

Garcidepsidon B from *Garcinia parvifolia*: Antimicrobial Activities of The Medicinal Plants from North Kalimantan against Dental Caries and Periodontal Disease Pathogen

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Abstract

In this study, to find the potential of antibacterial materials, we focused on the plant used for oral treatment by native people of North Kalimantan. We have selected 10 medicinal plants usually used in daily life by native people. We determine samples using antimicrobial assay and Gtase Inhibitory activity. We obtained the most effective sample, *Garcinia parvifolia*, as antimicrobial activity against the *Streptococcus sobrinus* and *Porphyromonas gingivalis* with a MIC value of 0.5 mg/ml inhibition on both of bacteria and MBC value of 0.5 mg/ml and 1 mg/ml, respectively. The methanol extract of *G. parvifolia* leaf showed antimicrobial activity in a MIC, and MBC assay by activity-guide fractionation, garcidepsidone B (**1**) was isolated as an active compound. The MIC of (**1**) against *S. sobrinus* was 0.02 mg/mL and against *P. gingivalis* was 0.05 mg/mL. Based on these results, we validated that the leaf extract has been used by the traditional tribe of North Kalimantan.

Introduction

Oral disease, including dental caries, gingival inflammation, periodontal disease, and tooth loss, may significantly affect overall health, among this dental caries and periodontal disease are multifactorial diseases in which diet, nutrition, microbial infection, and host response all play important roles (1). Dental caries and periodontal disease were the most prevalent chronic diseases of people worldwide (2). In periodontal disease, the common pathogen is *Porphyromonas gingivalis*, which is involved in the pathogenesis of periodontitis, an inflammatory disease that destroys the tissues supporting the tooth which may eventually be lead to tooth loss (3). In the dental caries field, the most common pathogens are Mutan streptococci (*Streptococcus mutans* and *Streptococcus sobrinus*) are isolated from human dental plaque (4). Dental plaque is a complex biofilm that accumulates on the teeth' surface, composed of more than 500 bactericidal species (5). Their grow inside the oral cavity and convert sucrose to insoluble adhesive glucans cause tooth loss in children and young adults. Initially, it presents as a white stain on enamel (6). The acid produced by bacteria involves the mechanism of dental plaque formation, bacterial adhesion to the dental surface, and dental enamel demineralization. *S. mutans* has played a central role in the pathogenesis of the disease by producing glycosyltransferase and synthesizing insoluble glucan into sucrose, mediating bacterial adhesion and accumulation on the tooth's surface. After the formation of the plaque, the acids produced by bacteria demineralize the tooth surface (7).

The strategies for preventing oral disease caused by cariogenic bacteria, such as depression, the growth of *S. sobrinus* and *P. gingivalis*. Inhibition of biofilm formation, glucan synthesis, and inhibition of glucosyltransferase activity have been conducted (8). In addition, many studies have shown that some natural products can interfere with the survival and virulence of oral pathogens, and remarkable anti-cariogenic potency was also observed for natural bioactive compounds (9).

Garcinia parvifolia belongs to clusiaceae family and is distributed in lowland areas of the rainforests Asia, Africa, New Caledonia, and Polynesia (10). This tree's fruit is edible, and the young leaves are occasionally consumed as vegetables (11). Locally, they are known as asam kandis (12). The leaves (13), twigs (14), latex (15), and bark (16). include xanthone, benzophenones, triterpenes, parvifoliol, biflavonoids, and benzoquinone, according to the phytochemical analysis. The obtained compounds exhibit antibacterial (17), antioxidant (10), and antiplasmodial biological properties (18).

In Indonesia, *G. parvifolia* has been traditionally used for curing oral disease by some local tribes. In the previous chapter, antimicrobial activity and inhibition of glycosyltransferase and antioxidant activity in DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging assay, were reported as screening to select the bioactive compounds for further investigation on isolation and characterization. Therefore, the purpose of this chapter was to isolate and identify the active chemicals that block the activity of glycosyltransferase and inhibit the growth of cariogenic bacteria.

Results And Discussion

Plant extracts

The leave and roots of 10 medicinal plants were macerated by methanol at room temperature (Table 1). The methanol maceration of the plants provided 1.92 to 0.63 percent extracts based on the dry weight of the sample. *J. curcas* leaves yielded the least, while the highest extract was produced from *T. indica* leaves.

Table 1
Extracts of plants used for medicine

No.	Sample	Plant part	Yield		Extract Color
			Extract (g)	Percentage (%)	
1	<i>Uncaria gambir</i>	Leaves	6.96	16.79	Dark Brown
2	<i>Tamarindus indica</i>	Leaves	13.95	20.63	Dark Green
3	<i>Garcinia parvifolia</i>	Leaves	2.16	3.80	Dark Green
4	<i>Sellagenila intermedia</i>	Leaves	2.23	4.33	Transparent Brown
5	<i>Cinnamomum burmani</i>	Leaves	2.74	4.78	Dark Brown
6	<i>Cinnamomum iners</i>	Leaves	3.16	6.94	Dark Brown
7	<i>Cinnamomum parthenoxylon</i>	Leaves	4.39	9.80	Dark Brown
8	<i>Jatropha curcas</i>	Leaves	0.74	1.96	Dark Green
9	<i>Eurycoma longifolia</i>	Root	1.31	2.45	Yellow
10	<i>Cinnamomum sp</i>	Root	1.84	3.20	Dark Brown

