Scientific Foundation SPIROSKI, Skopje, Republic of North Macedonia
South East European Journal of Immunology. 2024 Mar 11; 7:50-55.
https://doi.org/10.3889/seejim.2024.6067
eISSN: 1857-9388
Category: *Review article*
Section: *Clinical Immunology*

OPEN ACCESS

The Antioxidant and Antibacterial Effects of Gambier Catechin (*Uncaria gambir* Roxb) in Streptococcal Gingivitis: A Review

Refa Rahmaddiansyah[1]*, Muhammad Zidan Amriza[1], Rauza Sukma Rita[2]

[1]*Medical Doctor Study Program, Department of Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia;* [2]*Department of Biochemistry, Faculty of Medicine, Universitas Andalas, Padang, Indonesia*

Edited by: Slavica Hristomanova-Mitkovska
Citation: Rahmaddiansyah R, Amriza MZ, Rita RS. The Antioxidant and Antibacterial Effects of Gambier Catechin (*Uncaria gambir* Roxb) in Streptococcal Gingivitis: A Review. SSEE J Immunol. 2024 Mar 11; 7:50-55. https://doi.org/10.3889/seejim.2024.6067
Keywords: Gambier; Catechin; Streptococcal gingivitis; Antibacterial; Antioxidant
***Correspondence:** Refa Rahmaddiansyah, Department of Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia. E-mail: refarahmad@gmail.com
Received: 23-Dec-2023
Revised: 24-Feb-2024
Accepted: 01-Mar-2024
Copyright: © 2024 Refa Rahmaddiansyah, Muhammad Zidan Amriza, Rauza Sukma Rita
Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist
Open Access: This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

Abstract

BACKGROUND: Oral health is very important for general health and well-being. Oral diseases such as caries and periodontitis are common throughout the world. Periodontal is the main cause of tooth loss in adults. This disorder begins with gingivitis (swelling of the gums due to plaque), which, if left untreated, will result in periodontitis or infection that can destroy the teeth and surrounding tissue. The current management of this disease is to give analgesia and antibiotics, but early prevention and treatment are needed, one of them by using toothpaste.

AIMS: This study aims to assess the effectiveness of Gambier catechin as a preventive approach for streptococcal gingivitis.

METHODS: The research design used is a literature review study conducted from preclinical and clinical studies extracted from indexed international journals. Studies from 2012 to 2022 in English and related to the keywords are reviewed and synthesized.

RESULTS: The pathophysiology of the majority of gingivitis is related to inadequate cleaning of the oral cavity, which leads to the accumulation of plaque and bacteria. Catechins from Gambier also have a stronger capacity as antioxidants. Preclinical studies stated that Gambier has a strong potential for antioxidants. Catechins have stronger antioxidant capabilities than vitamins C and E. Catechins from Gambier also have a stronger capacity as antioxidants than vitamin E. Gambier catechin contains polyphenolic compounds that have antibacterial activity so that they can inhibit the formation of dental plaque. The catechin compound as an antibacterial has two properties, namely being able to inhibit (bacteriostatic) and kill (bacteria) the growth of bacteria.

CONCLUSION: Gambier catechin has antioxidant and antibacterial effects and has potential for treating streptococcal gingivitis.

Introduction

Oral health, as defined by the Fédération Dentaire Internationale (FDI), encompasses various aspects, including speech, smile, smell, touch, and overall well-being, but it is not explicitly addressed in Sustainable Development Goal 3 [1]. Despite its importance for general health, oral health care remains a low priority in many countries, leading to widespread issues such as caries and periodontitis, with inadequate financial investment for prevention and care [2]. The untreated global burden of dental caries in both primary and permanent teeth has remained stable over the past three decades [3]. Effective chewing function (mastication) facilitates food intake, contributing to maintaining quality of life. Research indicates that periodontal inflammation is linked to various systemic conditions, including cardiovascular disease, lung disease, metabolic syndrome, psoriasis, digestive issues, and neuropsychiatric disorders [4].

