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MEGASTIGMANE GLYCOSIDES FROM THE LEAVES OF *SALACIA CHINENSIS*

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Abstract – Six new megastigmane glycosides, foliasalaciosides A₁ (**1**), A₂ (**2**), B₁ (**3**), B₂ (**4**), C (**5**), and D (**6**), were isolated from the methanolic extract of the leaves of *Salacia chinensis* (Hippocrateaceae) collected in Thailand together with 16 known constituents. The absolute stereostructures of **1–6** were elucidated on the basis of chemical and physicochemical evidence including the application of the modified Mosher's method.

Salacia chinensis L. (syn. *S. prnoides*, Hippocrateaceae) is widely distributed in Thailand, Myanmar, and India. The stems of *S. chinensis* have been used as a laxative and to relieve muscular pain in Thai traditional medicine.¹ On the other hand, the decoctions of the stems and leaves are given to cure diabetes mellitus in the Ayurvedic system of Indian traditional medicine.² Previously, we reported that the extract from the stems of *S. chinensis* showed inhibitory activities on rat lens aldose reductase and α -glucosidase and radical scavenging activity, and the structures of various triterpenes, nor-triterpenes, and sesquiterpenes were characterized.^{3–6} However, the chemical constituents as well as the pharmacological properties of the leaves of *S. chinensis* have not been characterized. During the course of our serial studies on the bioactive constituents from *Salacia* species,^{7–14} six new megastigmane glycosides, foliasalaciosides A₁ (**1**), A₂ (**2**), B₁ (**3**), B₂ (**4**), C (**5**), and D (**6**), were isolated from the methanolic extract of the leaves of *Salacia chinensis* together with 16 known constituents. This paper deals with the isolation and structure elucidation including the absolute configuration of **1–6**.

The leaves of *S. chinensis* were cut and extracted with methanol under reflux. The methanolic extract was partitioned into a mixture of ethyl acetate (EtOAc) and water to furnish an EtOAc-soluble portion and an aqueous layer. The aqueous layer was further extracted with *n*-butanol (*n*-BuOH) to give a *n*-BuOH-soluble portion. The *n*-BuOH-soluble portion was subjected to Diaion HP-20 column chromatography (H₂O → MeOH) to give the water- and methanol-eluted fractions. The methanol-eluted fraction was subjected to normal- and reversed-phase silica gel column chromatographies, and finally HPLC to give foliasalaciosides A₁ (**1**, 0.0003% from the natural medicine), A₂ (**2**, 0.0003%), B₁ (**3**, 0.0004%), B₂ (**4**,

0.0003%), C (**5**, 0.0001%), and D (**6**, 0.0001%), together with 7 known megastigman glycosides, blumenyl C β -D-glucopyranoside (**7**, 0.0032%),¹⁵ roseoside A (**8**, 0.0001%),¹⁶ dendranthemside A (**9**, 0.0004%),¹⁷ alangioside A (**10**, 0.0002%),¹⁸ (6*S*,7*E*,9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-*O*- α -L-arabinopyranosyl(1 $\rightarrow$ 6)- β -D-glucopyranoside (**11**, 0.0001%),¹⁶ icaricide B₁ (**12**, 0.0002%),¹⁹ and citroside B (**13**, 0.0004%),²⁰ and nine known flavonol glycosides, paeonoside (**14**, 0.0008%),²¹ kaempferol 3-*O*-rutinosyl-7-*O*- β -D-glucopyranoside (**15**, 0.0008%),²² kaempferol 3-*O*- α -L-rhamnopyranosyl(1 $\rightarrow$ 6)- β -D-galactopyranosyl-7-*O*- β -D-glucopyranoside (**16**, 0.0017%),²³ clitorin (**17**, 0.0045%),²⁴ kaempferol 3-*O*-(2,6- α -L-dirhamnopyranosyl)- β -D-glucopyranosyl-7-*O*- β -D-glucopyranoside (**18**, 0.0061%),²⁴ rutin (**19**, 0.027%),²⁵ quercetin 3-*O*-rutinosyl-7-*O*- β -D-glucopyranoside (**20**, 0.0016%),²⁶ manghaslin (**21**, 0.0019%),²⁴ and myricetin 3-*O*- β -D-rutinoside (**22**, 0.0015%).²⁷