Antimicrobial activity

Because some microorganisms have become resistant to antibiotics that are already on the market, scientists have been looking for new antimicrobial agents. The goal of the research was to find antimicrobial bioactivity in tropical medicinal plants. Ten medicinal plants from North Kalimantan, Indonesia, were found to have antimicrobial activity. Table 2 shows the results of antimicrobial activity. In the investigation against *S. sobrinus* (Table 2), four plants extract showed antimicrobial activity against *S. sobrinus*, methanol extracts of *Garcinia parvifolia*, *Cinnamomum burmani*, *Eurycoma longifolia*, and *Cinnamomum iners* showed activity at 0.03–4 mg/ml. With a value of 0.5 mg/ml, the MIC for the methanol extract of *G. parvifolia* was the highest. In the assay against *P. gingivalis* (Table 2), 5 plants extract showed antibacterial activity against *P. gingivalis*, methanol extracts of *U. gambir*, *T. indica*, *G. parvifolia*, and *E. longifolia*, showed high activity at 0.5-4 mg/mL. The methanol extract of *G. parvifolia*

showed the highest MIC with a value of 0.25 mg/mL and MBC 1 mg/mL.

Table 2
Antimicrobial and GTase inhibitory activity of the medicinal plants from North Kalimantan

No	Scientific name	Local name	Family name	Part	Inhibitory activity (%)	MIC (mg/ml)		MBC (mg/ml)	
					Gtase	S. s ^a	P. g ^b	S. s	P. g
1	<i>Uncaria gambir</i>	gambir	Rubiaceae	leave	33	4	1	4	4
2	<i>Tamarindus indica</i>	asam	Leguminosae	leave	35	4	2	4	4
3	<i>Garcinia parvifolia</i>	asam kandis	Clusiaceae	leave	13	0.25	0.5	1	0.5
4	<i>Sellagenila intermedia</i>	cakar ayam	Selaginellaceae	leave	26	4	4	4	4
5	<i>Cinnamomum burmani</i>	kayu manis	Lauraceae	leave	27	4	4	4	4
6	<i>Cinnamomum iners</i>	cinamon	Lauraceae	leave	17	4	4	4	4
7	<i>Cinnamomum parthenoxylon</i>	cinamon	Lauraceae	leave	17	4	4	4	4
8	<i>Jatropha curcas</i>	jarak	Euphorbiaceae	leave	29	4	4	4	4
9	<i>Eurycoma longifolia</i>	pasak bumi	Sumaroubaceae	root	48	4	2	4	2
10	<i>Cinnamomum sp</i>	ginseng	Lauraceae	root	59	4	4	4	4
11	Chlorhexidine	-	-	-	-	3.9µg	3.9µg	3.9µg	3.9µg

^aStreptococcus sobrinus

^bporphyromonas gingivalis

The antibacterial agent could have potential from tropical medical plants shown the ability to diminish antimicrobial activity utilizing 10 medicinal plants from Indonesia. In the screening studies, most of the substances had actions to depress *Streptococcus sobrinus* and *Porphyromonas gingivalis*. The result of the antimicrobial assay of the plant extracts is presented in Table 2. In the assay against *S. sobrinus* (Table 2), 4 botanical extracts had potential against *S. sobrinus* and GTase, methanol extracts of *G. parvifolia*, *Cinnamomum burmani*, *Eurycoma longifolia*, and *Cinnamomum iners* shown the activity at 31.25–4000 µg/ml. the methanol extract of *G. parvifolia* showed the highest MIC with a value of 31.25 µg/ml. In the GTase inhibitory activity (Table 2), *Cinnamomum sp.*, and *E. longifolia* showed significant efficacy in inhibiting enzyme glucosyltransferase with value of 59 and 48%.

Isolation of active compounds of *G. parvifolia*

In this study, methanol extract of 10 materials from North Kalimantan plants was investigated for their antibacterial activity and etiologic enzyme of oral illness. In the screening experiments, only a few compounds depressed *S. sobrinus* bacterial proliferation. *G. parvifolia* (asam kandis) was the most efficient to suppress *S. sobrinus*. *G. parvifolia* belongs to the Clusiaceae family and is popularly recognized as a cooking spices and traditional medicinal herb.

The pair of extracts were beginning to isolate using column chromatography silica gel and Fig. 1 exhibited the data of high-performance liquid chromatography (HPLC) of each extract sample. Five isolated substances were purified by preparative high-performance liquid chromatography (p-HPLC) and identified by nuclear magnetic resonance (NMR). All the compounds were compared to the ^1H and ^{13}C NMR data of references compounds 1 and 2. It was identified as Garcidepsidone B (1), Garcidepsidone A (2), respectively, as displayed in Fig. 2 and HPLC data Fig. 1.

