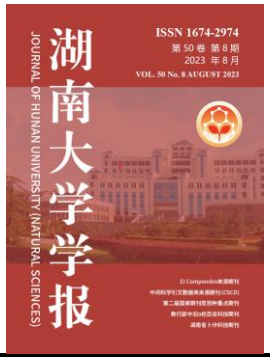

湖南大学学报（自然科学版）
Journal of Hunan University (Natural Sciences)

第 50 卷 第 8 期
2023 年 8 月

Available online at http://jonuns.com/index.php/journal/index

Vol. 50 No. 8
August 2023

Open Access Article

https://doi.org/10.55463/issn.1674-2974.50.8.9

Chemical Compounds and Pharmaceutical Properties of *Rhodomyrtus Tomentosa*: A Traditional Medicinal Herb from South Kalimantan, Indonesia

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Received: May 24, 2023 / Revised: June 18, 2023 / Accepted: July 10, 2023 / Published: August 31, 2023

Abstract: *Rhodomyrtus tomentosa* is an herbal plant that grows in Indonesia, especially in South Kalimantan, with the local name Karamunting. More than 100 compounds have been identified from the leaves, stems, buds, barks, roots, fruits, aerial parts, and flowers of this plant. Phloroglucinols, flavonoids, terpenoids, anthracene glycosides, tannins, and lipids are the groups of compounds that have been identified. The pharmacological and biological effects of extracts or isolated compounds from these plants are known to have anti-inflammatory, anti-cancer, antioxidant, antibacterial, antimalarial, antiviral, antifungal, and other activities. Rhodomyrtone is a bioactive compound from the phloroglucinols group, which is the most widely isolated and has several bioactivities as an antibacterial, anti-inflammatory, anticancer, cytotoxic, and antidepressant agent. Leaf ethanol extract is the most frequently studied extract and has bioactivity as an antibacterial, biocontrol, antioxidant, and cytotoxic agent.

Keywords: anti-cancer, antioxidant, bioactivity, *Rhodomyrtus tomentosa*.

毛白桃树的化学成分和药物特性：印度尼西亚南加里曼丹的传统药草

摘要：毛桃金娘（毛红桃）是一种草本植物，生长于印度尼西亚，尤其是南加里曼丹，当地名称为卡拉文丁。已从该植物的叶、茎、芽、树皮、根、果实、地上部分和花中鉴定出100多种化合物。间苯三酚、类黄酮、萜类化合物、蒽苷、单宁和脂质是已鉴定的化合物组。已知这些植物的提取物或分离的化合物具有抗炎、抗癌、抗氧化、抗菌、抗疟、抗病毒、抗真菌和其他活性的药理和生物学作用。红桃香酮是一种来自间苯三酚类的生物活性化合物，是分离最广泛的化合物，具有抗菌、抗炎、抗癌、细胞毒和抗抑郁等多种生物活性。叶乙醇提取物是最常研究的提取物，具有抗菌、生物防治、抗氧化剂和细胞毒剂的生物活性。

关键词： 抗癌, 抗氧化, 生物活性, 毛红桃.

1. Introduction

Rhodomyrtus tomentosa is a plant species from the Myrtaceae family that grows in South Kalimantan, Indonesia. Regional names for this plant include: karamunting (Kalimantan in general, including Sabah and Sarawak), karamuntiang (Minangkabau), kalimuntiong (Riau), harimonting (Batak), and harendong sabrang (Sunda). *R. tomentosa* is known as a potential medicinal plant. The leaves, roots, buds, and fruit of this plant have been used in traditional medicine. This herbal plant can be used to treat stomachaches, dysentery, abscesses, sepsis, antipyretics, antidiarrheals, and antidysentery [1]. *R. tomentosa* is widely distributed in Asia, including Vietnam, Japan, China, the Philippines, Malaysia and Thailand. Based on literature studies, the chemical compounds contained in *R. tomentosa* are obtained from the leaves, stems, bark and twigs, fruit, flowers, and buds. Meanwhile, compounds isolated from *R. tomentosa* include terpenoids, phenols, and lipids [2]. The groups of compounds isolated from *R. tomentosa* are phloroglucinols, flavonoids, terpenoids, anthracene glycoside, tannins, and other compounds [1]. In addition, *R. tomentosa* is used as an antioxidant, antibacterial, anticancer, and anti-inflammatory agent [3].

2. Research Methods

2.1. Data Collection

Data were taken from articles published in journals and scientific reports. The literature search covered various electronic databases such as Science Direct, Pubmed, etc. Literature search uses certain search terms such as "Medicinal plants", "Herbal" and "Traditional medicine", and Herbal plants".

2.2. Data Analysis

This review process uses reliable data and does not use data such as drafts, website articles, preprints of submitted articles, scientific reports, and conference papers.

3. Taxonomy and Botany

Based on literature studies, *R. tomentosa* is a plant species belonging to the kingdom (Plantae), phylum (Magnoliophyta), class (Magnoliopsida), order (Myrtales), family (Myrtaceae), and genus (Rhodomyrtus). *R. tomentosa* is a small bush that can grow up to 1 m, has pink flowers, and the fruit can be eaten [4]. *R. tomentosa* can be small or large, with a height of up to 12 feet. Leaf length of 2 to 3 cm with width can reach 1 inch. The leaves can be left alone, two or three. The petals are white outside with purplish red or all pink. The fruit is round in purple, with 3 or 4 cells, covered with persistent petal lobes, ½ inch wide, soft with two rows of seeds in each cell, and can be eaten [5].

3.1. Isolation of Compound from Plant Parts

3.1.1. Leaves

According to [6], triterpenes were isolated from petrol extracts of *R. tomentosa* leaves, namely lupeol [7], β-amyrin (2), β-amyrenonol (3β-hydroxyolean-12-en-11-one) (3), and betulin (4). Subsequently in 1976, Hui isolated the triterpenoid compound from the petrol extract of the leaves and stem of *R. tomentosa*. The isolated compounds were 21αH-hop-22(29)-en-3β,30-diol (5), 3β-hydroxy-21αH-hop-22(29)-en-30-al (6), 3β-acetoxy-11α,12α-epoxyoleanan-28,13β-olide (7), 3β-acetoxy-12α-hydroxyoleanan-28,13β-olide (8), and 3β-acetoxy-12-oxo-oleanan-28,13β-olide (9). Compounds (6) and (9) are new, whereas (5), (7), and (8) are well known compounds. Compound (6) from the leaves and (9) from the stem of *R. tomentosa* [8]. In addition to compounds 1-9, Hui also isolated betulonic (10), betulinic (11), and oleanolic acid (12) from the stem. From leaf ethanol extracts, betulinic (11), ursolic (13), and aliphitolic acids (14) were isolated [8]. Furthermore, four new compounds were isolated from the acetone extract of *R. tomentosa* leaves [9]. The new compounds are named rhodomyrtosone A (15), B (16), C (17), and D (18). In addition, compounds that have been isolated include rhodomyrtone (19), combretol (20), 3,3',4-tri-O-methylellagic acid (21), endoperoxide G3 (22), (6R,7E,9R)-9-hydroxy-4,7-megastigmadien-3-one (23), dan α-tocopherol (24) [9]. Apart from acetone extract, rodomyrtone (19) was isolated from ethyl acetate extract from the leaves of *R. tomentosa* [4].

Meanwhile, the compound from the ethanol extract of *R. tomentosa* leaves was also isolated [10]. The dry extract was dissolved in dimethylsulfoxide (DMSO) and then fractionated and purified with MPLC. Bioactive compounds were isolated using antibacterial misguided fractionation. The isolated compounds were [6,8-dihydroxy-2,2,4,4-tetramethyl-7-(3-methyl-1-oxobutyl)-9-(2-methylpropyl)-4,9-dihydro-1H-xanthene-1,3(2H)-di-one] or rhodomyrtone (19). The structure of these compounds was determined by conventional means using 1R and 2D NMR and comparing it with the literature that has been previously reported [10].

Tomentosone A (25) and B (26) were two phloroglucinols isolated from dichloromethane (CH_2Cl_2) extracts from *R. tomentosa* leaves. The structures of the two compounds were elucidated using NMR 2D spectroscopy [11]. Tomentodiones A (27)

and B (28) were isolated from leaf extract ethanol [12]. These compounds were meroterpenoid groups. Tomentosones A (25) and B (26) were also isolated with these compounds [12]. According to [13], several compounds were isolated from the ethanol extract of *R. tomentosa* leaves. The new compounds isolated were the acylphloroglucinol group, namely tomentosone C (29) and the flavonol glycoside group, myricetin-3,7,3-trimethyl ether 5′-O-β-glucopyranoside (30), and twelve known compounds, namely rhodomyrtone (19) [4], watsonianone C (31) [14], rhodomyrtosone C (17) [9], naringenin (32) [15], dihydroquercetin-4′-methyl ether (33) [16], myricetin (34) [17], quercetin (35) [18], 4,8,9,10-tetrahydroxy-2,3,7-trimethoxyanthracene-6-O-β-D-glucopyranoside (36) [18], 2,4,7,8,9,10-hexahydroxy-3-methoxyanthracene-6-O-α-L-rhamnopyranoside (37) [18], myricetin-3,7,3′-trimethyl ether (38) [19], trichocarpine (39), and gallic acid (40) [11]. Furthermore, meroterpenoid compounds were isolated from the ethanol extract of *R. tomentosa* leaves [12]. The isolated compounds were tomentosenol A (41), 4S-focifolidione (42), and 4R-focifolidione (43) [20].

Myricetin 3-O-α-L-furanoarabinoside (44) was also isolated from the leaves [1]. Other compounds isolated from *R. tomentosa* leaf extract were tomentodiones A (27), B (28), C (45), and D (46), rhodomyrtials A (47) and B (48), and rhodomentone A (49) [21], rhodomentones A (49) and B (50) [22], and tomentodiones E (51), F (52), G (53), H (54), I (55), J (56), K (57), L (58), and M (59) [23]. Rhodomyrtosones G (60) and H (61), rhodomyrtone (19), tomentose B (26), and rhodomyrtosone C (17) were isolated from leaf hexane extracts [24]. Furthermore, seven compounds were isolated from the phloroglucinol derivative named tomentodiones N (62), O (63), P (64), Q (65), R (66), S (67), and T (68) [25], as well as eleven known compounds, rhodomyrtosones A (15), B (16), C (17), D (18), and rhodomyrtone (19) [9]; tomentodione A (27) and B (28) [12]; rhodomyrtosone I (69) [26]; 4S-focifolidione (42) [20]; watsonianone A (70) [14] and [27]; rhodomyrtosone G (60) [24]. The compounds were isolated from leaves using the supercritical fluid CO_2 method.

The first meroterpenoid triketone-sesquiterpene was isolated from *R. tomentosa* were rhodomyrtusial A (71), B (72), and C (73), syncarpic acid derivate compounds, namely callistrilone A (74), rhodomyrtosone A (15), tomentodione M (59), and myrtucommulone K (75); and several biogenetically related dihydropyran isomers namely 7-αH-rhotomentodione A (76), 7-αH-rhotomentodione B (77), 7-βH-tomentodione Q (78), and 7-βH-tomentodione R (79) [28]. Tomentodione E (51), myrtucommulone K (75), tomentodione B (28), tomentodione C (45), and tomentosenol A (41) were isolated from leaf ethanol extract [29].

