# Inhibitory Effect of Single-Dose Herbal Betel Toothpaste on *Streptococcus mutans*

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**Abstract.** Dental caries remains one of the most prevalent oral diseases in Indonesia and globally, strongly associated with the activity of Streptococcus mutans, a bacterium capable of acid production, acid tolerance, and biofilm formation. Traditional Indonesian betel-chewing ingredients—areca nut, betel leaf, and gambier—contain bioactive compounds such as tannins, flavonoids, phenols, alkaloids, and catechins with recognized antibacterial activity. This laboratory experimental study aimed to evaluate the inhibitory effect of a 25% herbal toothpaste formulated from these ingredients compared with conventional toothpaste against S. mutans. A post-test only control group design was employed with two groups and five replications each. Antibacterial activity was assessed using the agar well diffusion method. Data were analyzed using the Shapiro–Wilk normality test followed by an independent t-test. Results showed that the 25% herbal toothpaste produced significantly larger inhibition zones than conventional toothpaste ($p < 0.05$). These findings indicate that the combined herbal formulation demonstrates strong antibacterial potential and may serve as a culturally relevant, locally sourced alternative for dental caries prevention.

**Keywords:** *dental caries, herbal toothpaste, Streptococcus mutans*.

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## A. Introduction

Dental caries remains one of the most prevalent chronic diseases affecting humans and continues to represent a major global public health challenge, particularly in developing countries such as Indonesia.[1] The disease is characterized by progressive destruction of dental hard tissues due to a prolonged imbalance between demineralization and remineralization processes occurring at the enamel surface. This imbalance is driven primarily by acid production from bacterial fermentation of dietary carbohydrates. When fermentable sugars such as sucrose are metabolized by oral microorganisms, organic acids—especially lactic acid—are produced, leading to a reduction in plaque pH. When the pH drops below the critical threshold of approximately 5.5, hydroxyapatite crystals in enamel begin to dissolve, causing mineral loss. Repeated acid exposure without sufficient remineralization results in structural weakening of enamel, formation of subsurface lesions, and eventually cavitation.[2]

Modern understanding describes dental caries as a biofilm-mediated ecological disease rather than a simple infection caused by a single pathogen. In a healthy state, the oral microbiome exists in a balanced ecosystem where commensal bacteria coexist with host defenses such as saliva flow, buffering capacity, and immune responses. However, frequent sugar intake alters the ecological balance by selecting for acidogenic and aciduric microorganisms that thrive in low pH conditions. This ecological shift, known as dysbiosis, favors pathogenic species capable of sustaining acidic environments and suppressing less acid-tolerant bacteria. Among these organisms, *Streptococcus mutans* is widely recognized as a primary etiological agent in the initiation of dental caries.[3]

*S. mutans* possesses several virulence characteristics that enhance its cariogenic potential. The bacterium is highly acidogenic, efficiently converting carbohydrates into organic acids. It is also aciduric, meaning it can survive and remain metabolically active in acidic environments that inhibit other oral microorganisms. Furthermore, *S. mutans* synthesizes extracellular polysaccharides through the glucosyltransferase enzyme system, which converts sucrose into sticky glucans.[3] These glucans form the structural framework of dental plaque biofilm, enhancing bacterial adhesion to tooth surfaces and stabilizing the extracellular polymeric substance matrix.. The biofilm matrix acts as a diffusion barrier, limiting penetration of saliva buffers and antimicrobial agents while trapping acids close to enamel surfaces. As a result, localized acidic microenvironments persist, accelerating enamel demineralization and promoting lesion progression.[5]

The impact of dental caries extends beyond localized tooth damage. Untreated caries can cause pain, infection, tooth loss, and functional limitations in chewing and speaking. In children, oral discomfort is associated with reduced concentration, school absenteeism, sleep disturbances, and impaired growth. From a socioeconomic perspective, treatment of advanced caries requires significant healthcare resources, emphasizing the importance of preventive strategies. Mechanical plaque removal through toothbrushing, combined with chemical suppression of bacterial activity via toothpaste, remains a cornerstone of caries prevention.[6]

Conventional toothpaste formulations typically include fluoride and synthetic antimicrobial agents.[7] Fluoride enhances enamel remineralization and inhibits bacterial metabolism; however, concerns exist regarding long-term exposure to chemical antibacterial substances that may contribute to microbial resistance or mucosal irritation.[8] Consequently, there has been growing interest in herbal-based oral care products that utilize plant-derived bioactive compounds. Herbal preparations are often perceived as safer, culturally acceptable, and environmentally sustainable.[9]