Compound 1 and 2 were studied for *S. sobrinus* and *P. gingivalis* growth inhibitory action. The data of MIC, MBC, and GTase inhibitory were reported in Table 3. The crude extract of *G. parvifolia* showed 0.25mg/ml of the MIC value, with the MBC value higher than the MIC values. Compounds 1 and 2 reduced the development of *S. sobrinus* at concentrations 25 and 175 µg/ml, and against *P. gingivalis* with a value of 50 and 350 µg/ml, respectively. Each compound inhibited the growth of *S. sobrinus* and *P. gingivalis* at a concentration range of 25–2000 µg/ml. In this study, two compound from depsidone are usually present in all activity against both bacteria. So there might be more active molecules than isolated chemicals in the crude extracts, however, we could not isolate the powerful active compound yet in our experiment. So further research isolate compounds must be conducted.

1, Garcidepsidone B; 2, garcidepsidone A.conditions: Colomn : Sunniest C18,5 µm, Analysis time:40 min, detector wavelength : 280 nm Flow late : 1.0 ml/min, Gradient program MeOH:0.05%TFAaq.=80%:20–100%:0% (60 min)

Figure 3 Compound 2 (Garcidepsidone A)

Table 3 Antimicrobial Activity and GTase Inhibitory of Garcidepsidone					
Compounds	Antimicrobial activity				GTase Inhibition (%)
	<i>S. sobrinus</i>		<i>P. gingivalis</i>		
	MIC (µg/ml)	MBC (µg/ml)	MIC (µg/ml)	MBC (µg/ml)	
Garcidepsidone B	25	100	50	200	50
Garcidepsidone A	175	350	100	> 500	25
Chlorhexidine (+)	3.9				-

The compounds activities have shown inhibition at garcidepsidone B and A. Garcidepsidone B showed action against MRSA with a MIC value of 128 µg/ml. In addition, this study showed garcidepsidone B had a higher impact against *S. sobrinus* and *P. gingivalis* with a value of 25 µg/ml and 50 µg/ml, respectively.

Discussion

The development of microbial resistance to currently available antibiotics prompted the quest for new antimicrobial agents (8). Chlorhexidine, triclosan, and delmopinol are employed as antibacterial agents against oral pathogens to minimize dental plaque-mediated diseases, such as dental caries (19). In this investigation, chlorhexidine was utilized as an antibacterial positive control.

S. sobrinus is one of the most cariogenic bacteria among mutans streptococci (20). Although the human flora is quite rich and complicated, one type of mutans streptococci, *S. sobrinus* have been implicated as key etiologic agent of dental caries (21). One of this species's most important virulence characteristics is its ability to generate glucosyltransferase (GTase), GTase is the primary enzyme that catalyses the introduction of a glucose moiety from sucrose to sticky glucans and contributes considerably to the establishment of dental caries (22). Therefore, potent efficacy of the plant extracts against *S. sobrinus* provides the prospect for the treatment of dental caries, by inhibiting the growth of *S. sobrinus*, glucosyltransferase, and other sobrinus-related illnesses.

P. gingivalis is a gram-negative oral anaerobe that is one of the pathogenic bacteria species that conduct initiation and causation periodontitis, an inflammatory disease that destroys the tissues supporting the tooth, which eventually may lead to tooth loss, rheumatoid arthritis, atherosclerosis and orodigestive cancers. Orodigestive cancers represent a high part of the total malignancies worldwide, including cancers of the oral cavity, gastrointestinal tract, and pancreas (3). The data revealed the possibility that the extracts may be employed for suppressing and destroying bacteria development, etiological agent, and other gingivalis- associated disorders (23).

According to Table 2, the most effective sample against these bacteria was *G. parvifolia*. The phytochemical examination of the leaves (17), twigs (10), latex (15), and bark (16) of this plant led to the separation of xanthenes, depsidones, and phloroglucinols. Several studies on the crude methanol extract from the leaves have demonstrated that *Garcinia* had robust and persistent inhibitory effects against diverse infections and antibacterial activity of *G. parvifolia* against *Staphylococcus aureus* (10).

E. longifolia also had potential against *P. gingivalis* and inhibited glucosyltransferase. The phytochemical screening of *E. longifolia* demonstrated the presence of phenolic chemicals, flavonoids, terpenoids, alkaloid, protein, and cardiac glycosides in the stem and root. Flavonoids are commonly known for healthare polyphenolic chemicals and forhealth-supporting features such as antioxidant, anti-allergic, antiinflammation, antibacterial, and anticancer properties (24). Alkaloid have been reported to possess analgesic, antiplasmodic, antibacterial, analgesic properties and anti-malaria (25). Among all the phytochemicals present, flavonoids and alkaloid might be possible as an inhibitor of GTase and antibacterial agents.

According to Table 2, *T. indica* has the capacity to inhibit *P. gingivalis* with value of 2mg/ml. The phytochemical of *T. indica* components were identified, including flavonoid, tannin, anthroquinone, saponin, alkaloid (26). These may have accounted for antibacterial action. These phytochemicals and some other aromatic secondary metabolites have been suggested to serve as natural agents that protect plants agents against microbial diseases and insect predators (27).