Meanwhile, rhodomyrtosone B (16) was an acylphloroglucinol compound isolated from the leaves of *R. Tomentosa* by [30] based on the method reported by [9]. The raw ethanol extract was fractionated with *n*-hexane and EtOAc. The *n*-hexane fraction was passed into the chromatography column to obtain rhodomyrtosone B (16) as determined by HPLC. In addition, myricetin 3-O-β-D-glucoside (80) and myricetin 3-O-α-L-rhamnoside (81) were isolated from the leaves [2].

3.1.2. Stems and Rods

Friedelin (82), lupeol (1), α-amyrin (83), taraxerol (84), betulin-3-acetate (85), and betulin (4) were isolated from the stem [6]. The compounds isolated from *R. tomentosa* rods extracted with CH_2Cl_2 and Me_2CO were 3,3',4,4'-tetra-*O*-methylflavellagic acid (86), trans-triacontyl-4-hydroxy-cinnamate (87), 3-*O*-*(E)*-coumaroyloleanolic acid (88), (-)-(2*R*,3*R*)-1,4-O-diferuloylsecoisolariciresinol (89), arjunolic acid (90), 4-hydroxy-3-methoxybenzoic acid (91), and gallic acid (40) [26].

3.1.3. Bark and Twigs

The compound 5-hydroxy-3,3',4',5',7-pentamethoxyflavone or combretol (20) is a phenolic compound isolated from the bark and twigs of *R. tomentosa*. Bark and twigs were extracted with *n*-hexane followed by ethyl acetate [31].

3.1.4. Fruits

Seven compounds were isolated from the methanol extract of *R. tomentosa* dried green fruit, namely stigmast-4-en-3-one (92), rhodomyrtone (19), rhodomyrtosone I (69), rhodomyrtosone D (18), oleanolic acid (12), methyl gallate (93), and 3-O-methylellagic acid 4-*O*-α-rhamnopyranoside (94) [26]. Triflouroacetic acid: methanol (1:9) extract from *R. tomentosa* fruit yielded anthocyanin compounds including cyanidin-3-*O*-glucoside (95), peonidin-3-*O*-glucoside (96), malvidin-3-*O*-glucoside (97), petunidin-3-*O*-glucoside(98),delphinidin-3-*O*-glucoside (99), and pelargonidin-3-glucoside (100) [3]. Piceatannol (101) was isolated from fruit extract (0.4 g) by freeze-dried fruit mixed with 8 mL of acetone: water: acetic acid in a ratio of50:49:1 (v/v/v), then shaken, and centrifuged. Supernatant and residue are further extracted until a compound was obtained [32].

The dried berry from *R. tomentosa* was extracted with 95% ethanol with reflux (70 ^{o}C). The extract obtained was evaporated under vacuum at 50 ^{o}C. The extract obtained from evaporation was then extracted with petroleum ether. The identified compounds were flavonoid compounds such as kaempferol (102), quercetin-7,4'-diglucoside (103), dihydromyricetin (104), vitexin (105), myricetin (34), and quercetin (35) [17]. Meanwhile, watsonianone A (70) was a

phloroglucinol derivative isolated in different parts of *R. tomentosa* [27] and [25]. It was isolated from the fruit [27], and later from the leaves [25].

Piceatannol (101) and piceatannol-4'-*O*-*β*-D-glucopyranoside (106) were obtained from the ethanol extract of *R. tomentosa* [33]. As reported in [34], the *R. tomentosa* fruit consisted of dietary fibre (69.94–87.43% of Recommended Daily Intake (RDI)), α-tocopherol (38.90–51.87% of RDI), manganese (>100% of RDI), copper (44.44% of RDI), protein (2.63% of RDI), lipid (1.59–3.5% of RDI) and sugars (5.65% of RDI). Linoleic acid was the main fatty acid in fruit, accounting for 75.36% of total fatty acids. Total phenolics (49.21 ± 0.35 mg gallic acid equivalent (GAE) / g dry weight) resulted in high antioxidants (431.17 ± 14.56 μmol Trolox equivalent (TE) / g dry weight) [34].

3.1.5. Flowers

Malvidin-3-glucoside (107) was identified from *R. tomentosa* flowers [35]. In addition, other compounds isolated from flowers include pelargonidin-3,5-biglucoside (108), delphinidin-3-galactoside (109), and cyanidin-3-galactoside (110) [1, 2].

3.1.6. Aerial Parts

Aerial parts that were percolated with methanol obtained anthracene glycoside compounds. These compounds were 4,8,9,10-tetrahydroxy-2,3,7-trimethoxyanthracene-6-O-β-D glucopyranoside (36) and 2,4,7,8,9,10-hexahydroxy-3-methoxyanthracene-6-O-*α*-L-rhamnopyranoside (37). Other compounds isolated from the aerial parts were quercetin (35), myricitrin (111), and (3S,5R,6R,7E,9S)-megastiman-7-ene-3,5,6,9-tetrol (112) [18].

3.1.7. Buds

Kaempferol 3-*O*-*β*-sambubioside (113) is a flavonol glycoside isolated from the methanol extract of *R. tomentosa* buds. The structure of the compound was analyzed by 1H- and 13C-NMR [36].

3.1.8. Stem Bark

Two new compounds were isolated derived from phloroglucinol from the methanol extract of *R. tomentosa* stem bark [37]. The new compounds are (±)-rhodomyrtosone F (114) and (±)-calliviminone C (115). In addition, known compounds such as betulinic acid (11) [38], ursolic acid-3-acetate (116) [39], ursolic acid (13) [39], and 1-(2,4,6-trihydroxyphenyl)-1-hexanone (117) [40] were also isolated from these new compounds.

3.1.9. Roots

Tomentoid A (118) and tomentoid B (119) are two new compounds isolated from the ethanol extract of the root of *R. tomentosa* [41].

4. Pharmacological Effects of *R. Tomentosa*

4.1. Antibacterial Effect

The bioactivity of rhodomyrtone (19) was tested on bacteria. This compound has bioactivity against *Eschericia coli* and *Staphylococcus aureus* [4]. Furthermore, the antibacterial activity of ethanol extract from *R. tomentosa* leaves was tested against Gram-positive bacteria [10]. The results of that research showed good antibacterial activity based on the values of minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC). MIC and MBC values are shown in Table 1.

In addition, antibacterial tests were also conducted for the fractions [10]. The ethyl acetate and *n*-hexane fractions showed significant antibacterial activity.

Table 1 Antibacterial test results of the ethanol extract of *R. tomentosa* on several pathogenic bacteria

Type of bacteria	MIC (mg/ml)	MBC (mg/ml)
S. aureus MRSA1 Methicillin-resistant clinical isolate	0.03	0.03
S. aureus MRSA2 Methicillin-resistant clinical isolate	0.25	1.0
S. aureus MRSA3 Methicillin-resistant clinical isolate	0.06	0.5
S. aureus MRSA4 Methicillin-resistant clinical isolate	0.06	0.25
S. aureus MRSA27 Methicillin-resistant clinical isolate	0.06	0.25
S. aureus MRSA28 Methicillin-resistant clinical isolate	0.06	0.12
S. aureus SH1000	0.06	0.12
S. epidermidis biofilm negative (ATCC 12228)	0.25	1.00
S. epidermidis biofilm positive (ATCC 35984)	0.12	0.5
Streptococcus gordonii	0.06	0.12
Streptococcus mutans	0.06	0.06
S. pneumoniae capsule negative (D39)	0.03	0.03
S. pneumoniae capsule positive (D39Δcps)	0.03	0.03
Streptococcus pyogenes	0.06	0.12
Streptococcus salivarius	0.25	0.50

The *n*-hexane fraction had MIC (μg/ml) and MBC (μg/ml) values in *Streptococcus mutans*, *Streptococcus salivarius*, and *Streptococcus gordonii*, respectively, 7.8 and 62.5, 15.6 and 31.2, 62.5 and 62.5. Meanwhile, the ethyl acetate fraction had MIC (μg/ml) and MBC (μg/ml) values in *S. mutans*, *S. salivarius*, and *S. gordonii*, respectively, 3.9 and 62.5, 62.5 and 62.5, 15.6 and 31.2. Furthermore, rhodomyrtone (19) was

isolated from an ethanol extract of *R. tomentosa* leaves and showed strong antibacterial activity against Gram-positive bacteria compared to reference antibiotics (vancomycin). Rhodomyrtone (19) has an antibacterial effect with MIC values = 0.19-1.56 μg/ml and MBC = 0.39-25 μg/ml in Gram-positive bacteria. The MIC and MBC values of rhodomyrtone (19) for some pathogenic bacteria are shown in Table 2 [10].

Table 2 MIC and MBC values of rhodomyrone against pathogenic bacteria

Bacteria	**MIC/MBC (μg/ml)**		
	Rhodomyrtone	**Antibiotic**	
		Penicilin G	**Vancomycin**
Bacillus cereus	0.39/0.39	0.062/0.062	
Bacillus subtilis	0.39/0.78	0.062/0.062	
Enterococcus faecalis	1.56/12.50	ND	ND
Methicillin-resistant *S. aureus* (n = 4)	0.39–0.78/0.39–0.78	-	1.25/125
Staphylococcus aureus ATCC 25923	0.39/0.39	-	0.62/1.25
Staphylococcus epidermidis biofilm positive (ATCC 35984)	0.39/25	-	0.78/1.56
Streptococcus gordonii	0.19/1.56	0.031/0.031	
Streptococcus mutans	0.19/1.56	0.031/0.031	
Streptococcus pneumoniae capsule positive	0.39/1.56	0.015/0.062	
Streptococcus pyogenes (n = 2)	0.39–0.78/1.56	0.015/0.015	
Streptococcus salivarius	0.39/1.56	0.062/0.062	

Leaf ethanol extract has good activity against isolates of *S. pyogenes* with MIC and MBC values by 3.91–62.5 μg/mL and 3.91–62.5 μg/mL, respectively. Meanwhile, rhodomyrtone (19) also has good activity against isolates of *S. pyogenes* with MIC and MBC values by 0.39-1.56 μg/mL and 0.39-1.56 μg/ml, respectively [42]. Previously, the antibiotic and anti-infectious potential of rhodomyrtone (19) was studied in *S. pyogenes* (bacterial pathogen). Rhodomyrtone (19) was isolated from the leaves of *R. tomentosa*. It was revealed that rhodomyrtone (19) has both antimicrobial and anti-infective activities [43]. Furthermore, as reported in [44], leaf ethanol extract showed antibacterial activity against *S. aureus* ATCC 25923, *S. mutans* (clinical isolate), and *Candida albicans* ATCC 90028 with MIC values of 31.25, 15.62, and 1000 μg/ml, respectively. Apart from ethanol extract, rhodomyrtone (19) has antibacterial activity against *S. aureus* ATCC 25923 and *S. mutans* with MIC values of 0.78 and 0.39 μg/ml, respectively.

Antibacterial activity test for leaves ethanol extract and rhodomyrtone (19) against 24 clinics of methicillin-resistant S. aureus (MRSA) and *S. aureus* was conducted by [45]. The MIC and MBC values of the leaf ethanol extract against 24 clinical MRSA isolates and *S. aureus* were around 312-624 μg/ml and 39-78 μg/ml, respectively. The MIC and MBC values of rhodomyrtone (19) against S. aureus and MRSA NPRC 001R were 0.5 and 1, and 0.5 and 1 μg/ml, respectively. Meanwhile, the MIC and MBC values of vancomycin (reference) against *S. aureus* ATCC 29213 and MRSA NPRC 001R were 0.5 & 1 and 0.5 & 1 μg/ml, respectively. These results indicate that rhodomyrtone (19) is an active compound in the ethanol extract from *R. tomentosa* leaves, which has antibacterial activity against all clinical MRSA isolates.