The results of Riskesdas 2018 state that the largest proportion of dental problems in Indonesia is tooth decay (45.3%). Meanwhile, the majority of oral health problems experienced by the Indonesian population are swollen gums and/or boils (abscess) by 14% [5]. According to the FDI World Dental Federation, the most common dental and oral problems are caries, cancer, and gum or periodontal disorders. Periodontal is the main cause of tooth loss in adults. This disorder begins with gingivitis (swelling of the gums due to plaque), which, if left untreated, will result in periodontitis or infection that can destroy the teeth and surrounding tissue. It can have serious consequences in daily life, such as difficulty chewing, speaking, and losing teeth [2], [5].

Periodontal disease is an infection in which specific bacteria play an important role. Specific bacterial infections of gingiva, which are subgroups of non-plaque-induced gingival lesions, may be caused by *Neisseria gonorrhea*, *Treponema pallidum*, *Streptococcal* species, and other organisms [6]. Acute streptococcal gingivitis has a microbiological origin (*Streptococcal* species) and clinical features that are specific and characterized by bright-red swollen gingiva associated with pain, fever, malaise,

and submandibular lymphadenitis. It has been given little attention in the generational literature in general because this disease is rarely seen [7]. Similarly, there are numerous significant implications, including the potential for systemic secondary infections such as septicemia, meningitis, pericarditis, rheumatic fever, and pneumonia [8].

Current management involves analgesia and antibiotics for the causative bacteria, with surgical therapy for severe cases. Microbiological evaluation confirms the disease [9], but early diagnosis and intervention, including antiseptic toothpaste, can improve the prognosis.

Gambier is an astringent extract prepared from the leaves and stems of *Uncaria gambir*, a climber native to Sumatra and Borneo. Gambier is known as a source of catechins whose content exceeds that of other plants, such as tea. Green tea catechine levels vary from 20% to 30%, while gambier catechine levels can reach 67.55–72.02% [10]. Exploring the advantages of Gambier involves utilizing Gambier as a means of improving various outcomes. Gambier catechins have an inhibitory effect on *Streptococcus mutans* bacteria [11]. These bacteria are part of the normal flora of the oral cavity and can become pathogens if oral hygiene is reduced. Based on research on catechin's antimicrobial properties, the development of catechin-based mouth rinses can inhibit glucan synthesis by glucosyltransferase by up to 48.9% at a concentration of 10 mg/mL and up to 32.2% at a concentration of 1.25 mg/mL, thereby reducing dental plaque formation [12]. The use of gambier catechins at a concentration of 1–5% has antibacterial activity ranging from 20.45% to 43.24%. The higher the concentration, the greater the capacity of the catechins to inhibit the growth of *S. mutans* bacteria [13].

Aim

The aim of this study is to assess the effectiveness of gambier catechin as a preventive approach for streptococcal gingivitis. The goal is to reduce morbidity and improve quality of life globally, especially by utilizing natural resources in Indonesia.

Materials and Methods

The research design used in this study is a literature review, specifically focusing on the antioxidant and antibacterial properties of gambier catechin. The literature review involved a systematic search for original articles in international journals using databases such as PubMed, Elsevier, and Google Scholar.

The inclusion criteria encompassed primary literature or journals presenting original research, full-text articles in English, published between 2012 and 2022, and investigating the role of catechins in streptococcal gingivitis through both *in vitro* and *in vivo* studies (Figure 1).

The exclusion criteria include the presence of mixed research groups with other compounds, the absence of a control group, a lack of explanation regarding the mechanism, and publication in non-indexed journals. The search was restricted to articles written in English and conducted using the following keywords: "anti-inflammatory," "catechin," "gambier," "inflammation," and "rheumatoid arthritis". Data collection involved extracting relevant information from the selected sources, including reading, synthesizing, and summarizing the essential data to fulfill the study's objectives.