Uncaria gambir inhibited the growth of *P. gingivalis* with a 1mg/ml value. The phytochemical screening of *U. gambir* was revealed to contain flavonoid, alkaloid, sterol, phenolic compounds resin, protein, and amino acids (28). There has been no report about the active compound of *U. gambir*, but another species, *U. tomentosa* was discovered to contain antibacterial chemicals such as uncarine E, rhynchophylline, isorhynchophylline (29).

After determining the highest MIC against *S. sobrinus* and *P. gingivalis*, we chose *G. parvifolia* as the following research cause of the strong action at low concentrations, and this plant has been utilized by local tribes as daily spices. Depending on these, we employed both samples as follows isolation of active chemicals.

The extract of *G. parvifolia* exhibited antibacterial activity against methicillin-resistant *staphylococcus aureus* (MRSA) and an antioxidant effect on the scavenging activity research of the stable DPPH free radical. *G. parvifolia* against *S. sobrinus* and *P. gingivalis* demonstrated high antibacterial activity with MIC of 0.25 and 0.5 mg/ml, respectively. Therefore, we studied the separation and identification compounds of inhibitory enzyme and active antibacterial chemicals included in *G. parvifolia*. Garcidepsidone A and B were successfully isolated components from *G. parvifolia*. These ingredients are well-known for their antimicrobial properties. This is most likely due to the presence of prenyl compounds in the xanthone group. Furthermore, when compared to the single synthesis compound chlorhexidine, this component performs natural ingredients

Cunclusions

In this investigation, ten medicinal plants from Indonesia were evaluated against antibacterial of *S. sobrinus* and *P. gingivalis* and the inhibitory activity of glucosyltransferase (GTase). As a result, the *G. parvifolia* was chosen for further exploration of the isolation and identification of bioactive chemicals because of its high activity against both of assays.

Two depsidones, garcidepsidone A and garcidepsidone B, were identified as bioactive chemicals. Among these isolated compounds, garcidepsidone B demonstrated a notably higher inhibitory effect than garcidepsidone A against *S. sobrinus* and *P. gingivalis*. On the other hand, the most effective against GTase inhibitory activity was garcidepsidone A. For additional pharmacological studies, Garcidepsidone A can create a natural anti-cariogenic agent for tooth caries. Although the isolate compounds were not the most active compounds, they may provide additional active chemicals from *G. parvifolia* crude extracts with high action. Therefore, the isolation and identification of additional chemicals should be studied.

Materials And Methods

Chemicals and plant parts

In North Kalimantan, Indonesia, in Bulungan regency, the leaves and roots of medicinal plants were taken. The chosen plants were *Uncaria gambir*, *Tamarindus indica*, *Garcinia parvifolia*, *Sellagenila intermedia*, *Cinnamomum burmani*, *Cinnamomum iners*, *Cinnamomum parthenoxylon*, *Jatropha curcas*, *Eurycoma longifolia*, and *Cinnamomum* sp. Raharjo S. Hut, a taxonomist at Mulawarman University, was able to name the plants confirmed by references. The plant parts were dried for three days, then dried for three days, and ground up in a blender. DPPH (1,1-diphenyl-2-picrylhydrazyl), was purchased from Tokyo Kasei Kogyo, (Tokyo, Japan). DMSO (dimethyl sulfoxide), was purchased from (Merck, Darmstadt, Germany). Ascorbic acid was purchased from (Sigma, St. Louis, MO, USA). Difco provided the nutrient broth (Detroit, MI, USA). Other chemicals were HPLC grade.

Extraction

Ground plant samples were extracted sequentially with methanol at room temperature using a shaker (7400 Tubingen; Edmun Buchler, Germany) with constant shaking for 48 hours. After the suspension has been filtered with Whatman filter paper. The crude methanol extracts were near-dried by roto evaporation at 40⁰ C in a vacuum oven

Antimicrobial assay

In this study, the MIC values of the extract against microorganisms were found using the microdilution method with 96-well microplates. The extracts diluted by one were put in the 96-well plate with *S. sobrinus* for 24 hours or *P. gingivalis* for 72 hours at 37 °C under anaerobic conditions with the inoculum, 10⁶ cell/ml for *P. gingivalis* and *sobrinus* for 10⁸ cell/ml. The final concentration of the extract ranged from 4 mg/ml to 0.015 mg/ml. The chlorhexidine was used as a positive control. When 50 µl of 0.2 mg/ml iodinitrotetrazolium chloride (INT) was added to each microplate well and the plate was left at 37 °C for 3 hours, the growth of microorganisms was observed. The MIC was the lowest concentration using INT from changing color. For sequential MBC determination, 10 µl from wells that didn't change color was added to 100 µl of fresh medium, and the mixture was left for 24 hours. *In anaerobic conditions, S. sobrinus* or 72 hours for *P. gingivalis* at 37 °C. The MBC was found by putting 50 µl of 0.2 mg/ml INT into each well of a microplate for 3 hours at 37 °C.