In addition, ethanol extract showed good antibacterial activity against MRSA and *S. aureus* ATCC 29213 with MIC values of 31.25 - 6.25 and MBC value was 250 μg/ml. Whereas, the MIC and MBC values of rhodomyrtone (19) were 0.5 μg/ml and 2 μg/ml, respectively. These results indicate that rhodomyrtone (19) has greater antibacterial potential than ethanol extract [46]. Other studies reported that ethanol extracts from the leaves of *R. tomentosa* and rhodomyrtone have antibacterial activity against *Propionibacterium acnes* using the broth macrodilution method. The test results showed that the MC_{50} values of the ethanol extract and rhodomyrtone were 32 and 0.5 μg/ml, respectively. Meanwhile, the IC_{50} values of the cytotoxicity test of ethanol extract and rhodomyrtone on human normal fibroblasts respectively was 476 and more than 200 μg/mL. This showed that both of them have very low cytotoxic properties to be applied as topical therapeutic anti-acne agents [47].

The antibacterial activity of rhodomyrtone (19), acylphloroglucinols isolated from the leaves of *R. tomentosa*, was tested on an important hospital-acquired antibiotic-resistant pathogenic bacteria. Rhodomyrtone (19) has antibacterial activity against key antibiotic-resistant pathogens, including epidemic meticillin-resistant S. aureus (EMRSA), vancomycin-intermediate *S. aureus*, and vancomycin-resistant enterococcal strains. The survival ability of strains EMRSA-16, Enterococcus faecalis ATCC 29212, and VRE-3 was reduced after treatment with rhodomyrtone at 1 x (0.5 μg/ml), 2x, 4x and 8x MIC for 24 h [48]. In addition, rhodomyrtone inhibits the biosynthesis of Staphyloxanthin in *S. aureus* bacteria. Rhodomyrtone-treated *S. aureus* showed reduced pigmentation, and rhodomyrtone (19) treatment caused an increase (depending on dose) in the susceptibility of the pathogen to H_2O_2 and singlet oxygen killing [49].

Colloidal silver nanoparticles (AgNPs) were manufactured in a cost effective and environmentally friendly manner. Acetone extract from *R. tomentosa* was used as an agent for reducing and capping the

reagent time during AgNP synthesis. The concentration of acetone extract of *R. tomentosa* and temperature played an important role in the green synthesis of AgNPs. AgNPs have antibacterial activity against *S. aureus* with MIC and MBC values 3.1-6.2 and 6.2-50 μg/ml, respectively [50]. Ethanol extract from the leaves of *R. tomentosa* has the potential as an antibacterial and anti-inflammatory agent against all Staphylococcus isolates. The extract showed good antibacterial activity with MIC values (16–64 μg/ml) and MBC (64 -> 128 μg/ml). The extract also has anti-denaturing protein activity, stabilizes human red blood cells, heals bovine mastitis, and reduces inflammatory injury caused by bacterial infections [51]. The ethanolic extract from *R. tomentosa* has the potential to be used as a biocontrol agent for Listeria monocytogenes (pathogenic bacteria) with MIC and MBC values of 16 to 32 μg/mL and 128 to 512 μg/mL, respectively [52].

As explained in [12], rhodomyrtone (19) and tomentosone C (29) have antibacterial activity. Rhodomyrtone (19) showed significant antibacterial activity against the Gram-positive microbe *S. aureus* with MIC = 1.83 μg/ml, which was almost the same as the positive control (erythromycin) with MIC = 1.83 μg/ml. Tomentosone C (29) also showed antibacterial activity with MIC = 3.66 μg/ml [13].

Leaf ethanol extract increased the killing activity of human neutrophils against *E. coli* O157:H7. *E. coli* O157:H7 is one of the most virulent causative agents of foodborne disease. Percentage survival of *E. coli* O157:H7 and E. coli ATCC 25922 after treatment for 45 min with neutrophils in the presence of the extract at 125–250 μg/mL was 58.48%–50.28% and 69.13%–35.35%, respectively. At 250 μg/mL of *R. tomentosa*, crystal violet of *E. coli* O157:H7 and *E. coli* ATCC 25922 increased to 40.07% and 36.16%, respectively [53].

Ethanol extract from the leaves of *R. tomentosa* had antibacterial activity against *S. pneumoniae* clinical isolates with MIC/MBC values ranging from 16 to 512 μg/ml. Meanwhile, the MIC and MBC values of purified and synthetic rhodomyrtone (19) were almost the same for clinical *S. pneumoniae* isolates, ranging from 0.125 to 4 μg/ml. Rhodomyrtone (19) showed anti-pneumococcal activity against clinical isolates. Rhodomyrtone-treated pneumococci had a small number of capsules when measured by a colorimetric assay and visualized by electron microscopy. Rhodomyrtone (19) has potential as an antibacterial *S. pneumoniae* agent in the future if there is resistance to conventional antibiotics that are used to cure infections [54]. Acetone extract of *R. tomentosa* has been used as a reducing capping agent for the manufacture of gold, silver, and gold-silver-alloy nanoparticles. *R. tomentosa* acetone extract capped on silver and Au-Ag-Alloy nanoparticles showed antibacterial activity against *E. coli* [55].

R. tomentosa extracts (crude, hexane, ethyl acetate, and methanol) from the leaves, stems, and fruits exhibited antibacterial activity. The inhibition zones (mm) and EC50 of the extracts are presented in Table 3. Table 3 shows that methanol extracts from leaves, fruits, and stems had stronger inhibitory activity than n-hexane and ethyl acetate extracts against *S. aureus* and *E. coli*. Meanwhile, the antioxidant test showed that the methanol partition extract of leaves, fruits, and stems showed good antioxidant activity [56]. Ethanol extract from leaves showed antibacterial activity against Gram-positive pathogenic bacteria. The extract showed good antibacterial activity against Streptococcosis in Nile tilapia (fish pathogen), with minimum inhibitory concentrations (MICs) ranging from 7.8-62.5 μg/ml [57].

Table 3 Inhibition zones (mm) and EC_{50} of the *R. tomentosa* extracts

Extracts	***R. tomentosa* extracts**	***S. aureus* (mm)**	***E. coli* (mm)**	**EC_{50}**
Leaves	Crude	11	10	262.1
	n-Hexane	6	8	567.3
	Ethyl acetate	7	8	321.4
	Methanol	10	10	144.2
Fruits	Crude	9	9	189.7
	n-Hexane	13	11	782.1
	Ethyl acetate	10	9	64.6
	Methanol	16	12	106.9
Stems	Crude	11	12	189.2
	n-Hexane	7	9	77.7
	Ethyl acetate	6	7	53.8
	Methanol	10	13	43.7

In vitro, rhodomyrtone (19) and vancomycin were tested for their bioactivity against *Clostridium difficile*. The MIC and MBC for rhodomyrtone (19) and vancomycin for ten C. difficile isolates showed that the MICs from rhodomyrtone (19) for C. difficile vegetative cells were 0.625-2.5 mg/L. It was comparable to vancomycin (1.25 mg/L), but the MBCs of rhodomyrtone (1.25-5 mg/L) were lower than vancomycin (5 mg/L to > 40 mg / L; P <0.001). In addition, the rhodomyrtone (19) killing time test against bacteria is ≥ 99% for up to 4 h4 hours. This suggests that rhodomyrtone (19) should be further investigated as a potential study for C. difficile infection (CDI) [58].

Meanwhile, reporter gene assays and proteomic profiling in *B. subtilis* showed that rhodomyrtone (19)

did not address classic antibiotic targets, such as translation, transcription, or DNA replication, but acted on the cytoplasmic membrane. For *S. aureus*, rhodomyrtone (19) reduces the membrane potential in a few seconds and at low doses causes the release of ATP and even excretion of cytoplasmic proteins, but does not induce pore formation as with nisin [59]. Rhodomyrtone (19) and nisin were known to have MRSA activity by the broth microdilution method. The MIC and MBC values of rhodomyrtone (19) against MRSA NPRC R001 were 1.0 and 4.0 g/ml, respectively. Whereas the MIC value of nisin against MRSA NPRC R001 was 256 μg/ml [60].

Anticarier test results from rhodomyrtone (19) showed that rhodomyrtone (19) suppresses acid production by *S. mutans*. This bacterium is a cariogenic agent in humans that inhibits the activity of enzymes responsible for acid production and tolerance, including membrane-bound enzymes F-ATPase, phosphotransferase systems, glycolysis enzymes glyceraldehyphosphate dehydrogenase (GAPDH), and pyruvate kinase (PK), in the cytoplasm with an IC_{50} value of 24 μM, 19 μM, 23 μM, and 28 μM, respectively. The anticarier activity test of rhodomyrtone (19) was performed by measuring pH reduction, enzyme activity test, and fluorescence staining [61].

Rhodomytosone B (16) has antibacterial activity against Gram-positive pathogenic bacteria that cause serious infections, including MRSA with MIC values of 0.62-1.25 μg/mL and vancomycin-resistant Enterococcus faecium (VRE) with MIC values of 2.5 μg/mL. Rhodomyrtosone B (16) bactericidal activity was faster against MRSA than vancomycin. Membrane-targeting experiments revealed that rhodomyrtosone B (16) had significant antibacterial activity with potential disruption of bacterial membranes and increased membrane permeability. Rhodomyrtosone B (19) has a weak cytotoxicity against mammalian cells (IC50 > 14 μg/ml) and has a favorable specificity against selected Gram-positive bacterial membranes compared to red blood cells [30].

4.2. Antimalarial Effect

Tomentosone A (25) and B (26) were isolated by [11] from CH_2Cl_2 extract of *R. tomentosa* leaves, which showed antimalarial activity. Tomentosone A (25) can inhibit the growth of chloroquine-resistant and sensitive strains of *Plasmodium falciparum* with IC_{50} values of 1.49 ± 0.45 μM (n = 2) and 1.0 μM (n = 1); however, tomentosone B (26) was less active.

4.3. Anti-Inflammatory Effect

Methanol extract from the leaves of *R. tomentosa* can inhibit the production of NO and PGE2 in lipopolysaccharide (LPS)-activated RAW264.7 cells and peritoneal macrophages in a dose-dependent manner. Methanol extract has anti-inflammatory effect by suppressing the Syk/Src/NF-kB and IRAK1/IRAK4/AP-1 pathways and was further developed as a herbal plant for preventive and/or healing purposes in various inflammatory diseases [62].

Rhodomyrtone (19) shows anti-inflammatory bioactivity where it is able to suppress the expression of TNF-α in THP-1 monocytes stimulated with high doses of heat-killed MRSA at a concentration of 108 to 109 cfu/ml [63]. Investigation of the protective effect of ethanol extract from the fruits of *R. tomentosa*, piceatannol (101) and piceatannol-4'-O-β-D-glucopyranoside (106) on UVB-induced damage and inflammation in cultured NHEK showed that 80% ethanol extract and piceatannol protected against UVB-induced cytotoxicity in NHEK [33]. Watsonianone A (70), a phloroglucinol derivative isolated from *R. tomentosa* fruit, also exhibited anti-inflammatory activity. Watsonianone A (70) inhibited RSV-induced NO production, with an inhibitory concentration of 37.2 ±1.6 μM. Watsonianone A (70) can attenuate RSV-induced inflammation by suppressing ROS-sensitive inflammatory signaling [27].