Results and Discussion

Pathophysiology of Streptococcal Gingivitis

Gingivitis is an inflammatory condition of the gingival tissue or gums which is generally caused by a bacterial infection. This inflammatory process often begins with the accumulation of a microbial biofilm that forms around the gingival tissue, also called dental plaque (dental plate). The inflammatory condition of gingivitis is limited to the soft tissue area of the epithelial and gingival connective tissue, without loss of attachment [14]. Gingivitis epidemiological data show that this disease is the most common periodontal disease. The prevalence is higher in men. This is associated with dental hygiene treatments which tend to be better for women [15]. Up to 50–90% of adults worldwide experience gingivitis [16]. In Europe, gingivitis is found in 30–60% of the population [17]. A study of 1000 adults in America showed that 55.7% of the participants had gingival inflammation on evaluation based on the evaluation of the gingiva index [18]. Based on the 2018 Basic Health Research Report of Indonesia (RiskesDas), the prevalence of gingivitis in Indonesia is 74% [19].

There are several types of gingivitis based on the etiology, clinical characteristics, duration of infection, and severity. Chronic gingivitis caused by plates is the best known. The general characteristics of clinical gingivitis are changes in gingival contour, swelling, redness, and soft structure (spongy) in the area of the infected gingiva, accompanied by bleeding when exposed to stimuli, such as when brushing teeth [20], [21].

The pathophysiology of the majority of gingivitis is related to inadequate cleaning of the oral cavity and leading to the accumulation of plaque and bacteria. If left untreated, plate accumulation can trigger an acute inflammatory response in less than a week. Based on

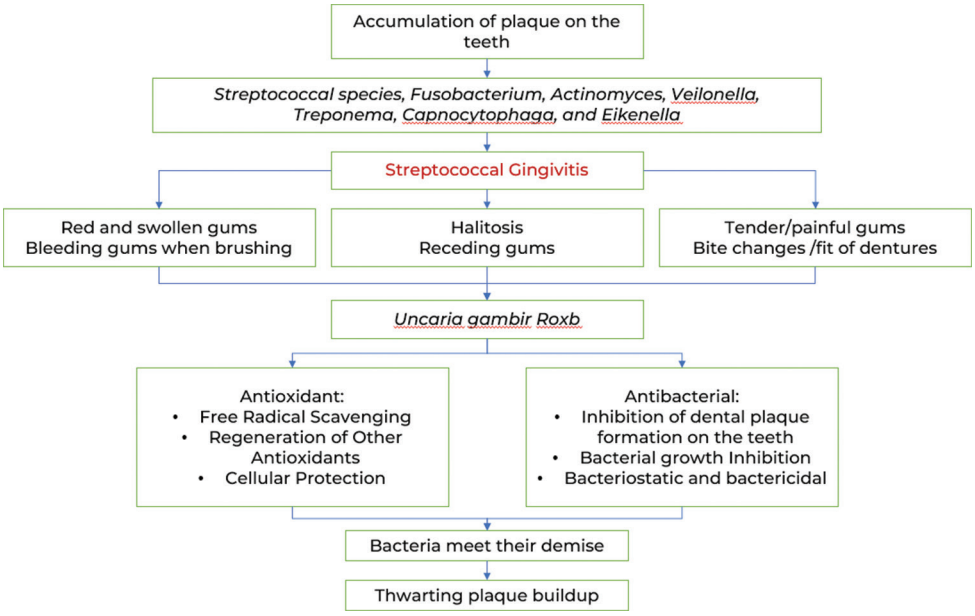

Figure 1: Mechanism of gambier catechins in managing streptococcal gingivitis [26], [28], [34], [35]

the histological characteristics, the pathophysiology of gingivitis can be divided into early lesions, early injuries, established injuries, and advanced injuries. Clinically, established lesions are manifestations of gingivitis, while advanced injuries are manifestations of periodontitis [22], [23]. Etymologically, streptococcal gingivitis is a non-plate non-induced gingivitis that is not triggered by plaque accumulation but can be activated by bacterial infection [24].

Gingivitis is caused by microbial plate deposits located in or near the gingival groove. The most strongly associated microorganisms with the etiology of gingivitis include *Streptococcal* species, *Fusobacterium*, *Actinomyces*, *Veilonella,* and *Treponema*. *Bact*, *Capnocytophaga,* and *Eikenella* are also potentially linked to the etiology of the disease. There may be other local or systemic etiological factors that intensify the deposition of the plate or the vulnerability of the fabric to microbial attack [24].

