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Solophenols B–D and Solomonin: New Prenylated Polyphenols Isolated from Propolis Collected from The Solomon Islands and Their Antibacterial Activity.

Saori Inui,[†] Takahiro Hosoya,[†] Yuko Shimamura,[†] Shuichi Masuda,[†] Takeshi Ogawa,[†] Hirokazu Kobayashi,[†] Kenichi Shirafuji,[‡] Reuben Toli Moli,[§] Ikuko Kozone,[∥] Kazuo Shin-ya,[⊥] and Shigenori Kumazawa[†,*]

[†]Department of Food and Nutritional Sciences, University of Shizuoka, 52-1 Yada, Suruga-ku, Shizuoka 422-8526, Japan

[‡]NPO APSD Japan, SAN-EI STUDIO 6B, 6-7-9 Sagamiono, Minami-ku, Sagamihara, Kanagawa 252-0303, Japan

[§]NGO APSD Solomon, P.O. Box 251, Auki Malaita, the Solomon Islands

[∥]Biomedicinal Information Research Center (BIRC), Japan Biological Informatics Consortium (JBIC), 2-4-7 Aomi, Koto-ku, Tokyo 135-0064, Japan

[⊥]Biomedicinal Information Research Center (BIRC), National Institute of Advanced Industrial Science and Technology (AIST), 2-4-7 Aomi, Koto-ku, Tokyo 135-0064, Japan

Supporting Information

ABSTRACT: Three new prenylated flavonoids, namely, solophenols B (**1**), C (**2**), and D (**3**), as well as a new prenylated stilbene, solomonin (**4**), were isolated from propolis collected from the Solomon Islands. In addition, 17 known compounds were identified. The structures of the new compounds were determined by a combination of methods, including mass spectrometry and NMR. These new compounds and several known compounds were tested for antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*. Most of them exhibited potent antibacterial activity. These findings may indicate that propolis from the Solomon Islands has potential applications as an ingredient in food additives or pharmaceuticals.

KEYWORDS: *Solomon Islands, propolis, solophenol, solomonin, prenylated polyphenols, antibacterial activity*

INTRODUCTION

Propolis is a natural resinous substance collected by honeybees from buds and exudates of certain trees and plants to protect their beehives from pathogens and predators. It is used as folk medicine in many regions of the world and has been reported to display various biological activities such as antibacterial, antioxidative, anti-inflammatory, and anticancer properties.[1−3] Generally, propolis is extensively used in food and beverages to improve health and prevent diseases such as inflammation, heart disease, diabetes, and cancer.[4]

Propolis usually contains a rich variety of chemical compounds such as polyphenols, terpenoids, steroids, and amino acids, depending on the vegetation at the site of collection. Geographical location has a bearing on the chemical composition, thus imparting distinctive qualities to propolis obtained from Europe, South America, and Asia. Propolis from Europe and China contains typical "poplar bud" phenolics such as flavonoid aglycones (flavones and flavanones), phenolic acids, and their esters.[5] In a previous study, we found that propolis from Okinawa, Japan had many prenylflavonoids that have potent antioxidant activity.[6] Propolis from the Solomon Islands has also been reported to contain some prenylflavonoids identical to those isolated from Okinawan propolis.[7] Recently, we also studied the Solomon Islands propolis and isolated a new prenylflavonoid, solophenol A (**16**).[8] It exhibited a potent 2,2′-diphenyl-1-picrylhydrazyl radical scavenging activity.

On further analysis of the Solomon Islands propolis, 4 new compounds **1**−**4** (Figure 1) and 17 known compounds were identified. Moreover, these selected compounds were tested for antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*. In the present study, we report their structure determinations and their antibacterial activity.