Tomentodione P (64), Q (65), and T (68), rhodomyrtosone I (69), rhodomyrtone (19), rhodomyrtosone B (16), watsonianone A (70), and rhodomyrtosone G (60) had potential anti-inflammatory activities with IC_{50} values of 3.80 ± 0.43 to 74.30 ± 1.26 μM. Meanwhile, IC_{50} (μM) value of indomecatin (positive control) was 126.25 ± 1.26. The presence of phloroglucinol derivatives allowed these compounds to exhibit anti-inflammatory activity [25].

Rhodomyrtone (19) inhibited 724/1587 transcripts >2-fold altered by IL-17A/TNF ($p<0.01$). These results were based on RNA-seq analysis of monolayer primary keratinocytes treated with IL-17A/TNF. The potential of rhodomytone as an anti-inflammatory agent was tested in vivo in mice. Test results showed that rhodomyrtone (19) reversed imiquimod-induced skin hyperplasia and epidermal thickening ($p<0.001$). Meanwhile, leaf extracts from *R. tomentosa* showed anti-inflammatory activity in rats. Inhibition (%) of the extracts were *n*-hexane extract (44.75%), ethyl acetate extract (56.93%), methanol extract (63.556%), and sodium diclofenac as a standard anti-inflammatory drug (64.82%). These results indicated that all leaf extracts from *R. tomentosa* (Aiton) Hassk. had anti-inflammatory activity [64].

4.4. Antitumor/Anticancer

Tomentodione D (46) shows inhibitory activity in metastatic tumors, especially in DLD-1 cells, by suppressing the activation of matrix metalloproteinase (MMP)-2 and MMP-9 [21]. Rhodomentones A (49) and B (50) showed weak inhibitory activity against human lung cancer cell lines [22]. Tomentosenol A

(41), 4S-focifolidione (42), and 4R-focifolidione (43) have been tested for cytotoxicities against four tumor cells, namely MCF-7, NCI-H460, SF-268, and HepG-2, with IC_{50} values were 5.8 ± 0.4 μM, 1.3 ± 0.1 μM, 1.9 ± 0.1 μM, and 1.7 ± 0.1 μM. This test used cisplatin as a positive control [20]. The anti-proliferative activity of rhodomyrtone (19) was tested on HaCaT cells [65]. Test results showed that the percentage of anti-proliferative activity of rhodomyrtone on HaCaT cells atconcentrations of 2-32 μg/ml after 24, 48, and 72 h ranged from 13.62-61.61%, 50.59-80.16%, and 61.82-85.34%, respectively [65].

The effect of rhodomyrtone (19) on the production of enzymes and biofilm formation by clinical isolates was studied in [66]. The level of hydrolysis of the lipase and protease enzymes significantly decreased with the treatment of rhodomyrtone (19) at 0.125-0.25 mg/mL ($p < 0.05$). The lipolytic zone was significantly reduced in all isolates and the proteolytic activity was decreased in only 50% of isolates. Rhodomyrtone (19) at 1/16 MIC and 1/8 MIC caused a significant reduction in biofilm formation in clinical isolates ($p < 0.05$). The percentage of survival of *Propionibacterium acne* biofilms until maturity in the treatment with compounds at 4 and 8 MIC ranged between 40% and 85%. The properties of rhodomyrtone (19) showed the way for developing new anti-acne agents [66]. Meanwhile, the results of research [67] showed that rhodomyrtone (19) inhibited A431 cell metastasis by reducing MMP-2/9 activities and expression by inhibiting ERK1/2, p38, and FAK/Akt signaling pathways via NF-κB activitie.

Ethyl acetate extract from the root of *R. tomentosa* has antiproliferative activity against HepG2 (IC_{50} 11.47 ± 0.280 mg/mL), MCF-7 (IC_{50} 2.68±0.529 mg/mL), and HT 29 (IC_{50} 16.18 ± 0.538 mg/mL) after 72 h of treatment [68]. The anticancer activity of tomentodione M (59) was investigated in [69]. Tomentodione M (59) is a syncarpic acid-conjugated monoterpene compound isolated from the petroleum ether soluble fraction of 95% ethanol extract of the leaves of *R. tomentosa*. Test results showed that tomentodione M (59) increased the cytotoxicity of chemotherapy drugs such as docetaxel and doxorubicin in MCF-7/MDR and K562/MDR cells, which were dose- and time-dependent. Tomentodione M (59) reduced the formation of colonies and increased apoptosis in MCF-7/MDR and K562/MDR cells treated with docetaxel, and it increased intracellular accumulation of doxorubicin and rhodamine 123 in multidrug- resistant cancer cells (MDR) by reducing drug efflux mediated by P-gp. Tomentodione M (59) decreased the expression of P-gp mRNA and protein by inhibiting p38 MAPK signaling [69].

Rhodomyrtone (19) showed bioactivity in inhibiting the proliferation of human epidermoid carcinoma A431 cells (IC_{50} = 8.04 ± 0.11 μg/mL), inducing cell apoptosis through the activation of caspase-7 and poly (ADP-Ribose) polymerase cleavage, and causing cell cycle arrest at the G1 phase [70].

Tomentodione O (63), P (64), Q (65), R (66), S (67), and T (68), tomentodione A (27), rhodomyrtosone I (69), rhodomyrtone (19), rhodomyrtosone B (16), rhodomyrtosone G (60), and A (15) showed largely differential cytotoxicities against HeLa cells with IC_{50} values ranging from 0.33 ± 0.05 to 68.20 ± 0.23μM. Tomentodione S (67) and T (68), rhodomyrtosone I (69), rhodomyrtone (19), and rhodomyrtosone B (16) showed inhibitory activities with IC_{50} values < 10μM. Tomentodione P (64) and Q (65) showed moderate cytotoxicities toward HeLa cells. The presence of isobutyryl may cause these compounds to have cytotoxic activities [25].

4.5. Antioxidant Effect

Antioxidant activity of anthocyanin extract and ascorbic acid was tested using the DPPH assay, ABTS assay, reduction assay, and ORAC test [3]. The IC_{50} values of DPPH radical-scavenging activity for anthocyanin extract and ascorbic acid were 6.27 ± 0.25 μg/ml and 17.4 ± 0.31 μg/ml, respectively. The IC_{50} values of ABTS radical-scavenging activity for anthocyanin extract and ascorbic acid were 90.3 ± 1.52 μg/ml and 206 ± 2.37 μg/ml, respectively. The IC_{50} values of reducing power activity for anthocyanin extract and ascorbic acid were 51.7 ± 0.74 μg/ml and 31.3 ± 0.93 μg/ml, respectively. The IC_{50} values of ORAC activity for anthocyanin extract and ascorbic acid were 9.29 ± 0.08 μmol TE/mg and 1.79 ± 0.03 μmol TE/mg, respectively [3].

The antioxidants of air-dried berries from *R. tomentosa* taken from China were tested in [17]. The air-dried berries were mashed (40 mesh) and extracted with 95% ethanol using reflux at a temperature of 70 ^{o}C. Flavonoid-rich extracts were tested for DPPH radical scavenging ability (DPPH-RSA), OH radical scavenging ability (OH-RSA), O_2-radical scavenging ability (O_2-RSA), ferric-reducing antioxidant power (FRAP), and lipid peroxidation inhibition. DPPH-RSA test results from flavonoid-rich extract at concentrations of 2.0 to 20 μg/mL were 11.6-73.3%, while ascorbic acid ranged from 15.9-87.1%. EC_{50} values were 10.97 ± 0.18 μg/mL and 8.03 ± 0.11 μg/ml for total flavonoids extract and ascorbic acid, respectively. Meanwhile, the OH-RSA test results at a concentration of 300 μg/mL for flavonoid-rich extract and ascorbic acid were 58.77% and 85.73%, respectively. EC_{50} values were 217.73 ± 3.46 μg/ml and 116.37 ± 1.40 μg/ml for total flavonoids extract and ascorbic acid, respectively. O_2-RSA test results showed EC_{50} values of total flavonoids extract, and ascorbic acid were 214.83 ± 6.54 μg/ml and 60.55 ± 1.35 μg/ml, respectively ($p < 0.05$). FRAP test results at a concentration of 40 μg/ml for total flavonoid extract and ascorbic acid (positive control) were 0.656

and 1.356, respectively. The reduction ability of flavonoid- rich extract was lower than that of ascorbic acid. EC_{50} (μg/ml) of flavonoid- rich extract and ascorbic acid were 28.67 ± 1.37 and 13.75 ± 0.88 ($p < 0.05$). Meanwhile, the results of the lipid peroxidation inhibiting test for the total flavonoid extract and BHT were 101.08 meq/kg and 73.34 meq/kg, respectively. This indicated that the lipid peroxidative inhibition effect of the flavonoid-rich extract was stronger than that of BHT [17].

The methanol extract of *R. tomentosa* root had antioxidant activity. Antioxidant activity was monitored by DPPH, copper reducing antioxidant capacity (CUPRAC) and β-carotene bleaching assay. EC_{50} of antioxidant test of the methanol extract were 110.25 ± 0.005 mg/ml (DPPH), 53.84 ± 0.004 (CUPRAC) and 58.62 ± 0.001 (β-carotene bleaching) [68].

4.6. Antivirus Effect

Myrtucommulone K (75) displayed comparable anti-respiratory syncytial virus (RSV) activity to that of ribavirin (positive control) with IC_{50} value of 10 μM. This indicated that the side chains of the phloroglucinol moiety may induce changes in their antiviral activity [29].

4.7. Anti-Fungus Effect

The test of the effect of extracts on *C. albicans* for germ tube production, adherence ability, and biofilm was carried out by [71]. The sample used was *R. tomentosa* leaf extracted with 95% ethanol. Suppression of germ tube production after exposure to extracts (256 μg/ml) for 30 minutes was significantly increased compared to cells not exposed ($P < 0.05$). Pathogenic microbes showed a reduction in adherence ability to the surface in a dose-dependent manner compared to controls ($P < 0.05$). The biofilm-forming ability of microorganisms was reduced up to 42.31-64.58% ($P < 0.05$) if exposed to extracts (512-1024 μg/ml) at 48 h. Phagocytosis and killing activity of neutrophils against the microbe increased when exposed to extract 50 μg/ml compared to the control ($P < 0.05$).

4.8. Other Biological Effects

The alkaline phosphatase activity, collagen synthesis, and mineralization of the nodules of MC3T3-E1 osteoblastic cells were tested for several compounds isolated from *R. tomentosa* aerial parts [18]. Test results showed that 4,8,9,10-tetrahydroxy-2,3,7-trimethoxyanthracene-6-O-β-D-glucopyranoside (36), 2,4,7,8,9,10-hexahydroxy-3 -methoxyanthracene-6-O-α-L-rhamnopyranoside (37), and (3S, 5R, 6R, 7E, 9S)-megastiman-7-ene-3,5,6,9-tetrol (111), respectively, had alkaline phosphatase activity, collagen synthesis, and mineralization of the nodules of MC3T3-E1 osteoblastic cells compared to those of the control [18]. Meanwhile, rhodomyrtusial A (71) and B (72), and 7-βH-tomentodione Q (78) showed acetylcholinesterase (AChE) inhibitory activity [28].