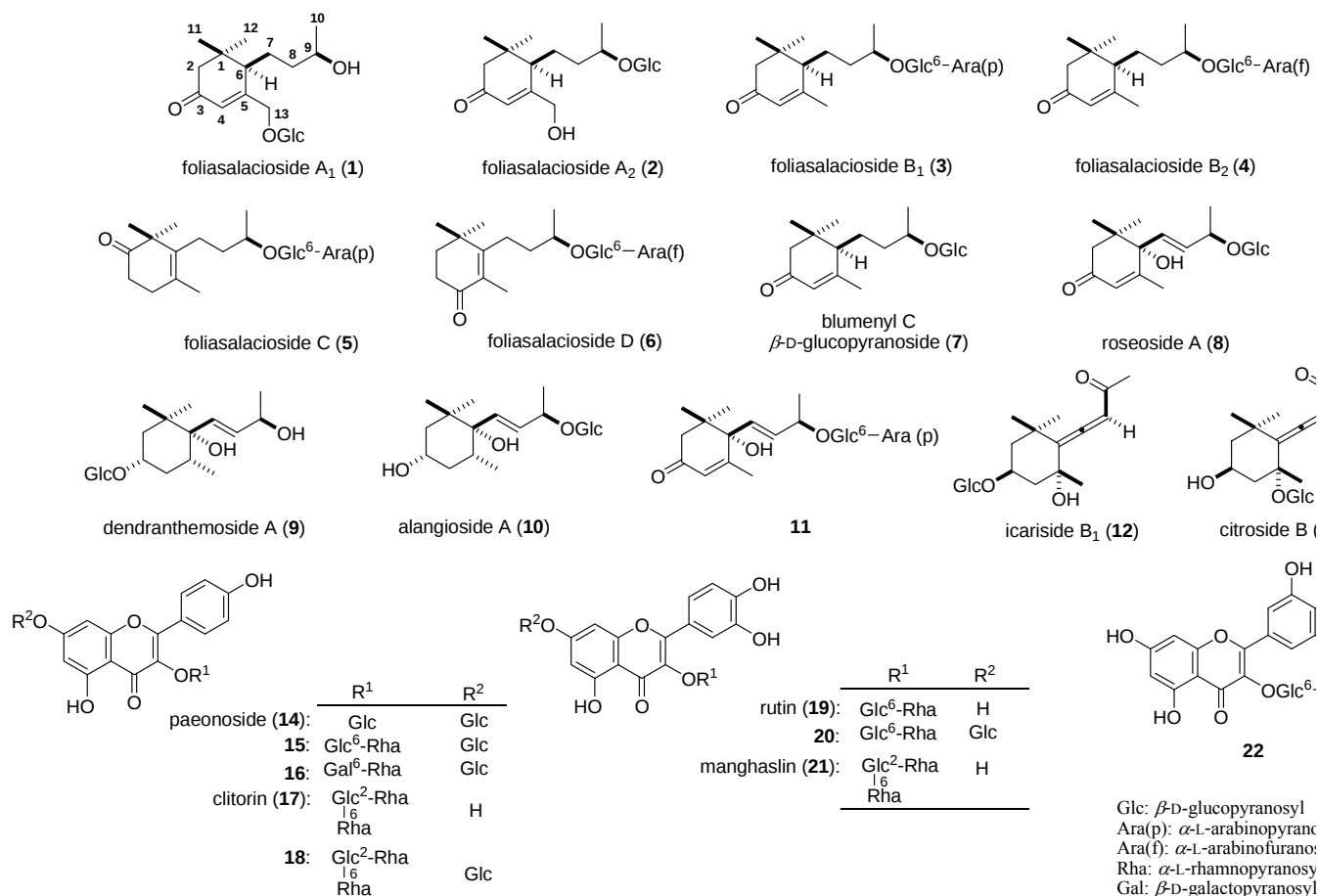


Chart 1

Structures of Foliasalaciosides A₁ (**1**), A₂ (**2**), B₁ (**3**), B₂ (**4**), C (**5**), and D (**6**)

Foliasalaciosides A₁ (**1**) and A₂ (**2**) were obtained as an amorphous powder with positive optical rotation (**1**: $[\alpha]_D^{28} +24.3^\circ$; **2**: $[\alpha]_D^{26} +30.9^\circ$, both in MeOH), respectively. The IR spectra of **1** and **2** showed absorption bands assignable to hydroxyl, α,β -unsaturated carbonyl, and ether functions [**1**: 3420, 1653, and 1078 cm⁻¹; **2**: 3423, 1653, and 1078 cm⁻¹]. The common molecular formula, C₁₉H₃₂O₈, of both **1** and **2** were determined from the quasimolecular ion peaks in the positive-ion FAB-MS [m/z 411 (M + Na)⁺] and by high-resolution (HR) FAB-MS measurement. Acid hydrolysis of **1** and **2** with 1 M HCl liberated