MATERIALS AND METHODS

General Experimental Procedure. Optical rotation values were determined with a SEPA-200 polarimeter (Horiba, Kyoto, Japan). UV spectra were obtained using a V-560 spectrometer (Jasco, Tokyo, Japan). IR spectra were recorded by a FT/IR-550 spectrometer (Jasco, Tokyo, Japan). ^{1}H (400 MHz), ^{13}C (100 MHz), and all 2D NMR spectra were run on an AVANCE III 400 spectrometer (Bruker BioSpin, Rheinstetten, Germany), and chemical shifts were reported using the residual solvent signals in acetone-d_6 (δ_H 2.05, δ_C 29.8). Coupling constants (J values) are given in Hz. High-resolution electrospray ionization mass spectrometry (HRESIMS) data were recorded using an LCT-Premier XE mass spectrometer (Waters, MA). Analytical reversed-phase ultrahigh-performance liquid chromatography (UPLC) (Waters, MA) was performed using a BEH ODS column (50 × 2.1 mm i.d.;

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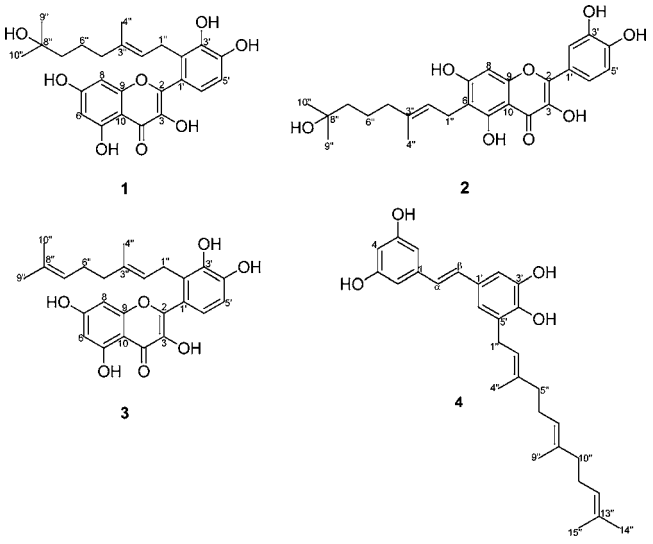

Figure 1. Structures of new compounds **1**−**4** from the Solomon Islands propolis.

Waters) in conjunction with a Waters Acquity UPLC photodiode array eλ detector and an LCT-Premier XE mass spectrometer.

Extraction and Isolation. Propolis was collected in March 2011 from Malaita, the Solomon Islands. The dried propolis sample (49.5 g) was extracted with 500 mL of ethanol at room temperature for 24 h with stirring and then concentrated under reduced pressure to give a crude extract (34.8 g). The extract dissolved in EtOH was mixed with 20 g of silica gel 60 (Merck, Darmstadt, Germany), and concentrated to yield dried silica gel. The dried silica gel was placed on top of a silica gel column (360 mm ×50 mm i.d.) and eluted with a gradient of *n*-hexane/EtOAc followed by several washes with MeOH. In all 24 fractions, 100-mL eluates were collected. The elution profile was as follows: fr. 1, eluent *n*-hexane-EtOAc (9:1); fr. 2, *n*-hexane-EtOAc (8:2); fr. 3, *n*-hexane-EtOAc (7:3); fr. 4−13, *n*-hexane-EtOAc (6:4); fr. 14, *n*-hexane-EtOAc (5:5); fr. 15, *n*-hexane-EtOAc (4:6); fr. 16, *n*-hexane-EtOAc (3:7); fr. 17, *n*-hexane-EtOAc (2:8); fr. 18, *n*-hexane-EtOAc (1:9); fr. 19, EtOAc; and frs. 20−24, MeOH.