Rhodomyrtone (19) was able to prevent source consumption decrease, decreased social behavior, increase of immobility in the forced swimming test, and suggesting a protective effect of rhodomyrtone against depression-like behaviors. Additionally, rhodomyrtone (19) prevented the impalement of spatial memory in mice exposed to chronic unpredictable mild stress (CUMS). Rhodomyrtone (19) administration also reversed dendritic spine density defects in CUMS. Furthermore, rhodomyrtone (19) inhibited the increase of GSK3β activity and reversed the decrease of brain-derived neurotrophic factor and PSD-95 in CUMS mice. Therefore, the antidepressant effect of rhodomyrtone (19) involved the regulation of neurogenesis, neural survival, and synaptic plasticity in the hippocampus [72].

The list of chemical compounds isolated from *R. tomentosa* is shown in Figure 1. The bioactivity of the compounds and extracts is shown in Table 4.

Table 4 List of chemical compounds and their bioactivity

Compound/Extract	Bioactivity	Origin/part/extraction	Reference
Lupeol (1)		Hongkong/leaves/petrol	[6]
Lupeol (1)		Hongkong/stems	[6]
β-amyrin (2)		Hongkong/leaves/petrol	[6]
β-amyrenonol (3*β*-hydroxyolean-12-en-11-one) (3)		Hongkong/leaves/petrol	[6]
Betulin (4)		Hongkong/leaves/petrol	[6]
Betulin (4)		Hongkong/stems	[6]
21αH-hop-22(29)-en-3β,30-diol (5)		Hongkong/leaves/petrol	[8]
3β-hydroxy-21αH-hop-22(29)-en-30-al (6)		Hongkong/leaves/petrol	[8]
3β-acetoxy-11α,12α-epoxyoleanan-28,13β-olide (7)		Hongkong/leaves/petrol	[8]
3β-acetoxy-12α-hydroxyoleanan-28,13β-olide (8)		Hongkong/leaves/petrol	[8]
3β-acetoxy-12-oxo-oleanan-28,13β-olide (9)		Hongkong/stems/petrol	[8]
Betulonic acid (10)		Hongkong/stems	[8]
Betulinic acid (11)		Hongkong/leaves/ethanol	[8]
Betulinic acid (11)		Hongkong/stems	[8]

Continuation of Table 4

Betulinic acid (11)		Stem bark/methanol	[37]
Oleanolic acid (12)		Hongkong/stems	[8]
Oleanolic acid (12)		Thailand/fruits/methanol	[26]
Ursolic acid (13)		Hongkong/leaves/ethanol	[8]
Ursolic acid (13)		Stem bark	[37]
Aliphitolic acid (14)		Hongkong/leaves/ethanol	[8]
Rhodomyrtosone A (15)		Thailand/leaves/acetone	[9]
Rhodomyrtosone A (15)		Leaves	[28]
Rhodomyrtosone B (16)		Thailand/leaves/acetone	[9]
Rhodomyrtosone B (16)	Rhodomytosone B has antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) with MIC values 0.62-11.25 µg / mL and vancomycin-resistant Enterococcus faecium (VRE) with MIC values of 2.5 µg/mL	China/leaves/95% ethanol, n-heksan, and EtOAc	[30]
Rhodomyrtosone C (17)		Thailand/leaves/acetone	[9]
Rhodomyrtosone C (17)		China/leaves/ethanol	[13]
Rhodomyrtosone C (17)		Thailand/leaves/hexane	[24]
Rhodomyrtosone C (17)		China/leaves/supercritical fluid CO2	[25]
Rhodomyrtosone D (18)		Thailand/leaves/acetone	[9]
Rhodomyrtosone D (18)		China/leaves/supercritical fluid CO2	[25]
Rhodomyrtosone D (18)		Thailand/fruits/methanol	[26]
Rhodomyrtone (19)	Rhodomyrtone has bioactivity against *Escherichia coli* and *Staphylococcus aureus*.	Indonesia/leaves/ethyl acetate	[4]
Rhodomyrtone (19)		Thailand/leaves/acetone	[9]
Rhodomyrtone (19)	Antibacterial in some gram-positive bacteria (MIC = 0,19-1,56 µg/ml, MBC = 0,39-25 µg/ml)	Thailand/leaves/95% ethanol	[10]
Rhodomyrtone (19)	Rhodomyrtone has both antimicrobial and anti-infective activities on Streptococcus pyogenes.	Thailand/leaves/ethanol	[43]
Rhodomyrtone (19)	MIC and MBC values of rhodomyrtone against *S. aureus* and MRSA NPRC 001R were 0.5 & 1 and 0.5 & 1 µg / ml, respectively	Leaves/ethanol	[45]
Rhodomyrtone (19)	MIC and MBC values of rhodomyrtone against *S. aureus* were 0.5 µg/ml and 2 µg/ml, respectively.	Leaves/ethanol	[46]
Rhodomyrtone (19)	Rhodomyrtone has good anti-S. pyogenes activity against isolates of *Streptococcus pyogenes* with MIC and MBC values were 0.39-1.56 µg / mL and 0.39-1.56 µg / ml, respectively	Thailand/leaves/ethanol	[42]
Rhodomyrtone (19)	Rhodomyrtone has antibacterial activity against *Propionibacterium acnes* with an MC_{50} value of 0.5 µg/ml	Leaves	[47]
Rhodomyrtone (19)	Rhodomyrtone has antibacterial activity against *S. aureus* ATCC 25923 and *S. mutans* with MIC values of 0.78 and 0.39 µg/ ml, respectively.	Thailand/leaves/ethanol	[44]
Rhodomyrtone (19)		Thailand/dried green fruit/methanol	[26]
Rhodomyrtone (19)	Survival ability of EMRSA-16 strains, *Enterococcus faecalis* ATCC 29212 and VRE-3 was reduced after treatment with rhodomyrtone at 1 x (0.5 µg / ml), 2x, 4x and 8x MIC for 24 h.	Leaves	[48]
Rhodomyrtone (19)	Inhibiting biosynthetic Staphyloxanthin in *Staphylococcus aureus* bacteria	Leaves	[49]
Rhodomyrtone (19)	*Anti-imflamatory:* Suppress expression of TNF-α in THP-1 monocytes stimulated with high doses of heat-killed MRSA (108 to 109 cfu / ml)	Leaves	[63]
Rhodomyrtone (19)	MICs of rhodomyrtone for *Clostridium difficile* vegetative cells (0.625–2.5 mg/L) was comparable with that of vancomycin (1.25 mg/L). MBCs of rhodomyrtone (1.25–5 mg/L) was significantly lower than those for vancomycin (5 mg/L to > 40 mg/L; $P < 0.001$)	Leaves	[58]
Rhodomyrtone (19)	Rhodomyrtone showed significant antibacterial activity against gram-positive microbe *S. aureus* with MIC = 1.83 µg/ml, which was almost the same as positive control (erythromycin) with MIC = 1.83 µg/ml	China/leaves/ethanol	[13]
Rhodomyrtone (19)	Percentage anti-proliferative activity of rhodomyrtone on HaCaT cells at the concentrations of 2-32 µg/ml after 24, 48, and 72	Leaves/acetone	[65]

	h ranged from 13.62-61.61%, 50.59-80.16%, and 61.82-85.34%, respectively		
Rhodomyrtone (19)	*Anti-imfalamatory:* Rhodomyrtone inhibited 724/1587 transcripts >2-fold altered by IL-17A/TNF ($p < 0.01$). Rhodomyrtone reversed imiquimod-induced skin hyperplasia and epidermal thickening ($p < 0.001$)	Leaves/acetone	[73]
Rhodomyrtone (19)	Inhibits the production of lipases, proteases, and biofilm formation from *Propionibacterium acnes*	Leaves/95% ethanol	[66]
Rhodomyrtone (19)	Rhodomyrtone inhibited A431 cell metastasis by reducing MMP-2/9 activities and expression through inhibiting ERK1/2, p38 and FAK/Akt signaling pathways via NF-κB activitie	Leaves	[67]
Rhodomyrtone (19)	MIC and MBC values of purified and synthetic rhodomyrtone are similar to *Streptococcus. clinical* pneumoniae isolates, ranging from 0.125 to 4 μg / ml.	Leaves/ethanol	[54]
Rhodomyrtone (19)	Inhibiting proliferation of human epidermoid carcinoma A431 cells ($IC50 = 8.04 \pm 0.11$ μg/mL), Inducing cell apoptosis through the activation of caspase-7 and poly (ADP-Ribose) polymerase cleavage, and causing cell cycle arrest at the G1 phase	Leaves	[70]
Rhodomyrtone (19)	*Reporter gene assays and proteomic profiling experiments:* For *Bacillus subtilis*, rhdomyrtone does not address classical antibiotic targets like translation, transcription or DNA replication, but acts at the cytoplasmic membrane. In Staphylococcus aureus, rhodomyrtone decreases the membrane potential within seconds and at low doses, causes release of ATP and even the excretion of cytoplasmic proteins (ECP), but does not induce pore-formation as for example nisin	Leaves	[59]
Rhodomyrtone (19)	Antidepressant effect of rhodomyrtone involves the regulation of neurogenesis, neural survival, and synaptic plasticity in the hippocampus		[72]
Rhodomyrtone (19)	Rhodomyrtone has the potential as an anticaries agent against *S. mutans*.	Vietnam/Leaves	[61]
Rhodomyrtone (19)	MIC and MBC value of rhodomyrtone against MRSA NPRC R001 were 1.0 and 4.0 μg/ml, respectively. While, MIC value of nisin against MRSA NPRC R001 was 256 μg/ml.	Thailand/leaves/ethanol	[60]
Combretol (20)		Indonesia/bark and twigs/hexane then ethyl acetate	[31]
Combretol (20)		Thailand/leaves/acetone	[9]
3,3',4-Tri-O-methylellagic acid (21)		Thailand/leaves/acetone	[9]
Endoperoxide G (22)		Thailand/leaves/acetone	
(6R,7E,9R)-9-Hydroxy-4,7-megastigmadien- 3-one (23)		Thailand/leaves/acetone	
α-Tocopherol (24)		Thailand/leaves/acetone	
Tomentosone A (25)	Tomentosone A is able to inhibit the growth of chloroquine and sensitive strains of the malaria *Plasmodium falciparum* with IC50 values of 1.49 ± 0.45 μM ($n = 2$) and 1.0 μM ($n = 1$), respectively.	Leaves/dichloromethane	[11]
Tomentosone A (25)		China/leaves/ethanol	[12]
Tomentosone B (26)	Tomentosone B is less active in inhibiting the growth of chloroquine and sensitive strains of the malaria *Plasmodium falciparum*	Leaves/dichloromethane	[11]
Tomentosone B (26)		China/leaves/ethanol	[12]
Tomentosone B (26)		Thailand/leaves/hexane	[24]
Tomentodione A (27)		China/leaves/ethanol	[12]
Tomentodione A (27)		Leaves	[21]
Tomentodione B (28)		Leaves	[21]
Tomentodione B (28)		China/leaves/ethanol	[12]
Tomentodione B (28)		China/leaves/supercritical fluid CO2	[25]
Tomentodione B (28)		China/leaves/95% ethanol	[29]
Tomentosone C (29)	Tomentosone C showed antibacterial activity with	China/leaves/ethanol	[13]

