ORAL AND SYSTEMIC EFFECTS OF BROMELAIN

In the evolving world of dentistry, new options have surfaced which may be appealing to patients and have greater patient acceptance. One of these options is bromelain, which is a digestive enzyme acquired directly from the pineapple fruit. Bromelain can be extracted from either the stem or fruit of the pineapple plant, with a majority coming from the stem. Since the stem of the pineapple is a by-product and a bulk of the waste produced, this means that bromelain is inexpensive to acquire, possibly making it more economical for mass production, distribution, and utilization.⁸

In 2020, Ribeiro et al. conducted an in-vitro study which evaluated the effectiveness of peroxide free bleaching using bromelain. In addition, they examined Bromelain's effect on enamel hardness, surface texture and whether it was toxic to fibroblast cells. Ribeiro et al. obtained enamel-dentin discs from 50 bovine teeth and exposed the samples to bromelain for 45-minute intervals. They found that the discs exhibited an acceptable percentage of cell viability of nearly 100%. The cells from the enamel-dentin discs were still healthy and not damaged, aiding in the integrity of the fibroblasts.⁴ When fibroblasts become damaged from hydrogen peroxide-based whiteners, it may lead to sensitivity for some patients as noted in a study conducted by Lilaj et al. evaluating the effect of hydrogen peroxide on teeth cell viability.⁷ This is in part due to the anti-inflammatory response seen in bromelain, blocking the production of cytokines.⁸

Relating to the oral cavity, bromelain also can act directly on the tooth's pellicle by degrading the proteins that adhere and aid in staining. In 2020 Ribeiro et al. evaluated the effectiveness of peroxide-free whitening agent bromelain. They reported bromelain degraded the

stains on the tooth's surface into miniscule parts, allowing light to reflect off the surface of the tooth with more ease giving the appearance of a brighter smile.⁴ Ribeiro et al. found that bromelain reduced the superficial stain visible to the eye and it did not penetrate the tooth structure itself, which left the fibroblasts untouched.

In the same study conducted by Ribeiro et al. when comparing the potential of bromelain to peroxide based whiteners, bromelain showed promising results as being an equal alternative to peroxide-based bleaching. They also reported that color change caused by bromelain was greater than the human perceptibility threshold of 0.8–1.8.⁴ This range represents a scale in which color change of a tooth or its structure is seen to the naked eye in dentistry. This perceptibility threshold being in this range is promising because it shows that the use of the natural alternative does produce a noticeable change in tooth coloration comparable to peroxide based whiteners. Another important factor is hypersensitivity some patients may experience. The natural components of bromelain and the low levels of cytotoxicity associated with it, show how bromelain could be a bleaching alternative used in various media to help with the discomfort that may be experienced by patients using chemical forms of bleaching such as hydrogen peroxide.

Bromelain aids in more than bleaching teeth; it can be used for multiple ailments that occur in the body such as chronic inflammation, arthritis, autoimmune disorders, and malignancy relating to tumors.⁸ Patients experiencing the previously mentioned systemic issues may opt for bromelain since it can decrease inflammation and has antithrombotic and fibrinolytic functions as well.⁴ The therapeutic characteristics are due to the enzyme arising from fruits considered to be non-toxic. For dental professionals hoping to achieve patient acceptance, this can be considered a positive since there are no cyto-toxic effects that would alter the tooth structure. For someone with concerns when whitening and how things they consume in their daily lives affect

them, these benefits of bromelain would appeal to them. Although whitening with chemical agents, such as hydrogen peroxide-based gels and dentifrices, does not pose any issues for some individuals, bromelain could be an alternative for those who desire a more therapeutic agent.⁸

4. ANALYZE THE COMPARISONS BETWEEN HYDROGEN PEROXIDE AND BROMELAIN

Hydrogen peroxide is most commonly used in in-office bleaching, but has shown to negatively affect the oral tissues.¹² Despite the favorable whitening effects, adverse effects have been experienced such as soft tissue alterations and gingival irritation. The bleaching process is technique sensitive, which means experienced dental professionals cannot always prevent bleaching agents from occasionally adhering to the gingiva.¹² When the bleaching agents adhere, it can create white, opaque changes to the gingiva and a burning pain sensation.¹² These changes can resolve in several hours, but nonetheless affect the patient and create discomfort.