Patients with gingivitis may be prescribed an antiseptic oral rinse containing chlorhexidine. In severe cases of gingivitis, oral antibiotics and anti-inflammatory drugs can be recommended. Corrective measures can be made for several conditions in the oral cavity that can increase the risk of plate retention, such as overwritten or outstanding restorations, correction of contacts of the exposed teeth, malpositioned teeth, or badly adjusted dentures. In more severe cases, the correction of the gingival contour can also be performed surgically to improve access to the surface of the root for adequate debridement [9], [14].

Antioxidant capacity of Gambier catechin (Uncaria gambir Roxb)

Catechins, the primary constituents of the gambier plant, serve various medicinal purposes. Gambier contains catechins at levels ranging from 7% to 33%, along with catechin tannins, pyrocatechol, gambierin, red catechin, quercetin, fixed oil, wax, and trace amounts of alkaloids [25]. Conventionally, people in Southeast Asia and Southern Asia have utilized gambier plants to treat a range of ailments, including diarrhea, gastric diseases, as antioxidants and cancer preventatives, oral disorders, burns, acne, and as one of the components in betel quid chewing [26].

The results of the Amos research (2010) showed that the total catechin content of the Gambier extract in Indonesia varies widely, with a range of 40 to 80% [25]. Hilal and Engelhardt had obtained catechins of n tea in the market with a range of 8.5–20.6% and black tea with a 0.74–10% range [27]. According to the findings of Musdja *et al*., gambier demonstrates efficacy as an antibacterial agent [28]. This is attributed to gambier being a medicinal plant with exceptionally high catechin content, surpassing that of green tea leaves, where catechins have proven effective as antioxidants [27], [29].

In a study conducted by Rahmaddiansyah *et al*. in 2021, which investigated the utilization of gambier catechins in its potential on cancer, gambier catechins were shown to demonstrate effectiveness in inhibiting the growth of HeLa cells, which are cervical cancer cell lines [30]. In the *in vitro* experiments, the effects of gambier antioxidants were studied using the DPPH method already carried out by Anggraini *et al*., who reported that gambier has a strong potential for antioxidants [31].

In the *in vivo* experiments by Musdja *et al*., it was known that gambier catechins are a natural product that is potent for use as an antioxidant, as has been previously studied, that catechins in green tea have a stronger antioxidants capabilities than vitamins C and E. Catechins from gambier also have stronger capacity

as antioxidant than vitamin E [28]. This is good news for the management of gingivitis where inflammation is the basis of the pathophysiology of the disease in its early stages.

Antibacterial capacity of Gambier catechin (U. gambir Roxb)

Apart from its antioxidant capacity, gambir catechins also have the potential to be an antibacterial in streptococcal gingivitis. Gambier catechin is a kind of polyphenolic compounds that have antibacterial activity, so that they can inhibit the formation of dental plaque [32]. Polyphenol compounds can prevent bacterial adhesion to form pellicle dental plaque by inhibiting the activity of the glucosyltransferase enzyme that causes glucans. The glucan links form the extracellular polysaccharides that are part of the intercellular matrix of the plaque compilation. If glucan is not formed, plaque formation will be inhibited so that there is a decrease in the dental plaque index [33].

This is also in accordance with research by Ilmiawati *et al*., which proved the catechin content of gambier in toothpaste formulations was able to reduce dental plaque index in experimental patients [34].

Similarly, Ayuningsih explored the formulation of toothpaste containing purified catechins to target *S. mutans* bacteria, aiming to evaluate its effectiveness in inhibiting bacterial growth. The results of this study showed that there was an inhibition of the catechin toothpaste formulation on the growth of *S. mutans* bacteria that were sampled [35]. Previous research by Bayuarti also showed that brushing teeth with 0.1% gambier catechin toothpaste can function as an antibacterial against*S. mutans* which can reduce dental plaque index [36].

The catechin compound as an antibacterial has two properties, namely being able to inhibit (bacteriostatic) and kill (bacteria) the growth of bacteria that cause plaque on the teeth. Gambier catechins will inhibit the formation of insoluble glucan from sucrose by glucosyltransferase which causes inhibition of the glycosylation process, so that the process of the formation of extracellular polysaccharides by bacteria will be inhibited. Glucans play an important role in the process of bacterial attachment to teeth [37].