Indonesia has a rich ethnomedicinal heritage, including the traditional practice of betel chewing, locally known as *nginang*.[10] This practice involves the use of areca nut (*Areca catechu*), betel leaf (*Piper betle*), and gambier (*Uncaria gambir*).[11] Scientific investigations have identified numerous phytochemicals within these plants, including tannins, flavonoids, phenolic compounds, alkaloids, and catechins with demonstrated antibacterial properties.[12] Areca nut exhibits antibiofilm activity, betel leaf contains phenolic constituents capable of disrupting bacterial cell membranes, and gambier is rich in catechins known to inhibit bacterial enzymes, including glucosyltransferase. The combination of these ingredients may produce synergistic antibacterial effects that are potentially more effective than single-agent formulations.[13] Despite their traditional use, scientific evaluation of combined herbal formulations in toothpaste remains limited, providing the basis for this study to assess the inhibitory effect of a 25% herbal betel toothpaste against *Streptococcus mutans*.[14].

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## B. Method

This study was conducted as an experimental laboratory investigation using a post-test only control group design to compare the antibacterial activity of a 25% herbal betel toothpaste formulation with that of conventional toothpaste against *Streptococcus mutans*. The research was performed in a microbiology laboratory under sterile conditions to ensure reliability and reproducibility of results. The test organism used was *S. mutans* ATCC 25175, a standardized reference strain widely used in antimicrobial studies related to dental caries.

The herbal toothpaste formulation was prepared using extracts derived from areca nut, betel leaf, and gambier. Plant materials underwent maceration to preserve thermolabile phytochemicals, followed by filtration and evaporation to obtain concentrated extracts. These extracts were incorporated into a toothpaste base designed to maintain homogeneity, stability, and suitable viscosity, achieving a final active concentration of 25%. The formulation process emphasized preservation of phytochemical integrity and diffusion capacity during antibacterial testing.

Antibacterial activity was evaluated using the agar well diffusion method, a standard technique for assessing inhibitory potential of semi-solid preparations. A bacterial suspension equivalent to 0.5 McFarland turbidity standard was prepared to ensure uniform cell density. The suspension was evenly spread onto Mueller–Hinton Agar plates to create a confluent bacterial lawn. Wells with a diameter of 6 mm were made in the agar medium, and 50 µL of each toothpaste sample was introduced into the wells. Plates were incubated at 37°C for 24 hours to allow bacterial growth and interaction with test substances. After incubation, inhibition zone diameters were measured using a digital caliper with millimeter precision. Each group was tested in five replications to enhance statistical reliability.

Data obtained were analyzed using the Shapiro–Wilk test to assess normality of distribution. An independent t-test was then applied to compare inhibition zone diameters between groups, with statistical significance set at $p < 0{,}05$.

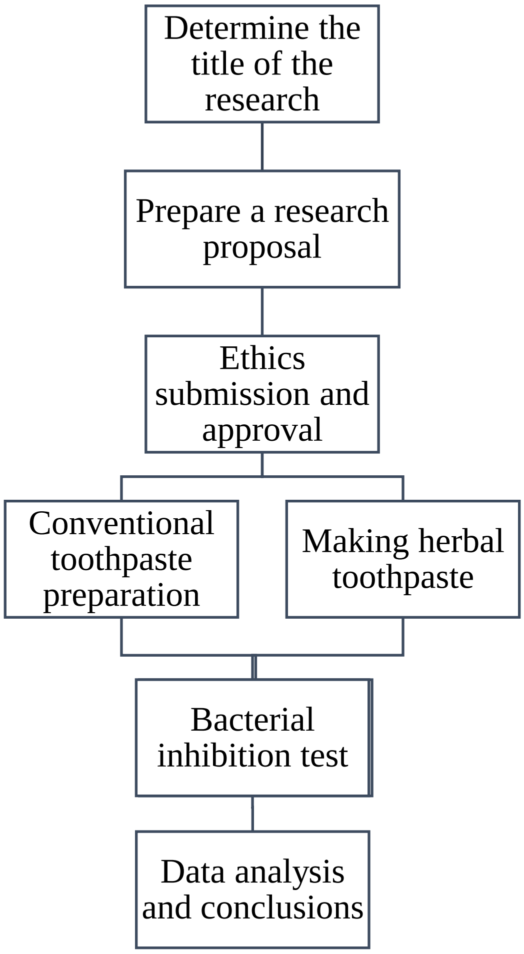


**Figure 1.** Research Flowchart

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The calculation of the inhibition zone is based on the classification of bacterial inhibitory strength as strong or weak. According to David and Stout, supported by the studies of Satrianawaty, Sumarno, and Prabowo, the classification of the inhibition zones is as follows:

**Table 1.** Inhibition Zone Classification

| Bacterial Inhibition Zone | Category |
|---|---|
| < 5 mm | Weak |
| 5-10 mm | Moderate |
| 10-20 mm | Strong |
| > 20 mm | Very Strong |

## C. Result and Discussion

This This study compared the inhibitory effect of 25% herbal betel toothpaste (F1) with conventional toothpaste against Streptococcus mutans. The test was conducted using the well diffusion agar method, and the diameter of the inhibition zones was measured after 24 hours of incubation at 37°C. The results of the inhibition zone measurements are presented in Table 2.