	MIC = 3.66 μg/ml		
Myricetin-3,7,3′-trimethyl ether 5′-O-β-glucopyranoside (30)		China/leaves/ethanol	[13]
Watsonianone C (31)		China/leaves/ethanol	[13]
Naringenin (32)		China/leaves/ethanol	[13]
Dihydroquercetin-4′-methyl ether (33)		China/leaves/ethanol	[13]
Myricetin (34)		China/leaves/ethanol	[13]
Myricetin (34)		China/Air-dried berries/95% etanol/reflux	[17]
Quercetin (35)		China/leaves/ethanol	[13]
Quercetin (35)		Vietnam/aerial parts/methanol	[18]
Quercetin (35)		China/Air-dried berries/95% ethanol/reflux	[17]
4,8,9,10-Terahydroxy-2,3,7-trimethoxyanthracene-6-O-β-D-glucopyranoside (36)		China/leaves/ethanol	[13]
4,8,9,10-Terahydroxy-2,3,7-trimethoxyanthracene-6-O-β-D-glucopyranoside (36)	4,8,9,10-tetrahydroxy-2,3,7-trimethoxyanthracene-6-O-β-D-glucopyranoside had alkaline phosphatase activity	Vietnam/aerial parts/methanol	[18]
2,4,7,8,9,10-Hexahydroxy-3-methoxyanthracene-6-O-α-L-rhamnopyranoside (37)		China/leaves/ethanol	[13]
2,4,7,8,9,10-Hexahydroxy-3-methoxyanthracene-6-O-α-L-rhamnopyranoside (37)	2,4,7,8,9,10-hexahydroxy-3-methoxyanthracene-6-O-α-L-rhamnopyranoside had collagen synthesis activity	Vietnam/aerial parts/methanol	[18]
Myricetin-3,7,3′-trimethyl ether (38)		China/leaves/ethanol	[13]
Trichocarpine (39)		China/leaves/ethanol	[13]
Gallic acid (40)		China/leaves/ethanol	[13]
Gallic acid (40)		Thailand/stem/CH_2Cl_2 and Me_2CO	[26]
Tomentosenol A (41)		China/leaves/95% ethanol	[29]
Tomentosenol A (41) 4S-focifolidione (42) 4R-focifolidione (43)	IC_{50} cytotoxic activity values of tomentosenol A, 4S-focifolidione, and 4R-focifolidione on four tumor cells namely MCF-7, NCI-H460, SF-268, and HepG-2 were 5.8 ± 0.4 μM, 1.3 ± 0.1 μM, 1.9 ± 0.1 μM, and 1.7 ± 0.1 μM. Cisplatin as positve control	Leaves/ethanol	[20]
4S-focifolidione (42)		China/leaves/supercritical fluid CO2	[25]
Myricetin 3-O-α-L-furanoarabinoside (44)		Leaves	[1]
Tomentodione C (45)		Leaves	[21]
Tomentodione C (45)		China/leaves/95% ethanol	[29]
Tomentodione D (46)	Tomentodione D has inhibitory activity in metastatic tumors, especially in DLD-1 cells by suppressing the activation of matrix metalloproteinase (MMP) -2 and MMP-9	Leaves	[21]
Rhodomyrtial A (47)		Leaves	[21]
Rhodomyrtial B (48)		Leaves	[21]
Rhodomentone A (49)	Rhodomentone A showed weak inhibitory activity against human lung cancer cell lines	China/leaves/ethanol	[22]
Rhodomentone B (50)	Rhodomentone B showed weak inhibitory activity against human lung cancer cell lines	China/leaves/ethanol	[22]
Tomentodione E (51)		China/leaves/95% ethanol	[29]
Tomentodione E (51)		China/leaves/95% ethanol	[23]
Tomentodione F (52)		China/leaves/95% ethanol	[23]
Tomentodione G (53)		China/leaves/95% ethanol	[23]
Tomentodione H (54)		China/leaves/95% ethanol	[23]
Tomentodione I (55)		China/leaves/95% ethanol	[23]
Tomentodione J (56)		China/leaves/95% ethanol	[23]
Tomentodione K (57)		China/leaves/95% ethanol	[23]
Tomentodione L (58)		China/leaves/95% ethanol	[23]
Tomentodione M (59)		China/leaves/95% ethanol	[23]
Tomentodione M (59)	Tomentodione M reverses MDR in cancer cells by decreasing P-gp expression via p38 MAPK inhibition	Leaves/petroleum ether soluble fraction of 95% ethanol extract	[23]
Tomentodione M (59)		Leaves	[28]
Rhodomyrtosone G (60)		Thailand/leaves/hexane	[24]
Rhodomyrtosone H (61)		Thailand/leaves/hexane	[24]
Tomentodione N (62)		China/leaves/supercritical fluid CO_2	[25]

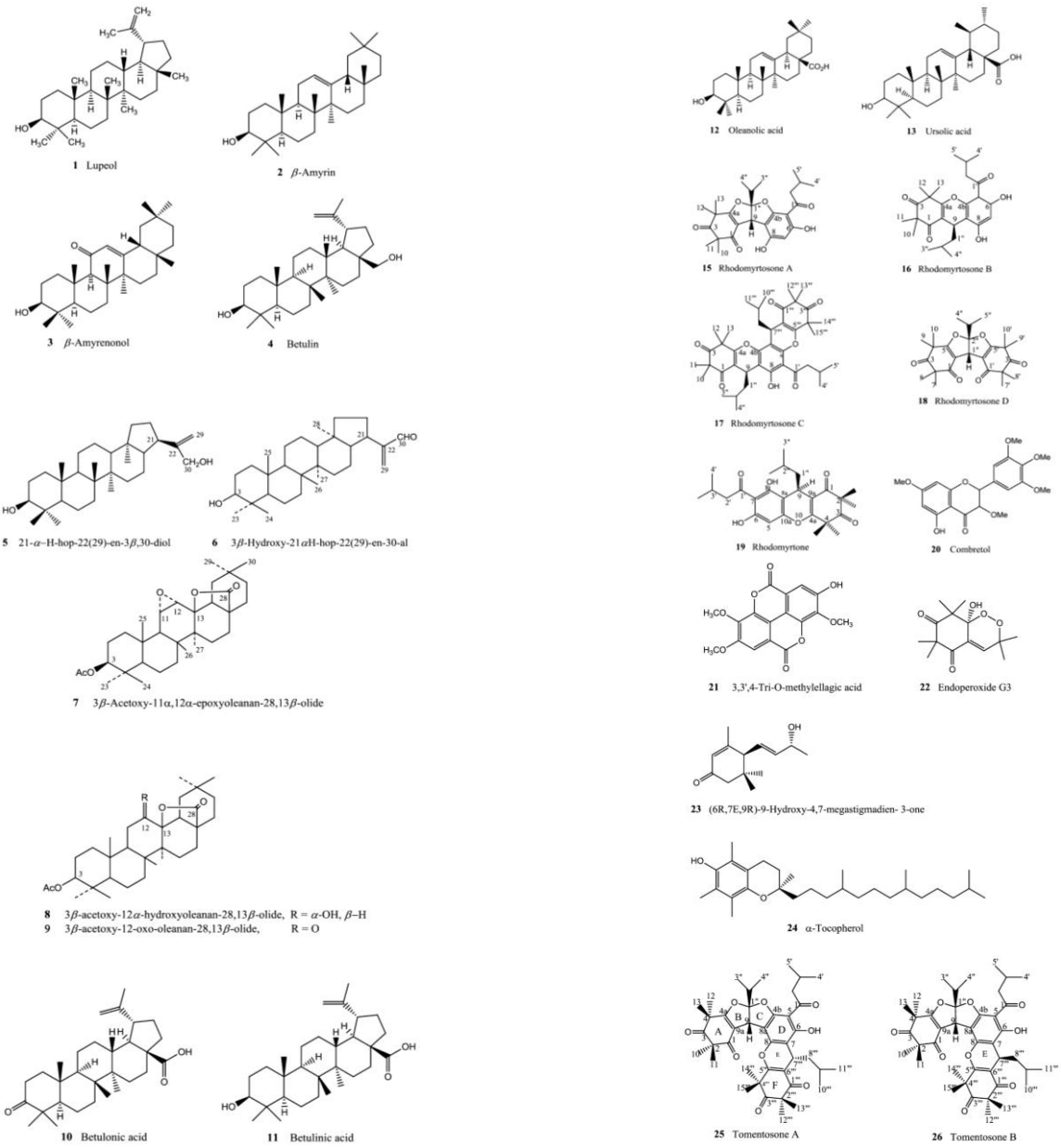
Continuation of Table 4

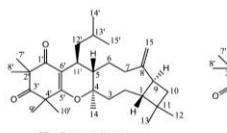
Tomentodione O (63) Tomentodione P (64) Tomentodione Q (65) Tomentodione R (66) Tomentodione S (67) Tomentodione T (68) Tomentodione A (27) Rhodomyrtosone I (69) Rhodomyrtone (19) Rhodomyrtosone B (16) Rhodomyrtosone G (60) Rhodomyrtosone A (15)	*Cytotoxic activity:* Tomentodione O,P,Q,R,S, and T, tomentodione A, rhodomyrtosone I, rhodomyrtone, rhodomyrtosone B, rhodomyrtosone G and A, showed largely differential cytotoxicities against HeLa cells with IC_{50} values ranging from 0.33 ± 0.05 to 68.20 ± 0.23 μM. Tomentodione S and T, rhodomyrtosone I, rhodomyrtone, and rhodomyrtosone B showed inhibitory activities with IC50 values < 10 μM. Tomentodione P and Q showed moderate cytotoxicities toward HeLa cells. *Anti-inflammatory activity:* Tomentodione P, Q and T, rhodomyrtosone I, rhodomyrtone, rhodomyrtosone B, and rhodomyrtosone G had potential anti-inflammatory activities with IC_{50} values of 3.80 ± 0.43 to 74.30 ± 1.26 μM.	China/leaves/supercritical fluid CO_2	[25]
Rhodomyrtosone I (69)		Thailand/buah/methanol	[26]
Watsonianone A (70)	Antiimflamatory	China/leaves/supercritical fluid CO_2	[25]
Watsonianone A (70)	*Antiinflamatory:* Watsonianone A had inhibitory effect on RSV-induced NO production, with inhibitory concentration of 37.2 ±1.6 μM	Fruits	[27]
Rhodomyrtusial A (71)	Rhodomyrtusial A showed acetylcholinesterase (AChE) inhibitory activity	Leaves	[28]
Rhodomyrtusial B (72)	Rhodomyrtusial B showed acetylcholinesterase (AChE) inhibitory activity	Leaves	[28]
Rhodomyrtusial C (73)		Leaves	[28]
Callistrilone A (74)		Leaves	[28]
Myrtucommulone K (75)	Myrtucommulone K displayed comparable anti-RSV activity to ribavirin (positive control) with the IC50 value of 10 μM.	China/Leaves/95% ethanol	[29]
Myrtucommulone K (75)		Leaves	[28]
7-αH-Rhotomentodione A (76)		Leaves	[28]
7-αH-Rhotomentodione B (77)		Leaves	[28]
7-βH-Tomentodione Q (78)	7-*β*H-tomentodione Q showed acetylcholinesterase (AChE) inhibitory activity	Leaves	[28]
7-βH-Tomentodione R (79)		Leaves	[28]
Myricetin 3-O-*β*-D-glucoside (80)		Leaves	[2]
Myricetin 3-O-α-L-rhamnoside (81)		Leaves	[2]
Friedelin (82)		Hongkong/stem	[6]
α-amyrin (83)		Hongkong/stem	[6]
Taraxerol (84)		Hongkong/stem	[6]
Betulin-3-acetate (85)		Hongkong/stem	[6]
3,3',4,4'-tetra-O-methylflavellagic acid (86)		Thailand/stem/CH_2Cl_2 and Me_2CO	[26]
Trans-triacontyl-4-hydroxy-cinnamate (87)		Thailand/stem/CH_2Cl_2 and Me_2CO	[26]
3-O-(*E*)-coumaroyloleanolic acid (88)		Thailand/stem/CH_2Cl_2 and Me_2CO	[26]
(-)-(2R,3R)-1,4-O-diferuloylsecoisolariciresinol (89)		Thailand/stem/CH_2Cl_2 and Me_2CO	[26]
Arjunolic acid (90)		Thailand/stem/CH_2Cl_2 and Me_2CO	[26]
4-hydroxy-3-methoxybenzoic acid (91)		Thailand/stem/CH_2Cl_2 and Me_2CO	[26]
Stigmast-4-en-3-one (92)		Thailand/fruit/methanol	[26]
Methyl gallate (93)		Thailand/fruit/methanol	[26]
3-*O*-Methylellagic acid 4-*O*-α-rhamnopyranoside (94)		Thailand/fruit/methanol	[26]
Cyanidin-3-O-glucoside (95)		China/fruit/triflouroacetic acid: metanol (1:9)	[3]
Peonidin-3-O-glucoside (96)		China/fruit/triflouroacetic acid: metanol (1:9)	[3]
Malvidin-3-O-glucoside (97)		China/fruit/triflouroacetic acid: metanol (1:9)	[3]
Petunidin-3-O-glucoside (98)		China/fruit/triflouroacetic acid: metanol (1:9)	[3]
Delphinidin-3-O-glucoside (99)		China/fruit/triflouroacetic	[3]