Conversely, bromelain has not shown to have negative side effects to the oral tissues, and instead has an anti-inflammatory reaction when administered orally.¹⁵ To test the effects of Bromelain on oral tissues, a study conducted in East Africa used rats with experimental burns.¹⁵ Burns are characterized by a formation of burned and traumatized tissue. The burned and traumatized tissue can be susceptible to infection, contamination, and bacterial growth. Rapid debridement can reduce morbidity and lessen the risk of infection.¹⁵ There is non-selective surgical debridement and chemical debridement, which only removes burned skin. Since surgical excision can expose the patient to a risk of pain and significant bleeding, enzymatic debridement has been experimented, yielding positive results. A bromelain topical (35% lipid base) was applied to the rats with experimental burns to test the success with complete debridement. Complete debridement was achieved in 2 days and there were no side effects or damage to the adjacent burned tissue.¹⁵ Additional human studies have shown Bromelain combined with animal proteases can have therapeutic effects on the oral tissues and even limit biofilm and gingivitis.¹³

Since bromelain is a group of enzymes, it can be used as an active ingredient with a whitening effect. To test the whitening and tooth structure effects of Bromelain compared to hydrogen peroxide, one study used standard enamel dentin discs from fifty bovine teeth and submerged them in a coffee solution for a week. Bromelain was applied to the coffee-stained teeth four separate times for 15 minutes each over a seven-day period.⁹ The results determined Bromelain had similar teeth whitening effects when compared to the peroxide whitening gel.⁹ The optimum pH level for Bromelain is 7 and it does not affect the whitening process, nor does it alter the tooth enamel, microhardness, or tooth structure. Hydrogen peroxide has a pH level of 4.5 and the effects on tooth enamel, microhardness, and tooth structure are opposite compared to Bromelain.

A separate study was conducted by the department of restorative dentistry at the Sao Paulo State University, to test different pH levels of 35% hydrogen peroxide to evaluate the effects of whitening and the effects on the tooth structure. Ninety enamel-dentin bovine teeth were obtained and then divided into two groups. One group of teeth was submerged in a staining broth for fourteen days and the other group was not stained and placed in distilled water. After twenty-four hours, each group was further divided into three subgroups. Each subgroup was whitened by different pH levels of hydrogen peroxide of 5, 7, and 8.4 for half an hour.¹³ The color was evaluated seven days after whitening and compared to the baseline. Microhardness results were measured immediately, then at twenty-four hours, and again in one month in comparison to the baseline.¹³ The results determined the pH of hydrogen peroxide did not affect the whitening process, but did affect the microhardness of enamel. The microhardness decreased at every measurement interval and none of the subgroups returned to their initial values.¹³

Bromelain as an active ingredient is used in dentifrices for the whitening effects. Contraindications for Bromelain-containing dentifrices are present if the patient is allergic to pineapples since Bromelain is derived from the stems of pineapples.¹⁴ People who are allergic to latex, fennel, grass pollen, celery, and carrots should also use Bromelain with caution, as it may elicit an allergic reaction similar to those with a pineapple allergy.¹⁴ Bromelain is a natural, accessible, and cost-effective product available in the market. The applications of hydrogen peroxide gels can be in various forms, such as strips or trays, which are applied directly on the teeth and both are set for a specific amount of time.⁹

CONCLUSION

Multiple studies conclude natural tooth whitening agents allow a patient to achieve a smile several shades lighter without the enamel and tissue damage and the side effects which tend to accompany hydrogen peroxide.^{2,4} While peroxide whitening is time efficient and a relatively low-cost procedure, the goal of a whiter smile may come at a greater cost. Whitening teeth using hydrogen peroxide has been shown to be unpredictable, yielding unfavorable side effects such as hypersensitivity. A study combining the natural effects of bromelain with the powerful effects of hydrogen peroxide are promising but limited.² Bromelain based whiteners provide multiple therapeutic effects that not only work in the oral cavity but throughout the rest of the body as well.⁴ Despite the whitening effects of hydrogen peroxide, patients may experience adverse effects to the bleaching agent and have soft tissue alterations with gingival inflammation. Compared to hydrogen peroxide, Bromelain does not cause gingival irritation or enamel alterations and presents visible whitening effects.¹⁵ Peroxide in-office and at-home bleaching have chemical bleaching agents and are generally higher-priced, whereas Bromelain usage in dentifrice is natural and cost-effective.¹⁵ In conclusion, bromelain's natural components and low levels of cytotoxicity demonstrate how bromelain is a bleaching alternative used in various media without the side effects which may be experienced by patients using chemical bleaching agents containing peroxide.

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