By inhibiting those processes, the process of attachment of bacteria to the dental pellicle will also be inhibited, thereby preventing the initial colonization process in the formation of dental plaque with the obstruction of this early colony process. The following process is a secondary colonization process which is characterized by the occurrence of coagulation of other bacteria to bacteria in the early stages of colonization will also be inhibited and the process of maturation of the dental plates will be inhibited, as well as the formation of dental plaque in general will also be inhibited [38].

Gambier catechins inhibit bacteria by damaging the bacterial cytoplasmic membrane which causes leakage of important metabolites so that the bacterial enzyme system becomes inactive. Catechin compounds will release H+ ions that attack hydrophilic groups (hydroxy and phosphate groups) on the surface of cell membranes. The hydroxy groups on the ergosterol molecule that is hydrogen-bonded cannot maintain their linkage and position. The cell membrane cannot withstand internal pressure, so the cytoplasm will penetrate the cell [39]. The bactericidal capacity of catechins is able to reject bacterial proteins and reduce cell surface tension due to the phenol group contained in catechins. The phenol group is a toxic compound that causes the three-dimensional structure of the protein to be disrupted and opened randomly without destroying the covalent frame structure. The result is that the properties of the protein change, but the amino acid line of the protein remains intact. Furthermore, there is damage to biological activity, so that bacteria cannot survive [40].

Mechanisms of gambier catechins' effectiveness in managing streptococcal gingivitis through their antioxidant and antibacterial actions are illustrated in the following diagram:

Conclusion and Suggestion

Periodontal disease is an infection in which specific bacteria play an important role. Periodontal is the main cause of tooth loss in adults. This disorder begins with gingivitis (swelling of the gums due to plaque), which, if left untreated, will result in periodontitis or infection that can destroy the teeth and surrounding tissue. Apart from its antioxidant capacity, the gambier catechins toothpaste formulation also has the potential as an antibacterial in gingivitis. The catechin compound as an antibacterial has two properties, namely being able to inhibit (bacteriostatic) and kill (bacteria) the growth of bacteria that cause plaque on the teeth which will lead to streptococcal gingivitis.

Author Contributions

RR, MZA: conceptualization; RR, MZA, RSR: writing and review.

References

1. World Health Organization. Goal 3 : Sustainable Development Knowledge Platform. WHO SDGS Progress, Targets and

Indicators. Switzerland: World Health Organization; 2018.

2. Glick M, Williams DM, Kleinman DV, Vujicic M, Watt RG, Weyant RJ. A new definition for oral health developed by the FDI World Dental Federation opens the door to a universal definition of oral health. Br Dent J. 2016;221(12):915-17.
3. Peres MA, Macpherson LM, Weyant RJ, Daly B, Venturelli R, Mathur MR, *et al*. Oral diseases: A global public health challenge. Lancet. 2019;394(10194):249-60. https://doi.org/10.1016/S0140-6736(19)31146-8

   PMid:31327369
4. Yang LC, Yu HC, Chang YC. The recent new findings of periodontal systemic connection from Taiwan's National health insurance research database. J Dent Sci. 2021;16(2):789-90. https://doi.org/10.1016/j.jds.2021.01.006

   PMid:33854738
5. Kementerian Kesehatan RI. Info DATIN Kesehatan Gigi Nasional. Indonesia: Pusdatin Kemenkes RI; 2019. p. 1-6.
6. Armitage GC. Development of a classification system for periodontal diseases and conditions. Ann Periodontol. 1999;4(1):1-6. https://doi.org/10.1902/annals.1999.4.1.1

   PMid:10863370
7. Gursoy-Mert H, Altan-Koran M, Noyan U, Kadir T, Cologlu S, Yilmaz S. Evaluation of the effectiveness of Er: YAG laser and conventional periodontal treatment in a patient with acute streptococcal gingivitis: A 2-year follow-up. Photomed Laser Surg. 2010;28(6):841-5. https://doi.org/10.1089/pho.2009.2705