**Table 2.** Mean Diameter of Inhibition Zones for 25% Herbal Toothpaste and Conventional Toothpaste

| Group | Mean ± SD (mm) | Inhibitory Category |
|---|---|---|
| 25% herbal toothpaste | 20,90 ± 0,48 | Very Strong |
| Conventional toothpaste | 16,64 ± 0,35 | Strong |

The herbal toothpaste formulation demonstrated a mean inhibition zone diameter of 20.90 ± 0.48 mm, whereas conventional toothpaste produced a mean inhibition zone of 16.64 ± 0.35 mm. Based on inhibition zone classification, the herbal formulation was categorized as very strong, while conventional toothpaste was categorized as strong. Statistical analysis revealed a significant difference between groups, indicating superior antibacterial activity of the herbal formulation.

The observed inhibitory effect can be explained by the phytochemical composition of the herbal ingredients. Tannins present in areca nut exert antibacterial effects through protein precipitation and membrane disruption, leading to leakage of intracellular components. Flavonoids and phenolic compounds in betel leaves interfere with nucleic acid synthesis and membrane integrity, disrupting metabolic pathways essential for bacterial survival. Catechins from gambier strongly inhibit glucosyltransferase activity, preventing extracellular glucan synthesis and weakening biofilm structure.[16]

The extracellular polymeric substance matrix produced by *S. mutans* plays a crucial role in cariogenicity by enhancing bacterial adhesion and protecting colonies from environmental stress. Interference with glucan synthesis therefore directly affects biofilm stability. The synergistic action of multiple phytochemicals in the herbal formulation allows simultaneous targeting of bacterial cell structures, metabolic pathways, and biofilm formation mechanisms, resulting in enhanced antibacterial effectiveness compared with single synthetic agents.[17]

Optimal activity at a 25% concentration may be related to diffusion dynamics in agar media. Excessively high extract concentrations can increase viscosity and reduce compound mobility, limiting effective diffusion.[18]This phenomenon explains why intermediate concentrations may yield stronger observable inhibition zones.[19]

From a clinical and public health perspective, herbal toothpaste derived from traditional ingredients offers advantages including cultural acceptance, local availability, and sustainability. Integrating traditional knowledge with scientific validation may improve community participation in preventive oral health practices.[20]

**Analysis and Discussion**

The pathogenesis of dental caries is currently understood as a biofilm-mediated ecological disease rather than a simple infection caused by a single organism. Within the oral cavity, microbial communities exist in a balanced state, but frequent sugar exposure leads to an ecological shift favoring acidogenic and aciduric bacteria such as Streptococcus mutans. This ecological plaque hypothesis explains how environmental changes select for pathogenic species that dominate cariogenic biofilms.[1] The ability of S. mutans to tolerate acidic conditions provides a competitive advantage, enabling it to outgrow less acid-resistant commensals. This shift results in sustained low pH at the tooth–biofilm interface, driving progressive enamel demineralization.[21]

The extracellular polymeric substance (EPS) matrix produced by S. mutans plays a central role in cariogenicity. The glucosyltransferase enzyme converts sucrose into sticky glucans that form the structural scaffold of dental plaque. This matrix enhances bacterial adhesion, mechanical stability, and resistance to antimicrobial agents. It also traps acids within the biofilm, intensifying enamel mineral loss. Herbal compounds capable of interfering with EPS synthesis therefore represent strategic agents for caries prevention. Catechins from gambier have been reported to inhibit glucosyltransferase activity, thereby limiting glucan formation and weakening biofilm integrity. This mechanism explains why the herbal formulation demonstrated strong inhibitory zones.[22]

At the cellular level, tannins in areca nut exert antimicrobial effects through protein precipitation and enzyme inactivation. Tannins bind to bacterial cell wall proteins, disrupting membrane permeability and leading to leakage of cellular contents. Flavonoids and phenolic compounds from betel leaves contribute by interacting with lipid bilayers, altering membrane fluidity, and interfering with electron transport chains. These disruptions impair ATP synthesis and metabolic processes essential for bacterial survival. The combined action of these compounds targets multiple cellular pathways simultaneously, increasing antibacterial effectiveness and reducing the likelihood of resistance development.[23]

