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Literature Review

Potential of Uncaria Gambir Extract Against Glucosyltransferase Enzyme: A Narrative Review

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KEYWORDS

Enzyme, glucosyltransferase, Uncaria gambir

ABSTRACT

Introduction: Glucosyltransferase (Gtf) enzyme is an enzyme produced by Streptococcus mutans (S. mutans) bacteria that plays an important role in the process of attachment and virulence of bacterial colonies on the tooth surface. Gambier plants (Uncaria gambir (Roxb.)) have the main content of catechins and tannins that can prevent the formation of extracellular glucans that bind S. mutans bacteria on the tooth surface. The purpose of this narrative review is to determine the potential of gambir extract on Gtf enzymes produced by S. mutans. This article is a narrative review, with databases sourced from PubMed, Wiley Online Library, Cochrane, and Science Direct.
Review: A total of 251 articles were identified, and 6 journals were filtered that met the inclusion and exclusion criteria for analysis. Catechins and tannins contained in gambir have inhibitory action against Gtfs, so that the activity of EPS synthesis by S. mutans is blocked. Inhibition of Gtf by catechins does not interfere with the existence of microbes in the oral environment. Therefore, the ability of catechins extracted from gambir plants is able to inhibit the Gtf enzyme selectively, and is developed as a material that can prevent the formation of dental caries.
Conclusion: Gambier extract has the potential to inhibit the formation of Gtf enzymes.

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INTRODUCTION

Indonesia is rich in diverse flora, many of which have been traditionally utilized as medicinal plants. In recent years, herbal materials have been increasingly developed by researchers and practitioners for the prevention, treatment, and maintenance of overall health. One Indonesian plant that has been extensively studied is gambir *(Uncaria gambir* (Roxb.)*)*.[1] As a plant that grows abundantly in Indonesia, gambir has been widely used in both traditional and modern medicine to treat various conditions, including oral and dental health.[2]

Oral health problems are highly prevalent among the Indonesian population, with dental caries being one of the most significant concerns. Dental caries is a disease of the hard dental tissues—enamel, dentin, and cementum—caused by the activity of microorganisms in fermentable carbohydrates. The primary etiological agent of dental caries is *Streptococcus mutans (S. mutans)*.[3]

S. mutans is a Gram-positive bacterial species in the oral cavity and is a major contributor to tooth decay.[4] It can form dental plaque by developing a robust biofilm on the tooth surface and rapidly metabolizing various carbohydrates derived from the host's diet. Biofilm formation enables *S. mutans* to survive in the oral environment and protects against external threats such as disinfectants and antibiotics.[5] This biofilm formation is a complex process involving protein–bacteria interactions and is strongly influenced by nutrient availability.[6]

The cariogenic potential of *S. mutans* is attributed to its ability to synthesize large amounts of extracellular glucan polymers from sucrose, facilitating colonization of tooth surfaces and the formation of an in situ extracellular polymeric matrix.[6] *S. mutans* metabolizes carbohydrates, resulting in an acidic environment within the oral cavity. A key enzyme involved in this process is Glucosyltransferase (Gtf), which plays a critical role in bacterial adhesion and virulence on tooth surfaces.[7] Gtf enzymes also catalyze the conversion of sucrose into fructose and glucan. An acidic environment continuously produced in the oral cavity can cause demineralization and dental caries.[8]

Gambir *(Uncaria gambir* (Roxb.)*)* contains major bioactive components, namely catechins and tannins, and exhibits antibacterial properties, particularly against Gram-positive bacteria.[9] Studies by Azmi et al.[10] have reported that catechins are widely utilized in maintaining oral health, including the management of dental caries, periodontal disease, pulp pathology, and oral cancer.[10] Previous research has demonstrated that catechins extracted from green tea are capable of inhibiting Gtf enzyme activity.[11] Other studies have also shown that gambir extract can inhibit the growth of *Streptococcus mutans* due to its active compounds, such as catechins and tannins.[12] Yauri and Mirawati[13] reported that rinsing with a decoction of gambir effectively reduces the plaque index.[13] This effect is attributed to gambir's ability to inhibit the formation of insoluble glucans from sucrose by glucosyltransferase enzymes produced by S. mutans.[12]