   PMid:21142726
8. Kennedy HF, Morrison D, Tomlinson D, Gibson BE, Bagg J, Gemmell CG. Gingivitis and toothbrushes: Potential roles in viridans streptococcal bacteraemia. J Infect. 2003;46(1):67-70. https://doi.org/10.1053/jinf.2002.1084

   PMid:12504614
9. Dilsiz A, Sevinc S. Therapy of a patient with acute streptococcal gingivitis : Case report and review of the literature. JSM Dent. 2014;2(2):1025. https://doi.org/10.47739/2333-7133/1025
10. Pambayun R, Hasmeda M, Saputra D, Suhel S. Peningkatan Produksi Dan Perbaikan Kualitas Gambir Toman, Musi Banyu Asin. In: Laporan Kegiatan Program Vucer Multi Years, Kerjasama DITBINLITABMAS DIKTI melalui UNSRI dengan Pemda Musi Banyuasin, Sumatera Selatan; 2001.
11. Pambayun R, Murdijati G, Slamet S, Kapti R. Sensitivity of Gram-Positive bacteria to catechin extracted from gambir (Uncaria Gambir). Agritech J Fak Teknol Pertan UGM. 2008;174-179.
12. Lucida H, Bakhtiar A, Putri WA. Formulation of oral antiseptic preparation from gambir catechin. J Sains Teknol Farm. 2007;12(1):41-47.
13. Amos A. Gambir as an antibacterial agent in mouthwash formulation. J Sains dan Teknol Indones. 2013;11(3):188-192.
14. Kementrian Kesehatan Republik Indonesia. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.02.02/MENKES/62/2015 Tentang Panduan Praktik Klinis Bagi Dokter Gigi. Jakarta: Kementerian Kesehatan RI; 2015.
15. Kashetty M, Kumbhar S, Patil S, Patil P. Oral hygiene status, gingival status, periodontal status, and treatment needs among pregnant and nonpregnant women: A comparative study. J Indian Soc Periodontol. 2018;22(2):164-70. https://doi.org/10.4103/jisp.jisp_319_17

   PMid:29769772
16. Albandar JM, Rams TE. Global epidemiology of periodontal diseases: An overview. Periodontology 2000. 2002;29:7-10. https://doi.org/10.1034/j.1600-0757.2002.290101.x

   PMid:12102700
17. König J, Holtfreter B, Kocher T. Periodontal health in Europe: Future trends based on treatment needs and the provision of periodontal services--position paper 1. Eur J Dent Educ. 2010;14(Suppl 1):4-24. https://doi.org/10.1111/j.1600-0579.2010.00620.x

   PMid: 20415972
18. Li Y, Lee S, Hujoel P, Su M, Zhang W, Kim J, *et al*. Prevalence and severity of gingivitis in American adults. Am J Dent. 2010;23(1):9-13.

   PMid:20437720
19. Riskesdas. Primary Findings of the 2018 National Health Survey by the Ministry of Health of the Republic of Indonesia. Indonesia: Kementrian Kesehat Republik Indones; 2018.
20. Hassan BM, Intan Suhana MM, Farha A. Inflammation of the gums. Malays Fam Physician. 2020;15(1):71-3.

   PMid:32284812
21. Pari A, Ilango P, Subbareddy V, Katamreddy V, Parthasarthy H. Gingival diseases in childhood-a review. J Clin Diagnostic Res. 2014;8(10):ZE01-04. https://doi.org/10.7860/JCDR/2014/9004.4957

   PMid:25478471
22. Syndergaard B, Al-Sabbagh M, Kryscio RJ, Xi J, Ding X, Ebersole JL, *et al*. Salivary biomarkers associated with gingivitis and response to therapy. J Periodontol. 2014;85(8):e295-303. https://doi.org/10.1902/jop.2014.130696

   PMid:24502627
23. Page RC, Schroeder HE. Pathogenesis of inflammatory periodontal disease. A summary of current work. Lab Invest. 1976;34(3):235-49.