Preparation GTase

S. Sobrinus was grown in 4 L of Todd Hewitt broth for 20 hours at 37 °C. After the culture was centrifuged at 5000 rpm for 10 minutes at 40°C, the cells were collected, extracted with 8 M urea, and stirred for 1 hour. The crude enzyme solution with urea was dialyzed against 10 mM sodium phosphate buffer (PH 6.0) until all of the urea was removed. Pipetting a milliliter of crude enzyme solution into a micro tube was then put in a freezer at -80 °C.

Assay for GTase inhibitory activity

GTase synthesized insoluble glucan. GTase was incubated in 300 µl of 0.1 M phosphate buffer (pH 6.0) containing 5% sucrose, 0.5% sodium azide, 0.5% dextran T-10, and in the presence or absence of sample at 37 °C for 3 hours. The

inhibition rate was expressed by the following equation. Inhibition rate (%) = $100 \times (\text{Ac}-\text{As})/\text{Ac}$. (Ac and As represent the absorbance obtained in the control and the sample dose, respectively).

Isolation of active compounds from *Garcinia parvifolia*.

The leaf of *G. parvifolia* (1.1 kg) was repeatedly extracted with methanol at room temperature. The methanol extract was concentrated in vacuo to obtain a residue (98 g). A part of the extract (11.7 g) was suspended in methanol-water (1:10) and successively partitioned with n-hexane and ethyl acetate to give the n-hexane-soluble part (3 g, 25% of the methanol extract), hexane precipitation-soluble part (6 g, 51%), ethyl acetate-soluble part (1.49 g, 12.7%), and aqueous portions (1.5 g, 12.8%). The n-hexane precipitation (4.55 g) was fractionated by column chromatography on silica gel (1 kg) by elution with n-hexane-ethyl acetate gradient [n-hexane: ethyl acetate = 9:1 1000 ml, 8:2 1600 ml, 7:3 4100 ml, 6:4 3100 ml, 5:5 3000 ml, 3:7 1466 ml, ethyl acetate 1000 ml, methanol 1000 ml. Fraction 1: 81 mg, Fraction 2: 88 mg, Fraction 3: 45.4 mg, Fraction 4: 89 mg, Fraction 5: 533.4 mg, Fraction 6: 96.5 mg, Fraction 7: 37.5 mg, Fraction 8: 1799.8 mg, Fraction 9: 1258.5 mg]. Nine fractions were collected. Fraction 8 has the most potential for antimicrobial activity, and the resultant material was then fractionated by column chromatography on silica gel (450 mg). Six fractions were collected, and Fraction 4 and 5 were subjected to preparative high-performance liquid chromatography (HPLC) (column oven: shimadzu CTO-20AC), eluting with aqueous 0.05% trifluoroacetic acid (TFA)/methanol (20/80) at 9 ml/min. Compound 1 (10 mg) was isolated as the main active compound by Preparative HPLC eluting with 0.05% trifluoroacetic acid (TFA) water/methanol (20/80) 45 min at 9 ml/min, and was identified as Garcidepsidone B and Garcidepsidone A by ^1H -NMR, ^{13}C -NMR, ^1H - ^1H COSY, HMQC, HMBC, NOESY (Jeol ECA 600 NMR spectrometer) and MALDI-TOF-MS (Shimadzu Biotech Axima Resonance 2.9.1.20100121). The compounds were identified by comparison of the spectral data with those in the literature (30),(17).

Garcidepsidone B. Compound 1 was a white powder that showed a $[\text{M}^+\text{H}]^+$ ion peak at m/z 481 ($\text{M}^+=\text{C}_{28}\text{H}_{32}\text{O}_7$) in positive TOF-MS. ^1H NMR (CD_3OD 600 MHz) : 6.19 (s, H-4), 6.49 (s, H-6), 3.23 (d, H-12), 5.13 (mt, H-13), 1.91 (m, H-15), 1.98 (s, H-26). ^{13}C NMR (CD_3OD 600 MHz) δ : 162.7 (C-1), 112.3 (C-2), 162.3 (C-3), 98.6 (C-4), 160.2 (C-4a), 142.4 (C-5a), 103.6 (C-6), 142.6 (C-7), 135.4 (C-8), 131.5 (C-9), 140.8 (C-9a), 169.0 (C-11), 97.1 (C-11a), 21.2 (C-12), 122.1 (C-13), 134.2 (C-14), 39.4 (C-15), 26.2 (C-16), 124.0 (C-17), 130.6 (C-18), 16.3 (C-19), 24.4 (C-20), 14.8 (C-21), 22.9 (C-22), 121.6 (C-23), 135.4 (C-24), 16.7, 24.6 (C-26).