The catechin content in gambir has been shown to reduce dental plaque formation. This reduction is associated with the ability of these active compounds to inhibit glucosyltransferase enzymes. These enzymes have emerged as novel molecular therapeutic targets, as their inhibition can prevent the development of dental caries without disrupting the normal oral microbiota. Therefore, this narrative review aims to evaluate

the potential of gambir extract in inhibiting Glucosyltransferase enzymes.

REVIEW

This article presents a narrative literature review conducted using a systematic literature review method. The stages carried out were: determining the topic to be reviewed, searching and identifying literature, selecting relevant sources, evaluating and analyzing articles, synthesizing the analyzed articles, and organizing and writing the narrative review.

The articles included in this review focus on the potential of gambier extract *(Uncaria gambir* (Roxb.)) against glucosyltransferase enzymes. The selected articles were original research articles and systematic reviews. The data search was conducted systematically and in a structured manner to identify relevant articles on the predetermined topic, namely the potential of gambier extract on glucosyltransferase enzymes.

The literature search was performed using several major scientific databases covering health and related scientific fields, such as pharmacy, agriculture, chemistry, and others. The databases used include PubMed, Wiley Online Library, Cochrane, and ScienceDirect. Keywords were formulated based on the chosen topic and applied in both English and Indonesian. The keywords were: ekstrak gambir/gambier [All Fields] OR Uncaria gambir extract [MeSH Terms] AND enzim glukosiltransferase [All Fields] OR glucosyltransferase enzyme [MeSH Terms], potensi gambir [MeSH Terms] OR gambier potential [All Fields] AND biofilm [MeSH Terms] OR [All Fields].

The inclusion criteria for this review were: articles published between 2014 and 2024, written in English or Indonesian, relevant to the predetermined topic, and consisting of original articles and systematic reviews. The exclusion criteria were: articles not available in full text and articles not relevant to the selected topic.

Data extraction was conducted using a standardized form specifically designed for this narrative review. The standardized form included information on the authors, year of publication, study design, population, details of the intervention, outcome measurement methods (specifically, Glucosyltransferase enzyme activity), research findings, and conclusions. Data synthesis was performed qualitatively by integrating the results from the studies included in this review. The extracted data were analyzed to identify key themes and relationships among the variables under consideration. The analysis results were then organized into a narrative format explaining the potential of gambier extract against glucosyltransferase enzymes.

The literature search yielded a total of 251 articles identified from national and international databases obtained through PubMed, Wiley Online Library, Cochrane, and ScienceDirect, using the predetermined keywords aligned with the narrative review topic. After screening by title and abstract, 97 articles remained. A total of 154 articles were excluded due to irrelevance to the search topic. Of these, 14 articles were fully accessible and met the title and research objectives. Eighty-three articles were excluded because they did not match the narrative review topic. Finally, six articles were assessed for eligibility and included in the review.

Table 1. Results of Literature Search

Type of Article	Risk of Bias	Study Sample	Type of Intervention	Study Duration	Reference
Original article	Low risk	Premolar teeth	Gambier toothpaste	30 days	Dewi et al., 2016
Original article	Low risk	Male Wistar rats	Gambier extract	60 days	Dewi et al., 2017
Original article	Low risk	Streptococcus mutans	Gambier extract	30 days	Herdiana et al., 2020
Systematic review	Low risk	Streptococcus mutans	Gambier extract	7 days	Zhang et al., 2021
Original article	Low risk	Dental plaque	Gambier extract	30 days	Dharsono et al., 2022
Original article	Low risk	Human oral cavity	Gambier candy	14 days	Dewi et al., 2023