The concept of synergistic phytochemical action is particularly relevant in herbal formulations. While synthetic antimicrobials often target a single pathway, plant-derived compounds act on diverse molecular sites, producing additive or synergistic effects. This multi-target mechanism aligns with current antimicrobial strategies aimed at minimizing resistance. In addition, herbal agents may exert anti-inflammatory and antioxidant effects that support oral tissue health, offering broader benefits beyond antibacterial activity.[24]

The observed optimal activity at a 25% concentration suggests a balance between active compound availability and diffusion capacity. Antimicrobial effectiveness in agar diffusion assays depends not only on concentration but also on solubility, stability, and mobility within the medium. At excessively high concentrations, increased viscosity and compound aggregation may limit diffusion, reducing apparent inhibition zones. This diffusion-related phenomenon explains why intermediate concentrations can produce stronger measurable activity.[25]

Comparatively, conventional toothpaste formulations rely on fluoride and chemical antibacterial agents. Fluoride acts primarily by enhancing enamel remineralization and inhibiting bacterial metabolism, but it does not directly disrupt biofilm matrix structure. Herbal phytochemicals that interfere with glucan synthesis may therefore complement fluoride’s mechanism by weakening biofilm architecture. Such complementary action highlights the potential role of herbal toothpaste as either an alternative or adjunctive preventive approach.[26]

From a safety perspective, herbal products derived from traditional use may offer favorable tolerability profiles when appropriately formulated. However, standardization of extract concentration and quality control remain essential to ensure consistent efficacy. The development of herbal toothpaste also supports sustainability and local resource utilization, aligning with culturally based healthcare approaches. In addition to its role in glucan synthesis, S. mutans demonstrates remarkable metabolic adaptability that further strengthens its cariogenic potential. The bacterium possesses a highly efficient phosphoenolpyruvate phosphotransferase system that allows rapid uptake of various carbohydrates. Once internalized, these sugars undergo glycolysis, producing pyruvate that is subsequently converted into lactic acid via lactate dehydrogenase. This continuous acid production contributes to prolonged acidification within the biofilm environment. Moreover, S. mutans can synthesize and store intracellular polysaccharides, enabling acid production even between meals.[27]

The persistence of low pH at the tooth–biofilm interface is a critical factor in enamel demineralization. Hydroxyapatite crystals dissolve when exposed to acidic conditions below the critical pH threshold. The EPS matrix limits diffusion of buffering agents from saliva, such as bicarbonate ions, into deeper biofilm layers. As a result, acid clearance is delayed, and localized acidic niches are maintained for extended durations.[28]

Herbal phytochemicals may also influence bacterial quorum-sensing systems. Disruption of membrane integrity by phenolic compounds and flavonoids can interfere with signaling molecule transport, impairing coordinated virulence expression. This interference reduces expression of genes involved in adhesion, glucan production, and stress tolerance. Oxidative stress further influences bacterial survival. Phenolic compounds can generate oxidative imbalance within bacterial cells, disrupting homeostasis. Their antioxidant properties may simultaneously reduce inflammatory responses in host tissues.[29]

Flavonoids and catechins have documented anti-inflammatory effects mediated through inhibition of pro-inflammatory cytokines and signaling pathways. These properties may indirectly support oral health by reducing gingival inflammation associated with plaque accumulation. Comparisons with synthetic antimicrobials highlight advantages of multi-compound herbal systems. Single-target agents may disrupt microbiome balance, whereas phytochemical mixtures exert broader modulatory effects aligned with ecological caries management.[17]

Future investigations should include multispecies biofilm models and clinical trials to confirm effectiveness. Standardization and toxicological evaluation are necessary to ensure safety for long-term use.[14] Taken together, these mechanistic insights reinforce the rationale for herbal toothpaste as a scientifically plausible preventive strategy targeting biofilm structure, bacterial metabolism, and host inflammatory responses.[30].

## D. Conclusion

The present findings demonstrate that a 25% herbal toothpaste formulated from areca nut, betel leaf, and gambier exhibits strong inhibitory activity against Streptococcus mutans. The antibacterial effect is attributed to synergistic phytochemical interactions that disrupt bacterial cell structures, inhibit metabolic pathways, and interfere with biofilm formation. These results support the potential of herbal betel toothpaste as a culturally rooted, scientifically supported alternative for caries prevention. Continued research and product development may contribute to more sustainable and accessible oral healthcare solutions.

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