Garcidepsidone A. Compound 2 was found as a white powder, and positive TOF-MS showed that it had a $[\text{M}^+\text{K}]^+$ ion peak at m/z 519 ($\text{M}^+ = \text{C}_{28}\text{H}_{32}\text{O}_7$). ^1H NMR (CDCl_3 600 MHz) : 11.00 (1H, s, OH-1), 6.32 (1H, s, OH-3), 6.67 (1H, s, H-6), 3.36 (2H, d, $J = 6.9\text{Hz}$, H-12), 5.17 (1H, s, H-13), 1.78 (3H, s, H-15), 1.71 (3H, s, H-16), 3.54 (2H, d, $J = 8$ (3H, s, H-26)). ^{13}C NMR (CDCl_3 600 MHz) δ : 160.9 (C-1), 111.5 (C-2), 160.4 (C-3), 111.2 (C-4), 156.8 (C-4a), 143.7 (C-5a), 105.4 (C-6), 141.9 (C-7), 139.7 (C-8), 119.9 (C-9), 136.6 (C-9a), 168.9 (C-11), 98.8 (C-11a), 22.2 (C-12), 121.2 (C-13), 135.0 (C-14), 18.1 (C-15), 23.9 (C-16), 22.2 (C-17), 121.9 (C-18), 134.8 (C-19), 18.0 (C-20), 25.8 (C-21), 22.6 (C-22), 120.2 (C-23), 136.0 (C-24), 17.9 (C-25), 25.8 (C-26).

Declarations

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CONFLICT OF INTEREST

The authors declare that they hold no competing interests.

References

1. Günther M, Karygianni L, Argyropoulou A, Anderson AC, Hellwig E, Skaltsounis AL, et al. The antimicrobial effect of *Rosmarinus officinalis* extracts on oral initial adhesion ex vivo. *Clin Oral Investig*. 2022 Jun 1;26(6):4369–80. <https://doi.org/10.1007/S00784-022-04400-5>
2. Al-Nasser L, 2000 IL-P, 2020 U. Prevention and management of periodontal diseases and dental caries in the older adults. *Wiley Online Libr [Internet]*. 2020 Oct 1 [cited 2022 Nov 23];84(1):69–83. <https://doi.org/10.1111/prd.12338>.
3. Mysak J, Podzimek S, ... PS-J of immunology, 2014 U. *Porphyromonas gingivalis*: major periodontopathic pathogen overview. <https://doi.org/10.1155/2014/476068>
4. Abranches J, Zeng L, Kajfasz JK, Palmer SR, Chakraborty B, Wen ZT, et al. Biology of Oral Streptococci. *Microbiol Spectr*. 2018 Sep 7;6(5). <https://doi.org/10.1128/MICROBIOLSPEC.GPP3-0042-2018>.
5. Larsen T, Apmis NF-, 2017 undefined. Dental biofilm infections—an update. *Wiley Online Libr [Internet]*. 2017 Apr 1 [cited 2022 Nov 23];125(4):376–84. <https://doi.org/10.1111/apm.12688>.
6. Kuspradini H, Mitsunaga T, Ohashi H. Antimicrobial activity against *Streptococcus sobrinus* and glucosyltransferase inhibitory activity of taxifolin and some flavanone rhamnosides from kempas (*Koompassia malaccensis*) extracts. Vol. 55, *Journal of Wood Science*. 2009. <https://doi.org/10.1007/s10086-009-1026-4>.
7. Vaernewyck V, Arzi B, Sanders NN, Cox E, Devriendt B. Mucosal Vaccination Against Periodontal Disease: Current Status and Opportunities. *Front Immunol*. 2021 Dec 2;12. <https://doi.org/10.3389/FIMMU.2021.768397/FULL>.
8. Figueiredo N, Aguiar S de, Falé P, Chemistry LA-F, 2010 U. The inhibitory effect of *Plectranthus barbatus* and *Plectranthus ecklonii* leaves on the viability, glucosyltransferase activity and biofilm formation of. Elsevier. 2010 <https://doi.org/10.1016/j.foodchem.2009.07.008>.
9. Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria: Potential application in the prevention and treatment of oral diseases. *Evidence-based Complement Altern Med*. 2011;2011. <https://doi.org/10.1093/ECAM/NEP067>.
10. Rukachaisirikul V, Naklue W, Phongpaichit S, Towatana NH, Maneenoon K. Phloroglucinols, depsidones and xanthenes from the twigs of *Garcinia parvifolia*. *Tetrahedron*. 2006;62(36). <https://doi.org/10.1016/j.tet.2006.06.059>
11. Iinuma M, Tosa H, Tanaka T, ... FA-J of P, 1996 undefined. Antibacterial Activity of Xanthenes from Guttiferaceous Plants against Methicillin-resistant *Staphylococcus aureus*. *academic.oup.com* 48(8):861–5. <https://doi.org/10.1111/j.2042-7158.1996.tb03988.x>.
12. KARTINA K, BATUBARA I, ... HK-BJ of, 2022 U. Diversity of medicinal plants used for skincare by Bulungan tribe in North Kalimantan, Indonesia and its melanin biosynthesis inhibition. <https://doi.org/10.13057/biodiv/d230308>.
13. Xu YJ, Chiang PY, Lai YH, Vittal JJ, Wu XH, Tan BKH, et al. Cytotoxic prenylated depsidones from *Garcinia parvifolia*. *J Nat Prod*. 2000;63(10):1361–3. <https://doi.org/10.1021/NP000141E>.
14. Rukachaisirikul V, Naklue W, Tetrahedron SP-, 2006 undefined. Phloroglucinols, depsidones and xanthenes from the twigs of *Garcinia parvifolia*. <https://doi.org/10.1016/j.tet.2006.06.059>
15. Pattalung P, Wiriyaichitra P, Thailand MO-JSS, 1988 undefined. The antimicrobial activities of rubraxanthone isolated from *Garcinia parvifolia* (Miq) Miq. <https://doi.org/10.2306/scienceasia1513-1874.1988.14.067>
16. Xu YJ, Lai YH, Imiyabir Z, Goh SH. Xanthenes from *Garcinia parvifolia*. *J Nat Prod*. 2001;64(9):1191–5. <https://doi.org/10.1021/NP0101393>.
17. Xu YJ, Chiang PY, Lai YH, Vittal JJ, Wu XH, Tan BKH, et al. Cytotoxic prenylated depsidones from *Garcinia parvifolia*. *J Nat Prod*. 2000;63(10). <https://doi.org/10.1021/np000141e>.
18. Abdillah S, Tambunan R, Farida Y, Sumarny R. In Vitro and In Vivo Antiplasmodial Activities of *Garcinia Parvifolia* (MIQ) MIQ Leaves From Indonesia. <https://doi.org/10.9790/3008-09652832>