D-glucose, which was identified by HPLC analysis using an optical rotation detector.^{28,29} The ^1H -NMR (CD_3OD) and ^{13}C -NMR (Table 1) spectra of **1** and **2**, which were assigned by various NMR experiment,³⁰ showed signals assignable to aglycon parts {**1**: δ 1.03, 1.11 (3H each, both s, 12, 11- H_3), 1.46, 1.94 (1H each, both m, 7- H_2), 2.01 (1H, m, 6-H), 2.02 (1H, d, $J = 17.9$ Hz, 2- H_α), 2.55 (1H, d, $J = 17.9$ Hz, 2- H_β); **2**: δ 1.01, 1.10 (3H each, both s, 12, 11- H_3), 1.49, 1.95 (1H each, both m, 7- H_2), 1.94 (1H, m, 6-H), 2.01 (1H, d, $J = 17.9$ Hz, 2- H_α), 2.56 (1H, d, $J = 17.9$ Hz, 2- H_β)}, together with β -D-glucopyranosyl moieties [**1**: δ 4.32 (1H, d, $J = 8.2$ Hz, 1'-H), **2**: δ 4.33 (1H, d, $J = 8.2$ Hz, 1'-H)]. As shown in Figure 1, the double quantum filter correlation spectroscopy (DQF COSY) experiment on **1** and **2** indicated the presence of partial structures written in bold lines, and in the heteronuclear multiple-bond correlations (HMBC) experiment, long-range correlations were observed between the following protons and carbons: (**1**: 2-H and 3-C; 4-H and 6-C; 7-H and 1-C; 8-H and 6-C; 10-H and 8, 9-C; 11-H and 1, 2, 6, 12-C; 12-H and 1, 2, 6, 11-C; 13-H and 4, 5, 6, 1'-C; 1'-H and 13-C; **2**: 2-H and 3-C; 4-H and 6, 13-C; 7-H and 1-C; 8-H and 6-C; 9-H and 1'-C; 10-H and 8, 9-C; 11-H and 1, 2, 6, 12-C; 12-H and 1, 2, 6, 11-C; 13-H and 4, 5, 6-C; 1'-H and 9-C). The planar structures of **1** and **2** were the same as those of glochidionoside **B**³¹ and (6*R*,9*S*)-megastigman-4-en-3-one-9,13-diol 9-*O*- β -D-glucopyranoside,³² respectively. The relative stereostructures of **1** and **2** except for the 9-positions were determined by NOESY experiments, in which correlations were observed between the following proton pairs: 2- H_α and 12- H_3 ; 2- H_β and 11-H; 6- H_α and 12- H_3 ; 11- H_3 and 7- H_2 . The absolute stereostructures of the 6-position in **1** and **2** were confirmed by circular dichroic (CD) spectra.¹⁵ The CD spectra (MeOH) of **1** and **2** showed Cotton effects at [**1**: 215 nm ($\Delta\epsilon +2.06$), 328 nm ($\Delta\epsilon +0.27$); **2**: 216 nm ($\Delta\epsilon +4.23$), 330 nm ($\Delta\epsilon +0.45$)], which was very similar to those of blumenyl C β -D-glucopyranoside (**8**) [216 nm ($\Delta\epsilon +3.74$), 333 nm ($\Delta\epsilon +0.99$)] reported by Buske et al.,¹⁵ so that the absolute configuration of the 6-position in **1** and **2** was determined to be *R* orientation. The absolute configurations of the 9-position on **1** and **2** were clarified by a modified Mosher's method. Namely, enzymatic hydrolysis of **1** and **2** with nariginase gave a common aglycon, foliasalaciol A (**1a**). Next, the (*R*)- and (*S*)-MTPA esters (**1b**, **1c**) were derived from **1a** upon reaction with (*R*)- and (*S*)-MTPA in the presence of EDC·HCl and 4-DMAP. The 10-methyl protons of the (*S*)-MTPA ester (**1c**) resonated at lower field than those of the (*R*)-MTPA ester (**1b**) [$\Delta\delta$: positive], while the protons on the 2, 4, 6, 7, 8, 11, 12, and 13-positions of **1c** were observed at higher fields compared to those of **1b** [$\Delta\delta$: negative].