Fraction 22 was subjected to reversed-phase preparative high-performance liquid chromatography (RP-HPLC) monitored by UV at 330 nm on a 250 × 20 mm i.d., 5 μm, Cholester column (Nacalai Tesque, Tokyo, Japan) using H_2O−CH_3CN (55:45) to give **1** (12.4 mg) followed by **2** (3.7 mg) and **18** (1.7 mg) in H_2O−CH_3CN (45:55). Fraction 19 was chromatographed by RP-HPLC monitored by UV at 330 nm on a 250 × 20 mm i.d., 5 μm, Cholester column in H_2O−CH_3CN (40:60) to provide **3** (5.3 mg) and on a 250 × 20 mm i.d., 5 μm, RP-18 GP column (Kanto Chemical, Tokyo, Japan) in H_2O−CH_3CN (20:80) to give **4** (2.4 mg). RP-HPLC monitored by UV at 270 nm of fraction 8 on a 250 × 20 mm i.d., 5 μm, UG-120 column (Shiseido, Tokyo, Japan) in H_2O−CH_3CN (20:80) furnished **8** (1.0 mg). Separation of fraction **9** on RP-HPLC monitored by UV at 330 nm Cholester column (250 × 20 mm i.d., 5 μm) with H_2O−CH_3CN (20:80) yielded **12** (13.9 mg), whereas RP-HPLC chromatography monitored by UV at 270 nm of fraction 13 carried out on a 250 × 20 mm i.d., 5 μm, UG-120 column in H_2O−CH_3CN (30:70) afforded **7** (4.0 mg) and **16** (6.1 mg); in H_2O−CH_3CN (27:73), **9** (11.0 mg); and in H_2O−CH_3CN (37:63), **10** (8.6 mg), **11** (3.5 mg), and **14** (34.3 mg). Lastly, fraction 11 was subjected to RP-HPLC monitored by UV at 270 nm on a 250 × 20 mm i.d., 5 μm, Cholester column in H_2O−CH_3CN (37:63) to obtain **20** (79.2 mg).

Solophenol B (1). Yellow oil; UV (EtOH) λ_{max} (log ε) 256.0 (4.30), 349.0 (4.02) nm; IR (KBr) ν_{max} 3111, 2954, 1702, 1655 cm^{-1}; HRESIMS m/z 455.1747 (calcd. for $C_{25}H_{27}O_8$, 455.1706 $[M-H]^-$); ^1H and ^{13}C NMR data are shown in Table 1.

Solophenol C (2). Yellow oil; UV (EtOH) λ_{max} (log ε) 260.0 (4.20), 374.0 (4.20) nm; IR (KBr) ν_{max} 3110, 2965, 1702, 1654 cm^{-1}; HRESIMS m/z 455.1687 (calcd. for $C_{25}H_{27}O_8$, 455.1706 $[M-H]^-$); ^1H and ^{13}C NMR data are shown in Table 1.

Table 1. ^1H (400 MHz) and ^{13}C (100 MHz) NMR Spectroscopic Data for Solophenols B (1), C (2), and D (3) in Acetone-d_6