		acid: metanol (1:9)	
Pelargonidin-3-glucoside (100)		China/fruit/triflouroacetic acid: metanol (1:9)	[3]
Piceatannol (101)		Vietnam/friut/ freeze-dried	[32]
Piceatannol (101)	*Anti-inflamatory:* Piceatannol memperlihatkan protection of UVB-induced cytotoxicity in NHEK	Japan/Fruits/ethanol	[33]
Kaempferol (102)		China/Air-dried berries/95% etanol /reflux	[17]
Quercetin-7,4'-diglucoside (103)		China/Air-dried berries/95% etanol /reflux	[17]
Dihydromyricetin (104)		China/Air-dried berries/95% etanol /reflux	[17]
Vitexin (105)		China/Air-dried berries/95% etanol /reflux	[17]
Piceatannol-4'-*O*-*β*-D-glucopyranoside (106)	No protection for UVB-induced cytotoxicity in NHEK	Japan/Fruits/ethanol	[33]
Malvidin-3-glucoside (107)		Flowers	[73]
Pelargonidin-3,5-biglucoside (108)		Flowers	[2]
Delphinidin-3-galactoside (109)		Flowers	[2]
Cyanidin-3-galactoside (110)		Flowers	[2]
Myricitrin (111)		Vietnam/aerial parts/methanol	[18]
(3S,5R,6R,7E,9S)-megastiman-7-ene-3,5,6,9-tetrol (112)	(3S,5R,6R,7E,9S)-megastiman-7-ene-3,5,6,9-tetrol had bioacitvity as mineralization of the nodules of MC3T3-E1 osteoblastic cells compared to those of the control	Vietnam/aerial parts/methanol	[18]
Kaempferol 3-O- β –sambubioside (113)		Buds/methanol	[36]
(±)-rhodomyrtosone F (114) and (±)-calliviminone C (115)		Stem bark/methanol	[37]
Ursolic acid-3-acetate (116)		Stem bark/methanol	[37]
1-(2,4,6-trihydroxyphenyl)-1-hexanone (117)		Stem bark/methanol	[37]
Tomentoid A (118) and tomentoid B (119)		Roots/ethanol	[41]
Crude ethanolic extract	Crude ethanolic extract had antibacterial activity against gram-positive bacteria with MIC (mg/ml) and MBC (mg/ml) values were 0.03-0.25 and 0.03-1.0, respectively.	Thailand/leaves/95% ethanol	[10]
Ethyl acetate and hexan extract	Ethyl acetate and hexane fractions showed antibacterial activity. The hexane fraction has MIC (μg/ml) and MBC (μg/ml) values in *Streptococcus mutans*, *Streptococcus salivarius*, and *Streptococcus gordonii*, respectively, 7.8 & 62.5, 15 & 31.2, and 62.5 & 62.5. Meanwhile, the ethyl acetate fraction has MIC (μg/ml) and MBC (μg ml) values in *Streptococcus mutans*, *Streptococcus salivarius*, and *Streptococcus gordonii*, respectively, 3.9 & 62.5, 62.5 & 62.5, and 15.6 & 31.2	Thailand/leaves/95% ethanol	[10]
Acetone extract	The concentration of acetone extract of *Rhodomyrtus tomentosa* and temperature played an important for green synthesis of AgNPs. AgNPs have antibacterial activity against *Staphylococcus aureus* with MIC and MBC values 3.1–6.2 and 6.2–50 μg/ml, respectively	Acetone ekxtract	[50]
	Acetone extract of *Rhodomyrtus tomentosa* capped on silver and Au-Ag-Alloy nanoparticles showed antibacterial activity against *Escherichia coli*.	Acetone extract	[55]
Anthocyanins extract	The IC_{50} value of DPPH radical-scavenging activity for anthocyanins extract and ascorbic acid were 6.27 ± 0.25 μg/ml and 17.4 ± 0.31 μg/ml, respectively. The IC_{50} value of ABTS radical-scavenging activity for anthocyanins extract and ascorbic acid were 90.3 ± 1.52 μg/ml and 206 ± 2.37 μg/ml, respectively. The IC_{50} value of reducing power activity for anthocyanins extract and ascorbic acid were 51.7 ± 0.74 μg/ml and 31.3 ± 0.93 μg/ml, respectively. The IC_{50} value of ORAC activity for	China/fruits/triflouroacetic acid: metanol (1:9)	[3]

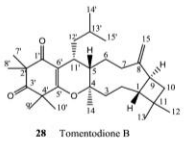
	anthocyanins extract and ascorbic acid were 9.29 ± 0.08 µmol TE/mg and 1.79 ± 0.03 µmol TE/mg, respectively.		
Ethanol extract	MIC and MBC values of leaves ethanol extract on 24 clinical MRSA isolates and *S. aureus* were 312-624 µg/ml and 39-78 µg/ml, respectively.	Leaves/ethanol	[45]
	Ethanol extract showed good antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) *and S. aureus* ATCC 29213 with MIC and MBC values of 31.25 & 6.25 and 250 µg/ml, respectively.	Leaves/ethanol	[46]
	Ethanol extract showed good anti-S. pyogenes activity against isolates of *Streptococcus pyogenes* with MIC and MBC values of 3.91-62.5µg/mL) and MBC, 3.91-62.5 µg/mL), respectivsly.	Thailand/leaves/ethanol	[42]
	Ethanol leaf extract showed antibacterial activity against Staphylococcus aureus ATCC 25923, *Streptococcus mutans* (clinical isolate), and *Candida albicans* ATCC 90028 with the MIC values of 31.25, 15.62, and 1000 µg/ml, respectively.	Thailand/ leaves/ethanol	[44]
	Inhibiting staphylococcal bacteria, MIC (16–64 µg/ml) and MBC (64- > 128 µg/ml)	Leaves /95% ethanol	[51]
	Ethanol extract has antibacterial activity against Propionibacterium acnes with MC50 value of 32 µg/ml	Leaves/ethanol	[47]
	The ethanolic extract from *R. tomentosa* had the potential to be used as a bio-control agent for *Listeria monocytogenes* (pathogenic bacteria) with MIC and MBC values of 16 to 32 µg/mL and 128 to 512 µg/mL, respectively	Thailand/leaves/ethanol	[52]
	Percentage survival of *E. coli* O157:H7 and *E. coli* ATCC 25922 after treated at 45 min with neutrophils in the presence of the extract at 125–250 µg/mL were 58.48%–50.28% and 69.13%–35.35%, respectively. At 250 µg/mL of *R. tomentosa*, crystal violet of *E. Coli* O157:H7 and *E. coli* ATCC 25922 were increased to 40.07% and 36.16%, respectively.	Thailand/leaves/ethanol	[53]
	Ethanol extract showed good antibacterial activity against streptococcosis in Nile tilapia (fish pathogen) with minimum inhibitory concentrations (MICs) ranging from 7.8 to 62.5 µg/ml.	Thailand/leaves/ethanol	[57]
	Ethanol extract from the leaves of *Rhodomyrtus tomentosa* had antibacterial activity against *Streptococcus pneumoniae* clinical isolates with MIC/MBC values ranging from 16 to 512 µg/ml.	Leaves/ethanol	[54]
	Ethanol extract inhibited virulence factors of *Candida albicans*, including germ tube formation, adhesion, and biofilm.	Leaves/ethanol	[71]
Flavonoids rich extract	Reducing power (EC_{50}, 28.67 ± 1.37 µg/mL), scavenging superoxide radicals (EC_{50}, 214.83 ± 6.54 µg/mL), hydroxyl radicals (EC_{50}, 217.73 ± 3.46 µg/mL), DPPH radicals (EC_{50}, 10.97 ± 0.18 µg/mL), and inhibiting lipid peroxidation of total flavonoids extract and BHT were 101.08 meq/kg and 73.34 meq/kg, respectively.	China/Air-dried berries/95%etanol/reflux	[17]
Ethyl acetate extract	*Anticancer:* Ethyl acetate extracts showed anti-proliferative acttivity on HepG2 (IC_{50} = 11.47 ± 0.280 µg/mL), MCF-7 (IC_{50} = 2.68 ± 0.529 µg/mL), and HT29 (IC_{50} = 16.18 ± 0.538 µg/mL) after 72 h of treatment	Root/Ethyl acetate extract	[68]
Methanol extract	*Antioxidant:* DPPH assay (EC_{50} 110.25±0.005 mg/ml), CUPRAC assay (EC_{50} 53.84±0.004) and β-carotene bleaching assay (EC_{50} 58.62±0.001)	Root/methanol	[68]
Methanol extract	Methanol extract showed anti-inflammatory properties by suppressing Syk/Src/NF-kB and IRAK1/IRAK4/AP-1 pathways and will be	Korea/daun/methanol	[62]

	further developed as a herbal remedy for preventive and/or curative purposes in various inflammatory diseases		
Dietary fibre, α-tocopherol, manganese, copper, protein, lipid, sugars, linoleic acid, and total phenolic	Dietary fibre (69.94–87.43% of Recommended Daily Intake (RDI)), α-tocopherol (38.90–51.87% of RDI), manganese (>100% of RDI), copper (44.44% of RDI), protein (2.63% of RDI), lipid (1.59–3.5% of RDI), and sugars (5.65% of RDI). Linoleic acid is the main fatty acid in fruit as much as 75.36% of total fatty acids. Total phenolics (49.21 ± 0.35 mg gallic acid equivalent (GAE) / g dry weight). Total phenolic has high antioxidant activity (431.17 ± 14.56 µmol Trolox equivalent (TE) / g DW)	Vietnam/friuts	[34]
Crude extract, hexane extract, ethyl acetate estract, and methanol extract	Leaves, stems and fruits of *R. tomentosa* showed antimicrobial activity. Methanol partition extract of leaves, fruits and stems showed good antioxidant and antimicrobial activity.	Malaysia/leaves, fruit, and stem/methanol	[56]
n-hexan, ethyl acetate, and methanol extract	*Anti-imflamatory:* The inhibition percentage (%) of R. tomentosa leaf extracts were n-hexane extract (44.75%), ethyl acetate extract (56.93%), methanol extract (63.556%), and sodium diclofenac as a standard anti-inflammatory drug (64, 82%).	Indonesia/leaves/n-hekxane, ethyl acetate, and methanol	[64]