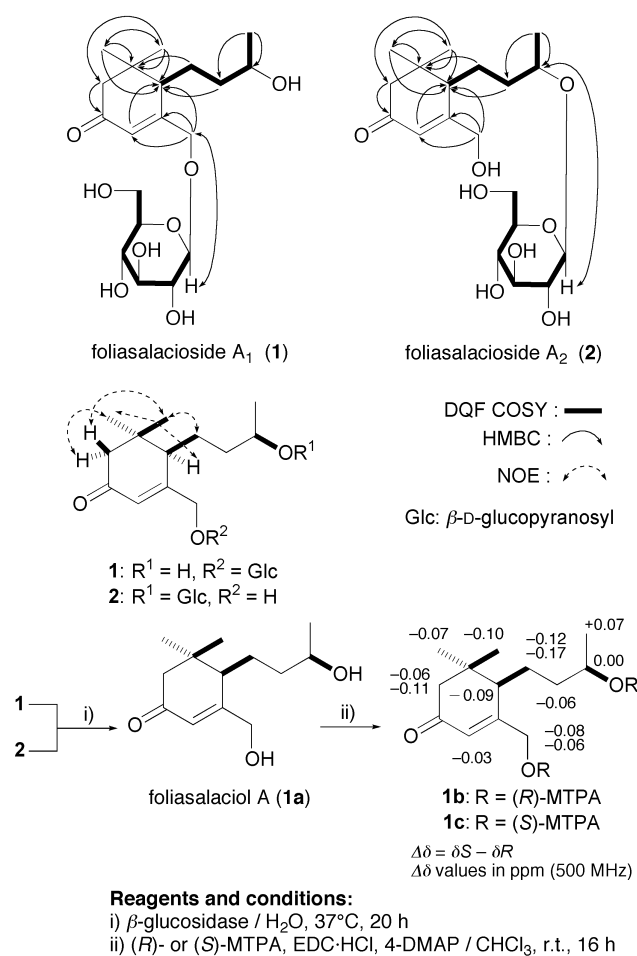


Figure 1

Consequently, the absolute configurations of the 9-position in **1** and **2** were elucidated to be *R* orientation. On the basis of above-mentioned evidence, the structures of foliasalaciosides A (**1**) and B (**2**) were characterized as shown.³³

Table 1. ¹³C-NMR Data (125 MHz, ^aCD₃OD, ^bCDCl₃) for Foliasalaciosides A₁ (**1**), A₂ (**2**), B₁ (**3**), B₂ (**4**), C (**5**), and D (**6**).

	1^a	1a^b	2^a	3^a	4^a	5^a	6^a
1	37.3	36.3	37.4	37.4	37.4	49.4	37.7
2	48.6	47.6	48.6	48.1	48.2	218.3	38.5
3	202.2	199.7	202.4	202.5	202.6	37.1	35.1
4	123.2	121.7	121.5	125.3	125.4	32.6	201.7
5	167.9	167.6	172.5	170.4	170.3	128.7	131.7
6	47.5	46.0	47.6	52.4	52.4	138.0	168.9
7	27.5	26.2	27.1	27.0	26.9	26.1	28.1
8	39.6	38.1	37.8	37.9	37.8	39.0	37.3
9	68.4	67.6	75.2	75.7	75.9	76.0	76.0
10	23.7	23.8	20.0	20.1	20.1	19.94	20.0
11	27.7	27.4	27.8	27.6	27.6	25.2	27.3
12	28.9	28.7	28.8	29.1	29.1	25.2	27.3
13	70.8	64.8	65.1	25.1	25.1	19.89	11.8
1'	103.5		102.1	102.3	102.3	102.3	102.4
2'	75.1		75.2	75.1	75.2	75.2	75.2
3'	78.1		78.2	78.0	78.1	78.1	78.1
4'	71.7		71.8	71.8	72.2	71.8	72.2
5'	78.2		78.0	76.9	76.8	76.9	76.9
6'	62.8		62.9	69.4	68.2	69.4	68.2
1''				105.3	109.9	105.2	111.0
2''				72.4	83.2	72.4	83.2
3''				74.2	79.0	74.2	79.0
4''				69.8	86.0	69.8	85.9
5''				66.7	63.2	66.6	63.1

Foliasalaciosides B₁ (**3**) and B₂ (**4**) were obtained as an amorphous powder with positive optical rotation (**3**: $[\alpha]_D^{27} +25.2^\circ$; **4**: $[\alpha]_D^{26} +30.5^\circ$, both in MeOH), respectively. The IR spectra of **3** and **4** showed absorption bands assignable to hydroxyl, α,β -unsaturated carbonyl, and ether functions [**3**: 3405, 1651, and 1075 cm⁻¹; **4**: 3397, 1655, and 1075 cm⁻¹]. The same molecular formula, C₂₄H₄₀O₁₁, of both **3** and **4** were determined from the positive- and negative-ion FAB-MS [m/z 527 (M + Na)⁺, m/z 503 (M – H)[–]] and by HRFABMS measurements. Acid hydrolysis of **3** and **4** with 1 M HCl liberated D-glucose and L-arabinose, which were identified by HPLC analysis using an optical rotation detector.^{28,29} The ¹H-NMR (CD₃OD) and ¹³C-NMR (Table 1) spectra³⁰ of **3** and **4** showed signals due to aglycon parts {**3**: δ 1.01, 1.09 (3H each, both s, 12, 11-H₃), 1.97 (1H, m, 6-H), 1.97 (1H, d, J = 17.2 Hz, 2-H α), 2.46 (1H, d, J = 17.2 Hz, 2-H β); **4**: δ 1.01, 1.09 (3H each, both s, 12, 11-H₃), 1.97 (1H, d, J = 17.4 Hz, 2-H α), 1.98 (1H, m, 6-H), 2.47 (1H, d, J = 17.4 Hz, 2-H β)}, together with β -D-glucopyranosyl moieties [**3**: δ 4.31 (d, J = 7.6 Hz, H-1'); **4**: δ 4.31 (d, J = 7.6 Hz, H-1')], an α -L-arabinopyranosyl moiety [**3**: δ 4.28 (d, J = 6.8 Hz, H-1'')], and an α -L-arabinofuranosyl moiety [**4**: δ 4.96 (d, J = 1.5 Hz, H-1'')]. The proton and carbon signals in the ¹H- and ¹³C-NMR spectra of **3** and **4** were superimposable on those of blumenyl C β -D-glucopyranoside (**7**)¹⁵ except for the glycoside moiety, while the signals due to the 9-*O*-diglycosyl moiety