	solophenol B (**1**)		solophenol C (**2**)		solophenol D (**3**)	
position	δ_C, type	δ_H (J in Hz)	δ_C, type	δ_H (J in Hz)	δ_C, type	δ_H (J in Hz)
2	150.6, C		146.5, C		149.7, C	
3	137.6, C		136.8, C		136.7, C	
4	176.9, C		176.3, C		176.0, C	
5	162.2, C	12.27, s (−OH)	158.7, C	12.43, s (−OH)	161.4, C	12.30, s (−OH)
6	99.1, CH	6.26, d (2.0)	111.7, C		98.1, CH	6.28, d (1.7)
7	164.8, C		162.6, C		163.9, C	
8	94.5, CH	6.45, d (2.0)	93.8, CH	6.61, s	93.6, CH	6.40, d (1.7)
9	158.2, C		155.6, C		157.4, C	
10	104.6, C		103.9, C		103.7, C	
1′	120.8, C		123.8, C		122.5, C	
2′	129.3, C		115.6, CH	7.82, d (2.1)	128.4, C	
3′	144.3, C		145.7, C		143.3, C	
4′	147.0, C		148.1, C		146.2, C	
5′	113.2, CH	6.87, d (8.2)	116.2, CH	7.00, d (8.5)	112.2, CH	6.87, d (8.2)
6′	123.3, CH	6.96, d (8.2)	121.4, CH	7.70, dd (8.5, 2.1)	121.8, CH	6.95, d (8.2)
1″	26.9, CH_2	3.46, d (6.6)	21.8, CH_2	3.40, d (7.1)	25.7, CH_2	3.50, d (6.6)
2″	123.8, CH	5.21, brt (6.6)	122.8, CH	5.31, brt (7.1)	122.7, CH	5.16, brt (6.6)
3″	135.4, C		135.8, C		134.4, C	
4″	16.2, CH_3	1.49, s	16.1, CH_3	1.80, s	15.3, CH_3	1.48, s
5″	40.9, CH_2	1.84, m	41.0, CH_2	1.97, m	39.4, CH_2	1.83, m
6″	23.3, CH_2	1.37, m	23.4, CH_2	1.47, m	26.4, CH_2	1.88, m
7″	44.3, CH_2	1.37, m	44.3, CH_2	1.39, m	124.2, CH	5.00, brt (7.0)
8″	70.6, C		69.9, C		130.7, C	
9″	29.2, CH_3	1.14, s	29.7, CH_3	1.13, s	24.8, CH_3	1.59, s
10″	29.2, CH_3	1.14, s	29.7, CH_3	1.13, s	16.7, CH_3	1.52, s

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Solophenol D (3). Yellow oil; UV (EtOH) λ_{max} (log ε) 256.0 (4.30), 351.0 (4.02) nm; IR (KBr) ν_{max} 3111, 2956, 1702, 1654 cm^{-1}; HRESIMS m/z 437.1576 (calcd. for $C_{25}H_{25}O_7$, 437.1542 $[M-H]^-$); ^1H and ^{13}C NMR data are shown in Table 1.

Solomonin (4). Yellow oil; UV (EtOH) λ_{max} (log ε) 329.0 (4.25) nm; IR (KBr) ν_{max} 3392, 2922 cm^{-1}; HRESIMS m/z 447.2524 (calcd. for $C_{29}H_{35}O_4$, 447.2535 $[M-H]^-$); ^1H and ^{13}C NMR data are shown in Table 2.

Table 2. ^1H (400 MHz) and ^{13}C (100 MHz) NMR Spectroscopic Data for Solomonin (4) in Acetone-d_6

	solomonin (4)		
position	δ_C, type		δ_H (J in Hz)
1	139.9	C	
2	104.7	CH	6.55, s
3	158.6	C	
4	101.6	CH	6.29, s
5	158.6	C	
6	104.7	CH	6.55, s
α	125.7	CH	6.81, d (16.2)
β	128.8	CH	6.96, d (16.2)
1′	139.9	C	
2′	110.4	CH	6.99, brs
3′	144.6	C	
4′	143.2	C	
5′	128.1	C	
6′	119.8	CH	6.87, s
1″	27.9	CH_2	3.40, d (7.0)
2″	122.8	CH	5.44, brt (7.0)
3″	135.2	C	
4″	15.3	CH_3	1.79, s
5″	39.5	CH_2	2.00, m
6″	26.4	CH_2	2.18, m
7″	124.1	CH	5.21, brt (7.0)
8″	134.6	C	
9″	15.2	CH_3	1.65, s
10″	39.6	CH_2	2.09, m
11″	26.5	CH_2	2.09, m
12″	124.2	CH	5.12, brt (6.9)
13″	130.6	C	
14″	24.9	CH_3	1.67, s
15″	16.8	CH_3	1.61, s