   PMid:765622
24. Trombelli L, Farina R, Silva CO, Tatakis DN. Plaque-induced gingivitis: Case definition and diagnostic considerations. J Periodontol. 2018;89(Suppl 1):S44-67. https://doi.org/10.1111/jcpe.12939

   PMid:29926492
25. Amos A. The catechin content of gambir: A primary product of Indonesia's production centers. J Stand. 2010;12(3):149. https://doi.org/10.20319/lijhls.2018.42.3446
26. Setyowati H. Gambir (*Uncaria gambir* Roxb) as natural cosmeceutical agent. Cermin Dalam Kedokteran. 2017;44(3):222-224.
27. Hilal Y, Engelhardt U. Characterisation of white tea-comparison to green and black tea. J fur Verbraucherschutz Leb. 2007;2(4):414-421. https://doi.org/10.1007/s00003-007-0250-3
28. Musdja MY, Rahman HA, Hasan D. Antioxidant activity of catechins isolate of uncaria gambier Roxb in male rats. Life Int J Health Life Sci. 2018;4(2):34-46. https://doi.org/10.20319/lijhls.2018.42.3446
29. Armoskaite V, Ramanauskiene K, Maruska A, Razukas A, Dagilyte A, Baranauskas A, *et al*. The analysis of quality and antioxidant activity of green tea extracts. J Med Plants Res. 2011;5(5):811-6.
30. Rahmaddiansyah R, Hasani S, Zikrah AA, Arisanty D. The effect of gambier catechin isolate on cervical cancer cell death (HeLa Cell Lines). Open Access Maced J Med Sci. 2022;10(B):1293-7. https://doi.org/10.3889/oamjms.2022.8779
31. Anggraini T, Rini R, Aini L. The extraction of gambier by using ultrasonic assisted at various temperature. IOP Conf Ser Earth Environ Sci. 2021;757(1):012058. https://doi.org/10.1088/1755-1315/757/1/012058
32. Hilmi HL, Rahayu D. Aktivitas farmakologi gambir (*Uncaria gambir* Roxb.). Farmaka. 2018;16(2):134-41.
33. Meulenbeld GH, Zuilhof H, Van Veldhuizen A, Van Den Heuvel RH, Hartmans S. Enhanced (+)-catechin transglucosylating activity of *Streptococcus mutans* GS-5 glucosyltransferase-D due to fructose removal. Appl Environ Microbiol. 1999;65(9):4141-7. https://doi.org/10.1128/AEM.65.9.4141-4147.1999

   PMid:10473427

34. Ilmiawati C, Nurhayati N, Bambang B. The influence of toothpaste containing gambir catechin (*Uncaria gambir* Roxb) on the reduction of dental plaque index. Andalas Dent J. 2020;8(2):57-63.
35. Ayuningsih F. Formulation of Toothpaste from Purified Catechin and Antibacterial Activity Test against *Streptococcus mutans*. Universitas Perintis; 2021. Available from: https://repo.upertis.ac.id/1348/1/draft skripsi-fitria ayuningsih.pdf
36. Bayuarti YD. Study on the Production Process of Gambir Toothpaste as an Antibacterial Agent. Bogor: Bogor Agricultural Institute; 2006.
37. Kozai K, Soto M, Yamaguchi N, Nagasaka N. Gambier as an inhibitor of dental plaque formation. Dent J. 1995;28:95-6.
38. Christianty F, Nurul D, Kemal Y. Comparison of the Effectiveness of Rinsing with 50% and 25% Concentration Brewed Green Tea Solutions in Clinically Inhibiting Dental Plaque Formation on Six Tooth Surfaces: A Clinical Study on Students of the Faculty of Dentistry, University of Indonesia. Universitas Indonesia; 2008. Available from: https://www.lontar.ui.ac.id/detail?id=125157&lokasi=lokal [Last accessed on 2023 Dec18].
39. Rustanti E, Jannah A, Fasya AG. Antibacterial activity test of catechin compounds from tea leaves (*Camellia sinensis* L. var. *Assamica*) against *Micrococcus luteus* bacteria. ALCHEMY. 2013;2(2):138-149.
40. Susilowati A, Sumarawati T. A study on the long-term effect of rinsing with gambir (*Uncaria gambir*) infusion on dental plaque formation. J Sains Med. 2012;4(1):58.