of **3** and **4** were very similar to those of (6*S*,7*E*,9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-*O*- α -L-arabinopyranosyl(1 $\rightarrow$ 6)- β -D-glucopyranoside (**11**)¹⁶ and floralginsenoside D,²⁸ respectively. As shown in Figure 2, the positions of the glycoside linkages in **3** and **4** were determined by a HMBC experiment, which showed long-range correlations between the following protons and carbons: 1'-H and C-9; 1''-H and C-6'. The relative stereostructures of **3** and **4** except for the 9-position were determined by a NOESY experiment, in which correlations were observed between the following proton pairs: 2-H α and 12-H₃; 2-H β and 11-H₃; 6-H and 12-H₃; 11-H₃ and 7-H₂. The absolute stereostructures of the 6-position in **3** and **4** were also confirmed by CD spectra.¹⁵

The CD spectra (MeOH) of **3** and **4** showed Cotton effects at [**3**: 214 nm ($\Delta\epsilon$ +1.92), 335 nm ($\Delta\epsilon$ +0.35); **4**: 214 nm ($\Delta\epsilon$ +1.26), 327 nm ($\Delta\epsilon$ +0.19)], so that the absolute configurations of the 6-position in **3** and **4** were determined to be *R* orientation. Finally, enzymatic hydrolysis of **3** and **4** with nariginase gave a same aglycon, blumenyl C.^{33,34} On the basis of above-mentioned evidence, the structures of foliasalaciosides B₁ (**3**) and foliasalaciosides B₂ (**4**) was characterized as shown.

Foliasalaciosides C (**5**), obtained as an amorphous powder with negative optical rotation ($[\alpha]_D^{23}$ -20.4° in MeOH), showed absorption bands at 3379, 1705, 1660, and 1084 cm⁻¹ due to hydroxyl, carbonyl, olefin and ether functions in the IR spectrum. The molecular formula, C₂₄H₄₀O₁₁, was determined from the positive- and negative-ion FAB-MS [m/z 527 (M + Na)⁺, m/z 503 (M - H)⁻] and by HRFABMS measurement. The acid hydrolysis of **5** yielded D-glucose and L-arabinose.^{28,29} The ¹H-NMR (CD₃OD) and ¹³C-NMR (Table 1) spectra³⁰ of **5** showed signals due to an aglycon part { δ 1.16 (6H, s, 11, 12-H₃), 1.20 (3H, d, J = 6.1 Hz, 10-H₃), 1.74 (3H, s, 13-H₃)}, together with a β -D-glucopyranosyl moiety [δ 4.34 (1H, d, J = 8.0 Hz, 1'-H)] and an α -L-arabinopyranosyl moiety [4.33 (1H, d, J = 6.7 Hz, 1''-H)]. The DQF COSY experiment on **5** showed correlations as shown in Figure 3. Furthermore, in the HMBC experiment, long-range correlations were observed between the following protons and carbons: 3-H and 2, 5-C; 4-H and 2, 5, 6-C; 7-H and 1, 5-C; 9-H and 1'-C; 10-H and 8, 9-C; 11-H and 1, 2, 6, 12-C; 12-H and 1, 2, 6, 11-C; 1'-H and 9-C; 1''-H and 6'-C. The proton and carbon signals of the 9-*O*-diglycosyl moiety in the ¹H- and ¹³C-NMR spectra of **5** were very similar to those of **3** and **11**.¹⁶ Furthermore, the configuration of the 9-position was characterized by comparison of the 9-, 10-, and 1'-carbon signals of **5** in the ¹³C NMR (CD₃OD) spectrum with those of synthetic known megastigmane glycosides, (1*R*/*S*)-3-[(4*R*)-4-hydroxy-