Antimicrobial Assay. *S. aureus* Food and Drug Administration (FDA) 209P, *B. subtilis* Biological Resourse Center, NITE (NBRC) 3134, and *P. aeruginosa* NBRC13275 were used for testing antibacterial activity. Initially, these strains were examined with microdilution assays, and minimum inhibitory concentration (MIC) values were determined using the microbroth dilution method according to the protocols of the National Committee for Clinical and Laboratory Standards. The bacterial strains were cultured in cation-adjusted Mueller-Hinton broth (CAMHB) (Sanko Pure Chemical, Tokyo, Japan) and incubated at 37 °C for 24 h. A dilution of 1.0×10^7 cfu/mL was obtained for each bacterial strain in CAMHB medium, of which 5 μL was added per well in a 96-well plate. A stock solution of each compound to be tested was prepared at a concentration of 12.8 mg/mL in EtOH, which was further diluted to a series of varying concentrations (final concentration of <1.0% EtOH (v/v)), of which 100 μL was added per well for each bacterial strain. Each plate was incubated at 37 °C for 18 h. MIC was defined as the minimum concentration at which the bacteria cannot propagate. In addition, quercetin (Cayman Chemical, Ann Arbor, MI) and eriodictyol (Extrasynthese, Genay, France) were tested as reference substances for comparison with each test compound. Streptomycin (Sigma Aldrich Chemical, St. Louis, MO) was used as a positive control. Compound **6** was used as nymphaenol A isolated from Okinawan propolis.

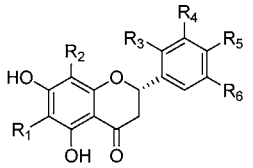
RESULTS AND DISCUSSION

Propolis from the Solomon Islands was extracted with EtOH at room temperature. The EtOH extracts were separated into 24 fractions by silica gel column chromatography with *n*-hexane, EtOAc, and MeOH, and further purified by RP-HPLC to give 3 new prenylflavonoids, **1**−**3**, and a new prenylstilbene, **4**, together with other several known compounds.

Compound **1** was obtained as a yellow, oily substance, and its molecular formula was determined to be $C_{25}H_{28}O_8$ by HRESIMS. The IR spectrum of **1** indicated the presence of hydroxyl (3111 cm^{-1}), alkyl (2954 cm^{-1}), and carbonyl (1702, 1655 cm^{-1}) functions. The UV absorption maxima occurred at 349 and 256 nm. In the ^1H NMR spectrum of **1** (acetone-d_6), the signal for the phenolic OH appeared as a singlet at δ_H 12.27 (s, OH-5), which was strongly hydrogen bonded to the C4-carbonyl group. These data suggested that the basic skeleton was identical to that of quercetin.[9] The appearance of the methyl groups (δ_H 2 × 1.14, 1.49), 3 methylene protons (δ_H 2 × 1.37, 1.84), a benzylic methylene proton (δ_H 3.46), and a vinyl proton (δ_H 5.21) in ^1H NMR spectrum of **1** (Table 1) suggested the presence of an 8″-hydroxy-3″,8″-dimethyl-oct-2″-enyl chain. The ^{13}C NMR spectrum of **1** showed 24 carbon signals and, it contained 25 carbons for the reason that the methyl group signals at 29.2 were doubled (Table 1). The signals in the ^1H- and ^{13}C NMR spectra were assigned from the heteronuclear single quantum coherence (HSQC) and heteronuclear multiple bond correlation (HMBC) data. In the HMBC spectrum of **1**, the methylene signal at δ_H 3.46 (H-1″) was observed to be correlated with C-1′ (δ_C 120.8), C-2′ (δ_C 129.3), and C-3′ (δ_C 144.3), indicating that the 8″-hydroxy-3″,8″-dimethyl-oct-2″-enyl chain was attached to C-2′ (Figure 3). Thus, compound **1** was determined to be 2′-(8″-hydroxy-3″,8″-dimethyl-oct-2″-enyl)-quercetin, a new prenylflavonoid named solophenol B (Figure 1).