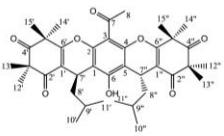




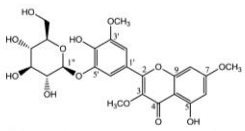
27 Tomentodione A



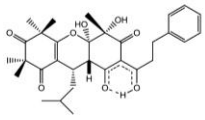
28 Tomentodione B



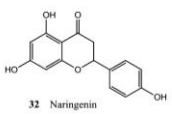
29 Tomentosone C



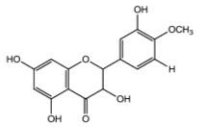
30 Myricetin-3,7,3'-trimethyl ether 5'-O-β–glucopyranoside



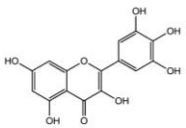
31 Watsonianone C



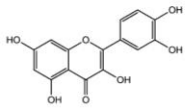
32 Naringenin



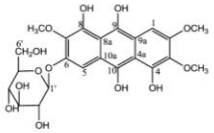
33 Dihydroquercetin-4'-methylether



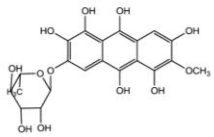
34 Myricetin



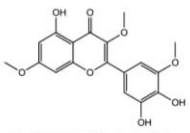
35 Quercetin



36 4,8,9,10-Tetrahydroxy-2,3,7-trimethoxyanthracene-6-O-β-D-glucopyranoside

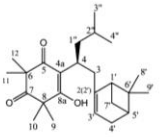


37 2,4,7,8,9,10-Hexahydroxy-3-methoxyanthracene-6-O-α-L-rhamnopyranoside

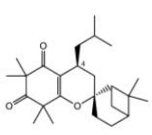


38 Myricetin-3,7,3'-trimethyl ether

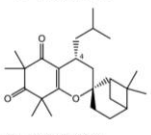
40 Gallic acid



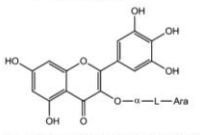
41 Tomentosenol A



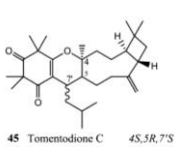
42 4S-Focifolidione



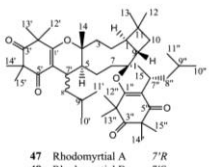
43 4R-Focifolidione



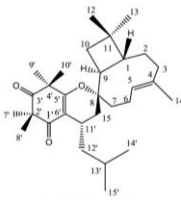
44 Myricetin 3-O-α-L-furanoarabinoside



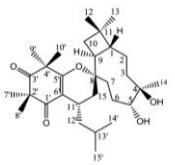
45 Tomentodione C *4S,5R,7'S*
46 Tomentodione D *4S,5R,7'R*



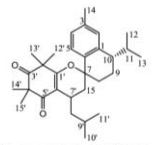
47 Rhodomyrtial A *7'R*
48 Rhodomyrtial B *7'S*



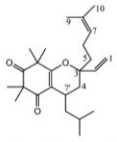
49 Rhodomentone A



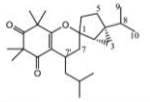
50 Rhodomentone B



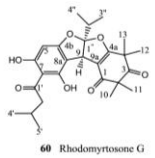
51 Tomentodione E, *7S,7'S,10S*
52 Tomentodione F, *7R,7'R,10S*
53 Tomentodione G, *7R,7'S, 10S*



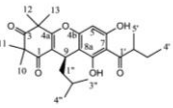
54 Tomentodione H, (+)*3S,7'S*
54a Tomentodione H, (-)*3R,7'R*
55 Tomentodione I, (+)*3R,7'S*
55a Tomentodione I, (-)*3S,7'R*



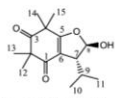
56 Tomentodione J, *1R,2S,4R,7'R*
57 Tomentodione K, *1R,2S,4R,7'S*
58 Tomentodione L, *1S,2S,4R,7'R*
59 Tomentodione M,*1S,2S,4R,7'S*



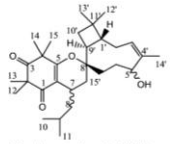
60 Rhodomyrtosone G



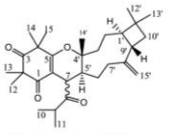
61 Rhodomyrtosone H



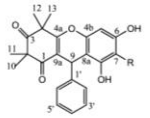
62 Tomentodione N



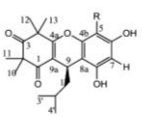
63 Tomentodione O, *7R 5'R*
64 Tomentodione P, *7S 5'S*



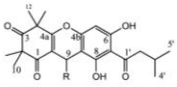
65 Tomentodione Q, *7R*
66 Tomentodione R, *7S*



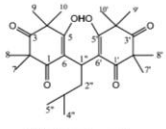
67 Tomentodione S, R= 2 methyl butyryl



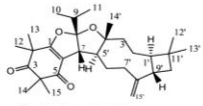
68 Tomentodione T, R= 2-methyl butyryl



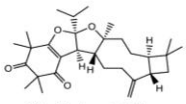
69 Rhodomyrtosone I, R=phenyl



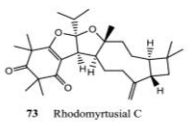
70 Watsonianone A



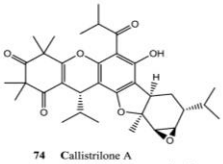
71 Rhodomyrtusial A



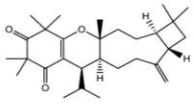
72 Rhodomyrtusial B



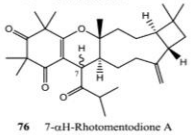
73 Rhodomyrtusial C



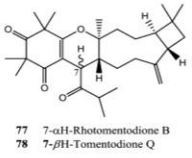
74 Callistrilone A



75 Myrtucommulone K



76 7-αH-Rhotomentodione A
79 7-βH-Tomentodione R



77 7-αH-Rhotomentodione B
78 7-βH-Tomentodione Q

81 Myricetin 3-O-α-L-rhamnoside

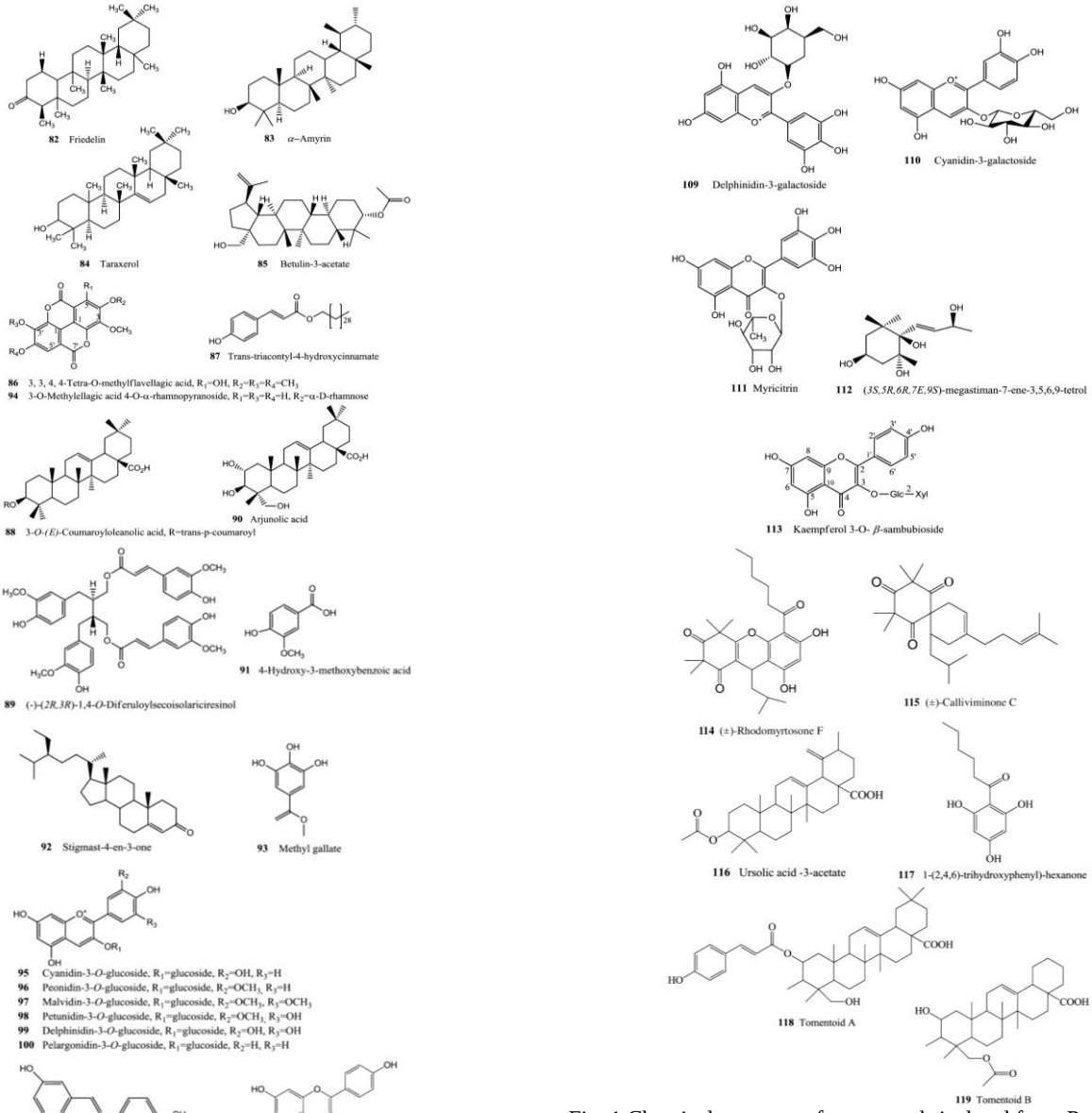


Fig. 1 Chemical structure of compounds isolated from *R. tomentosa*
Note: Structural of components 14, 39, and 80 are not available.

5. Conclusion

R. tomentosa (W. Ait) Hassk is an herbal plant that grows in Indonesia and is used as a traditional medicine by Indonesian people. This herbal plant contains many bioactive compounds with interesting bioactivity. The limitation of this paper is the scientific information from various journals and reports on extracts and compounds isolated from *R. tomentosa* and the bioactivity of these extracts and compounds. This plant has the potential to be developed as a natural remedy through systematic pharmacological and clinical studies. Research on this plant still needs to be continued to find new compounds and related extracts that are useful for health. A combination of compounds or extracts with other drugs can be used to increase the activity of these extracts or compounds. In addition, Structure–Activity Relationship (SAR) analysis of the compounds isolated from *R. tomentosa* needs to be performed to increase the bioactivity of these compounds as antioxidants, antibacterials,

antidiabetics, antifungals, anticancer, antimalarials, and others.

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