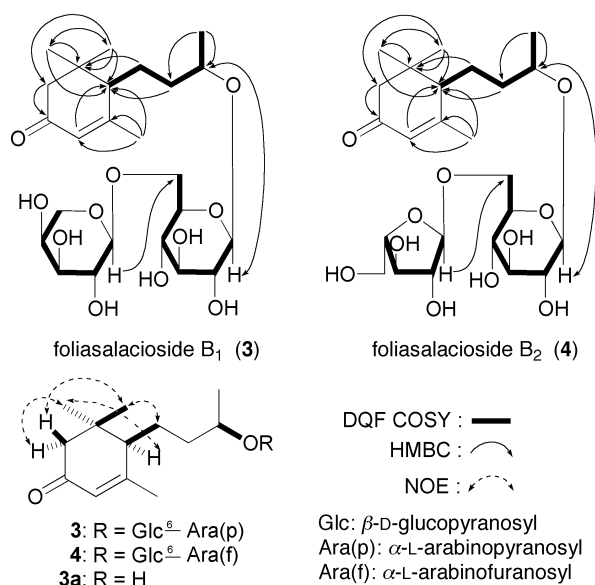


Figure 2

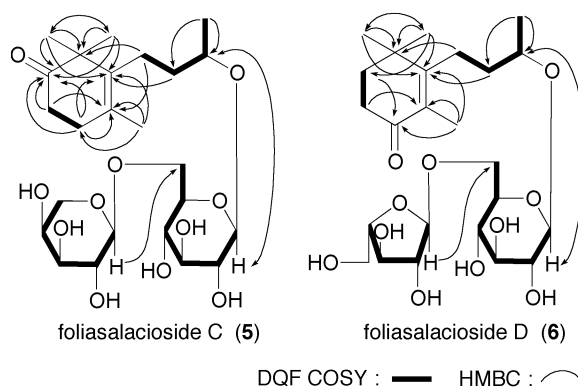


Figure 3

2,6,6-trimethylcyclohex-1-enyl]-1-methylpropyl- β -D-glucopyranoside,³⁶ having the same side chain (butanol *O*-glycoside moiety) as **5**. Namely, It was reported that the ^{13}C NMR signal [δ_{c} 76.1 (9-C); 19.8 (10-C); 102.2 (1'-C)] of the synthetic megastigmane having the *R*-configuration was shifted upfield relative to that [δ_{c} 77.9 (9-C); 21.8 (10-C); 103.9 (1'-C)] of the synthetic megastigmane having the *S*-configuration.³⁶ The 9-, 10-, and 1'-carbon signals of **5** were observed at δ_{c} 76.0 (9-C), 19.9 (10-C), and 102.3 (1'-C), so that the C-9 configuration of **5** was determined to be *R*. This evidence led us to formulate the structure of foliasalaciosides F (**5**) as shown.

Foliasalaciosides G (**6**), obtained as an amorphous powder with negative optical rotation ($[\alpha]_{\text{D}}^{26} -17.7^\circ$ in MeOH), showed absorption bands at 3339, 1653, and 1074 cm^{-1} due to hydroxyl, α,β -unsaturated carbonyl, and ether functions in the IR spectrum. The molecular formula, $\text{C}_{24}\text{H}_{40}\text{O}_{11}$, was determined from the positive- and negative-ion FAB-MS [m/z 527 ($\text{M} + \text{Na}$) $^+$, m/z 503 ($\text{M} - \text{H}$) $^-$] and by HRFABMS measurement. The acid hydrolysis of **6** yielded D-glucose and L-arabinose.^{28,29} The ^1H -NMR (CD_3OD) and ^{13}C -NMR (Table 1) spectra³⁰ of **6** showed signals due to an aglycon part [δ 1.20 (6H, s, 11, 12- H_3), 1.22 (3H, d, $J = 6.1$ Hz, 10- H_3), 1.76 (3H, s, 13- H_3)], together with a β -D-glucopyranosyl moiety [δ 4.34 (1H, d, $J = 7.6$ Hz, 1'-H)] and an α -L-arabinofuranosyl moiety [4.98 (1H, d, $J = 1.4$ Hz, 1''-H)]. The proton and carbon signals of the aglycon part of **6** in the ^1H - and ^{13}C -NMR spectra were superimposable on those of plataninoside F,³⁶ whereas the signals due to the 9-*O*-diglycosyl moiety of **6** were very similar to those of **4** and floralginsenoside D.²⁸ The structure of **6** was characterized by means of DQF COSY and HMBC experiments (Figure 3). The position of the glycosides linkage were determined by a HMBC experiment, which showed long-range correlation between 1'-H and 9-C; 1''-H and 6'-C. Furthermore, the configuration of the 9-position of **6** was characterized by comparison of the ^{13}C -NMR data.³⁶ Namely, the 9-, 10-, and 1'-carbon signals of **6** were observed at δ_{c} 76.0 (9-C), 20.0 (10-C), and 102.4 (1'-C), so that the 9-C configuration was determined to be *R* and the total structure of foliasalaciosides G (**6**) was characterized as shown.

EXPERIMENTAL

The following instruments were used to obtain physical data: specific rotations, Horiba SEPA-300 digital polarimeter ($l = 5$ cm); CD spectra, JASCO J-720WI spectrometer; UV spectra, Shimadzu UV-1600 spectrometer; IR spectra, Shimadzu FTIR-8100 spectrometer; ^1H NMR spectra, JEOL JNM-LA500 (500 MHz) spectrometer; ^{13}C NMR spectra, JEOL JNM-LA500 (125 MHz) spectrometer with tetramethylsilane as an internal standard; EIMS and HREIMS, JEOL JMS-GCMATE mass spectrometer; FABMS and HRFABMS, JEOL JMS-SX 102A mass spectrometer; HPLC detector, Shimadzu RID-6A refractive index and SPD-10A UV-VIS detectors. HPLC column, Cosmosil 5C₁₈-MS-II (Nacalai Tesque Inc., 250 $\times$ 4.6 mm i.d.) and (250 $\times$ 20 mm i.d.) columns were used for analytical and preparative purposes, respectively.