Compound **2** was also obtained as a yellow, oily substance, the molecular formula of which was found to be $C_{25}H_{28}O_8$ by HRESIMS. The NMR spectroscopic data for **2** closely resembled that of **1** (Table 1), thus indicating the presence of a quercetin skeleton, and an 8″-hydroxy-3″,8″-dimethyl-oct-2″-enyl chain was determined in a similar way as **1**. The signals of **2** in the ^1H and ^{13}C NMR spectra were assigned from the HSQC and HMBC data, and HMBC correlations from the methylene signal at δ_H 3.40 (H-1″) to C-5 (δ_C 158.7), C-6 (δ_C 111.7), and C-7 (δ_C 162.6) indicated that the 8″-hydroxy-3″,8″-dimethyl-oct-2″-enyl chain was attached to C-6 (Figure 3). Thus, compound **2** was determined to be 8-(8″-hydroxy-3″,8″-dimethyl-oct-2″-enyl)-quercetin, a new prenylflavonoid named solophenol C (Figure 1).

Compound **3**, procured as a yellow, oily substance, possessed the molecular formula $C_{25}H_{26}O_7$, as determined by HRESIMS. Its 1D/2D NMR showed features similar to those of **1** (Table 1), except for the presence of 2 vinyl protons at C-8″ (δ_C 130.7) and C-7″ (δ_C 124.2), and a geranyl chain was observed in the same way as **1**. From the HMBC spectrum of **3**, the methylene signal at δ_H 3.50 (H-1″) could be correlated with C-1′ (δ_C 122.5), C-2′ (δ_C 128.4), and C-3′ (δ_C 143.3), indicating that a geranyl group was attached to C-2′ (Figure 3). Thus, compound **3** was determined to be 2′-geranylquercetin, a new prenylflavonoid named solophenol D (Figure 1). The only difference between **1** and **3** is in the presence of a hydroxyl group at C-8″ position (terminus of a geranyl chain).



	R_1	R_2	R_3	R_4	R_5	R_6
5	geranyl-OH	H	H	OH	OH	H
6	geranyl	H	H	OH	OH	H
7	geranyl	H	H	H	OH	H
8	geranyl	H	H	H	H	H
9	farnesyl	H	H	OH	OH	H
10	H	geranyl	H	H	OH	H
11	H	prenyl	H	H	OMe	H
12	H	geranyl	H	H	OMe	H
13	H	H	geranyl-OH	OH	OH	H
14	H	H	geranyl	OH	OH	H
15	prenyl	H	geranyl	OH	OH	H
16	H	prenyl	geranyl	OH	OH	H
17	H	H	H	OH	OH	geranyl-OH
18	H	H	H	H	OH	geranyl-OH
19	H	H	H	OH	OH	geranyl
20	H	H	H	H	OH	geranyl

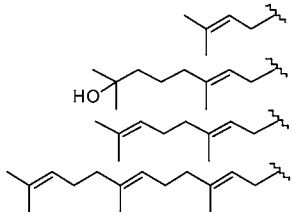


Figure 2. Structures of known compounds **5**−**20** from the Solomon Islands propolis.

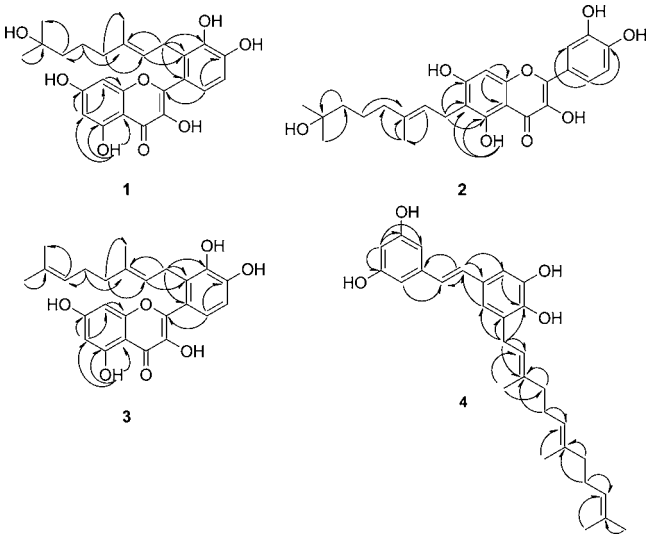


Figure 3. Key HMBC correlations (H to C) for **1**−**4**.