19. Duarte S, Rosalen P, Hayacibara M, ... JC-A of O, 2006 undefined. The influence of a novel propolis on mutans streptococci biofilms and caries development in rats. <https://doi.org/10.1016/j.archoralbio.2005.06.002>
20. Barrientos L, Herrera CL, Montenegro G, Ortega X, Veloz J, Alvear M, et al. Chemical and botanical characterization of Chilean propolis and biological activity on cariogenic bacteria *Streptococcus mutans* and *Streptococcus sobrinus*. <https://doi.org/10.1590/S1517-83822013000200038>
21. Besra M, Kumar V. Antimicrobial Activity of Essential Oils and Herbal Extracts Against Etiological Agent of Dental Caries. *J Essent Oil-Bearing Plants*. 2016 Oct 2;19(7):1807–15. <https://doi.org/10.1080/0972060X.2015.1029988>
22. Soumya M, Biological KN-IJ of, 2021 undefined. An overview of functional genomics and relevance of glycosyltransferases in exopolysaccharide production by lactic acid bacteria. Elsevier [Internet]. 2021 [cited 2022 Nov 24]; Available from: <https://www.sciencedirect.com/science/article/pii/S014181302101360X>
<https://doi.org/10.1016/j.ijbiomac.2021.06.131>
23. Alviano D, pharmaceutical CA-C, 2009 undefined. Plant extracts: search for new alternatives to treat microbial diseases. ingentaconnect.com [Internet]. 2009 [cited 2022 Nov 24]; Available from:
<https://www.ingentaconnect.com/content/ben/cpb/2009/00000010/00000001/art00008>
<https://doi.org/10.2174/138920109787048607>
24. Jubair N, Rajagopal M, ... SC-E-B, 2021 undefined. Review on the antibacterial mechanism of plant-derived compounds against multidrug-resistant bacteria (MDR). hindawi.com [Internet]. 2021 [cited 2022 Nov 24]; Available from:
<https://www.hindawi.com/journals/ecam/2021/3663315/> <https://doi.org/10.1155/2021/3663315>
25. Nugraha A, Damayanti Y, Wangchuk P, Molecules PK-, 2019 undefined. Anti-Infective and Anti-Cancer Properties of the *Annona* Species: Their Ethnomedicinal Uses, Alkaloid Diversity, and Pharmacological Activities. mdpi.com [Internet]. 2019 [cited 2022 Nov 24]; Available from: <https://www.mdpi.com/587354>
<https://doi.org/10.3390/molecules24234419>
26. Nwodo UU, Obiyeke GE, Chigor VN, Okoh AI. Assessment of tamarindus indica extracts for antibacterial activity. *Int J Mol Sci*. 2011;12(10). <https://doi.org/10.3390/ijms12106385>
27. Pandey R, Dubey R, Biotechnology SS-AJ of, 2010 undefined. Phytochemical and antimicrobial studies on essential oils of some aromatic plants. ajol.info [Internet]. 2010 [cited 2022 Nov 24];9(28):4364–8. Available from:
<https://www.ajol.info/index.php/ajb/article/view/82664>
28. Amir M, Mujeeb M, Khan A, Ashraf K, Sharma D, Aqil M. Phytochemical analysis and in vitro antioxidant activity of *Uncaria gambir*. *Int J Green Pharm*. 2012;6(1). <https://doi.org/10.4103/0973-8258.97136>
29. Zhang Q, Zhao JJ, Xu J, Feng F, Qu W. Medicinal uses, phytochemistry and pharmacology of the genus *Uncaria*. Vol. 173, *Journal of Ethnopharmacology*. 2015. <https://doi.org/10.1016/j.jep.2015.06.011>
30. Rukachaisirikul V, Trisuwan K, Sukpondma Y, Phongpaichit S. A new benzoquinone derivative from the leaves of *Garcinia parvifolia*. *Arch Pharm Res*. 2008;31(1). <https://doi.org/10.1007/s12272-008-1114-9>