The following experimental conditions were used for chromatography: normal-phase silica gel column chromatography, silica gel BW-200 (Fuji Silysia Chemical, Ltd., 150–350 mesh); reversed-phase silica gel column chromatography, Chromatorex ODS DM1020T (Fuji Silysia Chemical, Ltd., 100–200 mesh); Diaion HP-20 column chromatography (Nippon Rensui); TLC, pre-coated TLC plates with silica gel

60F₂₅₄ (Merck, 0.25 mm) (normal-phase) and silica gel RP-18 F_{254S} (Merck, 0.25 mm) (reversed-phase); detection was achieved by spraying with 1% Ce(SO₄)₂–10% aqueous H₂SO₄, followed by heating.

Plant Material

The dried leaves of *S. chinensis* were collected at Thailand in 2006 and identified by one of authors (Rajamangala University of Technology Srivijaya, Pongpiriyadacha Y.). A voucher of the plant is on file in our laboratory (2006. Thai-06).

Extraction and Isolation

The dried leaves of *S. chinensis* Linn. (5.8 kg) were finely cut and extracted 3 times with methanol (MeOH) under reflux for 3 h. Evaporation of the solvent under reduced pressure provided a methanolic extract (756 g, 13.0%). The MeOH extract (712 g) was partitioned into an EtOAc–H₂O (1:1, v/v) mixture to furnish an EtOAc-soluble fraction (222 g, 4.1%) and an aqueous phase. The aqueous phase was further extracted with *n*-BuOH to give a *n*-BuOH-soluble fraction (130 g, 2.4%) and a H₂O-soluble fraction (361 g, 6.6%).

The *n*-BuOH-soluble fraction (100 g) was subjected to Diaion HP-20 column chromatography (1.5 kg, H₂O → MeOH → acetone) to give H₂O-eluted fraction (49.8 g, 1.2%), MeOH-eluted fraction (39.2 g, 0.93%) and acetone-eluted fraction (11.0 g, 0.26%), respectively. The MeOH-eluted fraction (39.2 g) was subjected to ordinary-phase silica gel column chromatography {480 g, CHCl₃–MeOH (10:1, v/v) → CHCl₃–MeOH–H₂O [(10:3:1, v/vv, lower layer) → (7:3:1, v/vv, lower layer) → (6:4:1, v/vv, lower layer)] → MeOH} to give ten fractions [Fr. 1 (0.5 g), Fr. 2 (0.6 g), Fr. 3 (1.3 g), Fr. 4 (7.3 g), Fr. 5 (3.0 g), Fr. 6 (6.7 g), Fr. 7 (1.6 g), Fr. 8 (2.4 g), Fr. 9 (9.3 g), Fr. 10 (3.5 g)]. Fraction 3 (1.3 g) was subjected to reversed-phase silica gel column chromatography [480 g, MeOH–H₂O (10:90 → 20:80 → 30:70 → 40:60 → 50:50 → 60:40 → 100: 0, v/v)] to give five fractions [Fr. 3-1 (121 mg), Fr. 3-2 (111 mg), Fr. 3-3 (389 mg), Fr. 3-4 (131 mg), Fr. 3-5 (450 mg)]. Fraction 3-3 (389 mg) was separated by HPLC [MeOH–H₂O (40:60, v/v)] and finally purified with HPLC [MeCN–MeOH–H₂O (15:8:77, v/v/v)] to furnish blumenyl C β-D-glucopyranoside (**7**, 71.5 mg). Fraction 3-4 (131 mg) was subjected to HPLC [MeOH–H₂O (40:60, v/v)] and purified by HPLC [MeCN–MeOH–H₂O (15:8:77, v/v/v)] to give blumenyl C β-D-glucopyranoside (**7**, 17.2 mg). Fraction 4 (7.3 g) was subjected to reversed-phase silica gel column chromatography [220g, MeOH–H₂O (0:100 → 10:90 → 20:80 → 30:70 → 40:60 → 60:40 → 100: 0, v/v) → CHCl₃] to give ten fractions [Fr. 4-1 (783 mg), Fr. 4-2 (821 mg), Fr. 4-3 (1.12 g), Fr. 4-4 (577 mg), Fr. 4-5 (288 mg), Fr. 4-6 (652 mg), Fr. 4-7 (1.30 g), Fr. 4-8 (413 mg), Fr. 4-9 (253 mg), Fr. 4-10 (760 mg)]. Fraction 4-6 (652 mg) was separated by HPLC [MeOH–H₂O (30:70, v/v)] to furnish ten fractions [Fr. 4-6-1 (7.2 mg), Fr. 4-6-2 (15.6 mg), Fr. 4-6-3 (17.8 mg), Fr. 4-6-4 (18.6 mg), Fr. 4-6-5 (51.2 mg), Fr. 4-6-6 (20.5 mg), Fr. 4-6-7 (30.6 mg), Fr. 4-6-8 (35.8 mg), Fr. 4-6-9 (18.0 mg), Fr. 4-6-10 (44.6 mg)]. Fr. 4-6-8 (35.8 mg) was finally purified by HPLC [MeCN–MeOH–H₂O (12:8:80, v/v/v)] to give foliasalacioside A₁ (**1**, 13.9 mg), foliasalacioside A₂ (**2**, 11.1 mg), and icariside B₁ (**12**, 6.2 mg). Fraction 4-7 (1.30 g) was separated by HPLC [MeOH–H₂O (40:60, v/v)] and [MeCN–MeOH–H₂O (15:8:77, v/v/v)] to furnish foliasalacioside B₁ (**3**, 17.3 mg), foliasalacioside B₂ (**4**, 11.9 mg), foliasalacioside D (**6**,