Compound **4** was obtained as a yellow, oily substance, and its molecular formula was determined to be $C_{29}H_{36}O_4$ by HRESIMS. The IR spectrum of **4** indicated the presence of hydroxyl and alkyl functions. The ^{1}H NMR spectrum of **4** in acetone-d_6 showed the signals for 2 *trans* olefinic protons (δ_H 6.81, 6.96, d, J = 16.2 Hz).[10] In addition, the UV absorption maximum at 331 nm, together with ^{1}H and ^{13}C NMR data for **4** (Table 2), suggested that the basic skeleton was identical to that of stilbene.[10] The appearance of 4 olefinic methyl groups (δ_H 1.61, 1.65, 1.67, 1.79), 4 methylene protons (δ_H 2.00, 2 × 2.09, 2.18), and a benzylic methylene proton (δ_H 3.40) along with three vinyl protons (δ_H 5.12, 5.21, 5.44) pointed to the presence of a farnesyl group. The ^{13}C NMR spectrum of **4** showed 26 signals corresponding to carbon and it contained 29 carbons for the reason that the benzoic carbon signals at 158.6 and 104.7 were doubled (Table 2). The signals in the ^{1}H and ^{13}C NMR spectra were assigned from the HSQC and HMBC data. In the HMBC spectrum of **4**, the methylene signal at δ_H 3.40 (H-1″) was observed to be correlated with C-4′ (δ_C 143.2), C-5′ (δ_C 128.1), and C-6′ (δ_C 119.8), indicating that the farnesyl group was attached to C-5′ (Figure 3). Thus, compound **4** was determined to be 5′-farnesyl-3′-hydroxyresveratrol, a new prenylstilbene named solomonin (Figure 1). All the double bonds in the side chains for **1**−**4** were assigned as *E*, based on the ^{1}H and ^{13}C NMR chemical shifts of vinyl methyls in 8″-hydroxy-

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3″,8″-dimethyl-oct-2″-enyl (hydroxylated geranyl), geranyl, and farnesyl chains.[11]

The known compounds prokinawan (**5**),[6] nymphaenol A (**6**),[6] bonannione A (**7**),[12] 6′-geranylpinocembrin (**8**),[12] propolin I (**9**),[13] sophoraflavanone A (**10**),[12] (2*S*)-5,7-dihydroxy-4′-methoxy-8-prenylflavanone (**11**),[14] puyanin (**12**),[15] propolin A (**13**),[6] nymphaeol B (**14**),[6] nymphaeol C (**15**),[6] solophenol A (**16**),[8] propolin B (**17**),[6] propolin E (**18**),[6] isonymphaeol B (**19**),[6] 3′-geranylnaringenin (**20**),[6] and gallic acid (**21**) were determined by comparison of data from the isolated compounds and data available from the literature (Figure 2). The compounds **5**, **6**, **13**−**15**, **17**−**20**, which were isolated from Okinawan propolis, were identified by the retention time of RP-HPLC and HRESIMS.[6] The other compounds **7**−**12** and **16** were identified by their 1D/2D NMR, ESIMS, CD spectra and comparison with the reported data (Figure 2).

Most of the identified compounds are also present in the plants classified as *Macaranga*,[16,17] as well as in propolis collected in Indonesia,[18] Taiwan,[19,20] and Okinawa (South of Japan) [21] since it is known to originate from the genus *Macaranga*. These results suggest that propolis from the Solomon Islands also originates from the genus *Macaranga*.

Previous investigations have indicated that prenylated flavonoids in higher plants help in protection from diseases by exhibiting strong antibacterial and antifungal activity.[22] The isolated solophenols B−D (**1**−**3**), solomonin (**4**), and several compounds (**6**−**7**, **9**−**12**, **14**, **16**) were evaluated for antibacterial activity against *S. aureus*, *B. subtilis*, and *P. aeruginosa* (Table 3). Quercetin and eriodictyol were also tested as reference compounds.