Figures

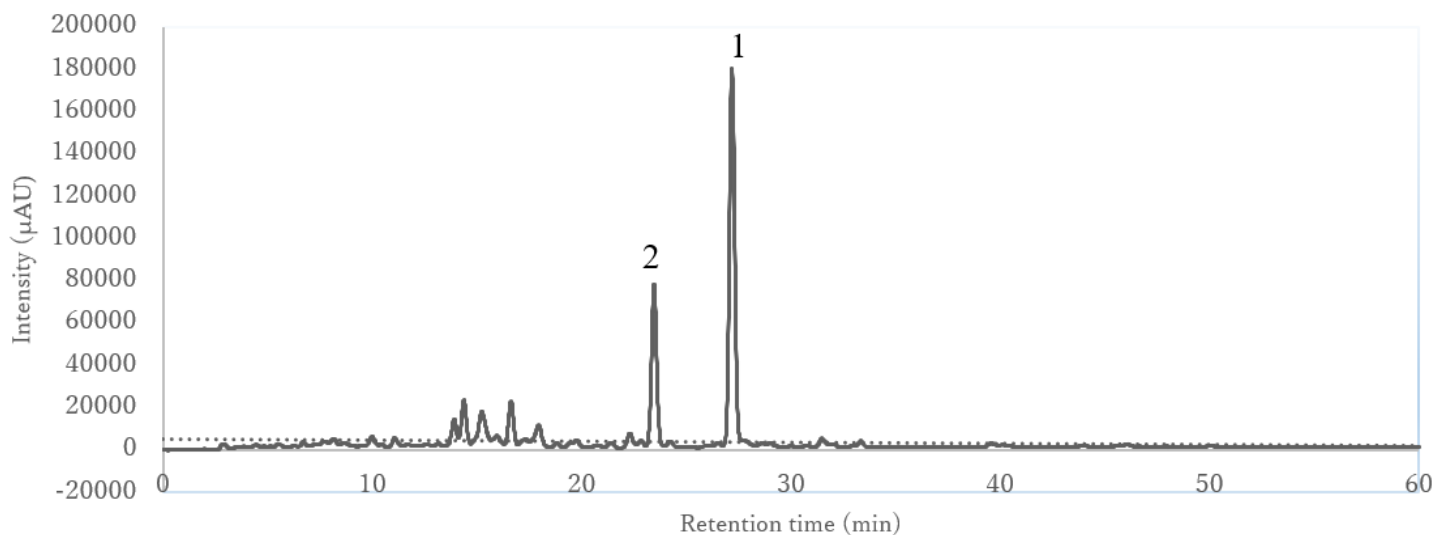


Figure 1

High-performance liquid chromatography chromatogram of *G. parvifolia* hexane precipitation..

1, Garcidepsidone B; 2, garcidepsidone A. conditions: Column : Sunniest C18,5 μm, Analysis time:40 min, detector wavelength : 280 nm Flow late : 1.0 ml/min, Gradient program MeOH:0.05 %TFAaq.=80 %:20 % to 100 %:0 % (60 min)

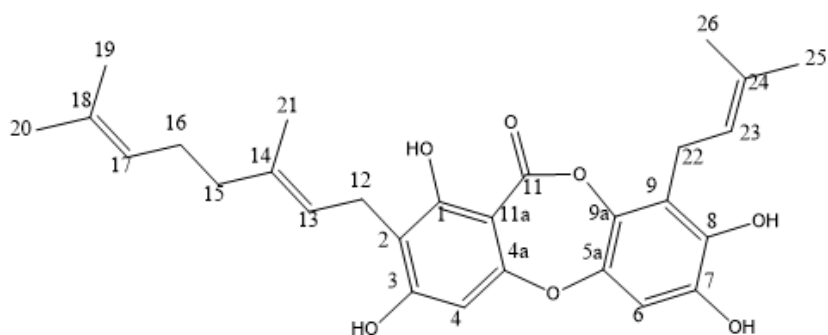


Figure 2

Compound **1** (Garcidepsidone B)

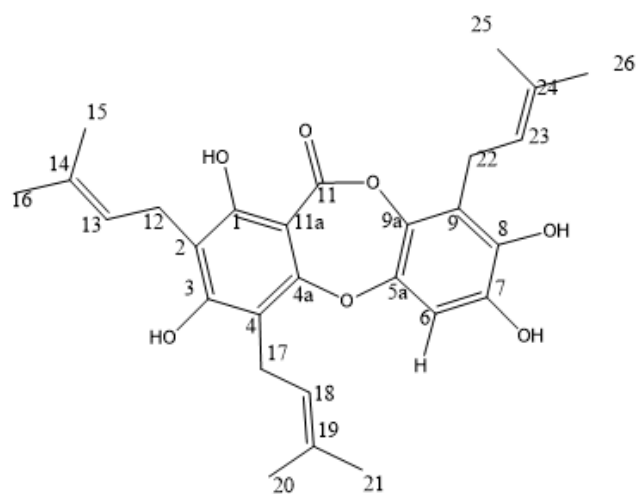


Figure 3

Compound **2** (Garcidepsidone A)

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