Based on a review of the literature, studies investigating the effects and mechanisms of gambir extract (*Uncaria gambir*) on glucosyltransferase enzymes—one of the key contributors to dental caries—remain limited. Dental caries is a disease affecting the hard tissues of the teeth, namely enamel, dentin, and cementum. It is multifactorial in nature and results from bacterial activity that ferments carbohydrates into acids on the tooth surface. Caries begins with the demineralization of enamel and progresses to cavitation due to ongoing bacterial activity.[3]

Streptococcus mutans is a Gram-positive bacterium capable of colonization and fermentation of carbohydrates and sugars into lactic acid. This process leads to an acidic oral environment, which promotes tooth demineralization.[4] Continuous demineralization ultimately results in the formation of dental caries. This bacterium produces glucosyltransferase (Gtf) enzymes, which play a crucial role in the etiology and pathogenesis of dental caries.[14] Gtf enzymes facilitate biofilm formation and enhance the colonization of cariogenic bacteria by producing extracellular polysaccharides (EPS), a major virulence factor in the cariogenic process.[8] These findings have encouraged researchers to explore Gtf enzymes as potential therapeutic targets for caries prevention.

Uncaria gambir, commonly known as gambir, is a plant that grows abundantly in Indonesia and has been widely utilized for health purposes. Its effectiveness in addressing various oral health conditions has been investigated. The primary bioactive compounds in gambir are catechins and tannins, which are capable of inhibiting the formation of extracellular glucans that facilitate the adhesion of S. mutans to tooth surfaces and the development of biofilm layers.[15] Previous studies have reported that catechins derived from Uncaria gambir exhibit inhibitory activity against enzymes involved in dental caries.[16] Catechins have also been shown to inhibit biofilm formation and glucosyltransferase activity in *Streptococcus gordonii*.[17]

A 2017 study conducted on Wistar rats inoculated with *S. mutans* demonstrated a reduction in caries lesions on occlusal surfaces.[18] This effect is attributed to the ability of catechins to exert bactericidal activity against *S. mutans* by disrupting the peptidoglycan layer of the bacterial cell wall.[15,18] A more recent study in 2023 reported that gambir-based lozenges reduced bacterial colony counts and dental plaque formation.[19] This effect is associated with gambir's ability to inhibit Gtf enzymes and prevent biofilm formation.

Fundamentally, *S. mutans* produces three types of glucosyltransferase enzymes: GtfB, GtfC, and GtfD.[20] The activity of these enzymes is mediated through catalytic functions. GtfB is responsible for synthesizing insoluble glucans, which facilitate bacterial adhesion and

accumulation on tooth surfaces. These insoluble glucans induce biochemical and structural changes in the biofilm matrix, thereby increasing microbial resistance to external disturbances.[4] Soluble glucans, on the other hand, can be readily metabolized and serve as an energy reserve when fermentable carbohydrates are depleted in the oral cavity.[20] This process contributes to a decrease in plaque pH. In addition to enhancing adhesion to tooth surfaces, GtfB also exhibits cohesive properties among microorganisms within the biofilm.[4,20]

The inhibition of Gtfs by catechins can prevent the synthesis of EPS by *S. mutans.*[20] Notably, this inhibition does not disrupt the presence of other microbial species within the oral environment. Therefore, the selective inhibitory activity of catechins on these enzymes continues to be explored as a promising strategy for preventing dental caries. Other studies have reported that catechins and tannins are capable of modulating GtfB gene expression, reducing GtfB enzyme activity, and inhibiting Gtf secretion.[21] Additionally, tannins present in gambir have demonstrated the ability to inhibit glucosyltransferase formation, thereby preventing biofilm development.[22]

Further research on the potential of gambir extract in targeting Glucosyltransferase enzymes is essential. This is particularly important given its selective inhibitory effect on Glucosyltransferase B, which offers a promising approach for preventing dental caries without disrupting the ecological balance of the normal oral microbiota.

CONCLUSION

Based on the narrative review conducted, it can be concluded that gambier extract (*Uncaria gambir*) has the potential to inhibit glucosyltransferase enzymes.

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