Table 3. Minimum Inhibitory Concentration (MIC) of the Compounds Isolated from Propolis from the Solomon Islands (μg/mL)

compound	*S. aureus*	*B. subtilis*	*P. aeruginosa*
1	64	64	64
2	64	64	64
3	32	32	16
4[a]	>32	>32	>32
6	4	4	4
7	8	4	4
9	16	8	16
10	4	16	64
11	32	32	128
12	8	8	8
14	16	16	16
16	4	8	32
quercetin	>256	>256	>256
eriodictyol	>256	>256	>256
streptomycin	16	4	4

[a]Compound **4** was tested for this assay since it was a new compound. However there was not enough amount of compound **4** to evaluate its effects at concentrations above 32 μg/mL.

Compounds **6**, **9**, **10**, **12**, **14**, and **16** (Figure 2), which have the flavanone skeleton with a geranyl or farnesyl chain, had potent antibacterial activity against gram-positive bacteria *S. aureus* and *B. subtilis*, with MIC values less than 16 μg/mL. By contrast, quercetin and eriodictyol, which are flavonoids without the prenylated chain, showed no antibacterial activity even at a concentration of 256 μg/mL. These results indicated that the geranyl or farnesyl chain on flavanone skeleton affect the antibacterial activity against gram-positive bacteria. It has been reported that the antibacterial activity of prenylflavonoids may cause damage to the cell membrane or the cell wall, possibly due to the lipophilic prenyl (e.g., geranyl and farnesyl) chains, thereby enabling rapid cell penetration.[7,22] Among the evaluated compounds, **6** had the most potent antibacterial activity against the test bacteria, with MIC values of 4 μg/mL. These results indicate that flavonoids with a geranyl chain at C-6 position could act as strong antibacterial agents.

Compound **3** displayed stronger antibacterial activity than **1** against the tested bacteria, showing MIC values below 32 μg/mL (Table 3), thus implying a weakening or depression of the antibacterial activity due to hydration of the geranyl chain terminus. Compound **1** has the quercetin skeleton with an 8″-hydroxy-3″,8″-dimethyl-oct-2″-enyl (hydroxylated geranyl) chain at C-2′ position, while compound **3** has the quercetin skeleton with geranyl chain at C-2′ position. In short, compounds **1** and **3** only differ whether a hydroxyl group is present at C-8″ position (terminus of a geranyl chain) or not (Figure 1). It is speculated that compounds with hydration of a geranyl chain may not attack the membrane or cause significant damage to the cell wall of bacteria because of the polarity of a hydroxylated geranyl chain, which is higher than that of an unsubstituted geranyl chain.

In conclusion, propolis from the Solomon Islands was found to comprise mostly prenylated polyphenols, similar to Okinawan propolis. Moreover, most prenylated polyphenols identified from propolis from the Solomon Islands displayed potent antibacterial activity. This study may indicate that propolis from the Solomon Islands can be used not only as food additives but also in pharmaceuticals against bacteria. Further, in-depth research on propolis from the Solomon Islands and its solophenols, solomonin, and prenylflavonoids is warranted in order to maximize its utilization.

■ ASSOCIATED CONTENT

Supporting Information

HRESIMS, ^{1}H NMR, ^{13}C NMR, HSQC, and HMBC spectra of **1**−**4** were used to be determined their structures. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Phone: +81-54-264-5523. Fax: +81-54-264-5523. E-mail: kumazawa@u-shizuoka-ken.ac.jp.

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Notes

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■ ABBREVIATIONS

CAMHB, cation-adjusted Mueller-Hinton broth; FDA, Food and Drug Administration; MIC, minimum inhibitory concentration; NBRC, Biological Resourse Center, NITE; UPLC, ultrahigh-performance liquid chromatography

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