5.8 mg), blumenyl C β -D-glucopyranoside (**7**, 48.1 mg), roseoside A (**8**, 3.6 mg), dendranthemoside A (**9**, 2.2 mg), and citroside B (**13**, 10.0 mg). Fraction 4-8 (413 mg) was subjected to HPLC [MeOH–H₂O (40:60, v/v)] to afford nine fractions [Fr. 4-8-1 (11.9 mg), Fr. 4-8-2 (22.2 mg), Fr. 4-8-3 (47.6 mg), Fr. 4-8-4 (16.2 mg), Fr. 4-8-5 (14.2 mg), Fr. 4-8-6 (11.4 mg), Fr. 4-8-7 (14.6 mg), Fr. 4-8-8 (16.8 mg), Fr. 4-8-9 (16.2 mg)]. Fr. 4-8-7 (14.6 mg) was further purified by HPLC [MeCN–MeOH–H₂O (15:8:77, v/v/v)] to give foliasalacioside C (**5**, 3.8 mg). Fraction 5 (3.0 g) was subjected to reversed-phase silica gel column chromatography [90 g, MeOH–H₂O (10:90 $\rightarrow$ 20:80 $\rightarrow$ 30:70 $\rightarrow$ 40:60 $\rightarrow$ 50:50 $\rightarrow$ 100:0, v/v)] to afford seven fractions [Fr. 5-0 (812 mg), Fr. 5-1 (196 mg), Fr. 5-2 (212 mg), Fr. 5-3 (224 mg), Fr. 5-4 (158 mg), Fr. 5-5 (400 mg), Fr. 5-6 (624 mg)]. Fraction 5-3 (224 mg) was purified by HPLC [MeOH–H₂O (26:74, v/v)] and [MeCN–MeOH–H₂O (10:8:82, v/v/v)] to furnish dendranthemoside A (**9**, 13.7 mg) and alangioside A (**10**, 7.1 mg). Fraction 6 (6.7 g) was subjected to reversed-phase silica gel column chromatography [220 g, MeOH–H₂O (10:90 $\rightarrow$ 20:80 $\rightarrow$ 30:70 $\rightarrow$ 40:60 $\rightarrow$ 50:50 $\rightarrow$ 60:40 $\rightarrow$ 100:0, v/v) $\rightarrow$ CHCl₃] to give eleven fractions [Fr. 6-1 (809 mg), Fr. 6-2 (859 mg), Fr. 6-3 (118 mg), Fr. 6-4 (103 mg), Fr. 6-5 (480 mg), Fr. 6-6 (300 mg), Fr. 6-7 (250 mg), Fr. 6-8 (1.28 g), Fr. 6-9 (239 mg), Fr. 6-10 (335 mg), Fr. 6-11 (1.25 g)]. Fraction 6-2 (859 mg) was separated by HPLC [MeOH–H₂O (25:75, v/v)] to afford thirteen fractions [Fr. 6-2-1 (18.2 mg), Fr. 6-2-2 (28.5 mg), Fr. 6-2-3 (36.3 mg), Fr. 6-2-4 (16.7 mg), Fr. 6-2-5 (42.5 mg), Fr. 6-2-6 (32.1 mg), Fr. 6-2-7 (38.9 mg), Fr. 6-2-8 (70.6 mg), Fr. 6-2-9 (37.5 mg), Fr. 6-2-10 (58.3 mg), Fr. 6-2-11 (21.2 mg), Fr. 6-2-12 (24.6 mg), Fr. 6-2-13 (18.9 mg)]. Fraction 6-2-12 (24.6 mg) was purified by HPLC [MeCN–MeOH–H₂O (7:7:86, v/v/v)] to furnish (6*S*,7*E*,9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-*O*- α -L-arabinopyranosyl(1 $\rightarrow$ 6)- β -D-glucopyranoside (**11**, 4.3 mg) and citroside B (**13**, 5.5 mg). Fraction 7 (1.6 g) was subjected to reversed-phase silica gel column chromatography [50 g, MeOH–H₂O (20:80 $\rightarrow$ 30:70 $\rightarrow$ 40:60 $\rightarrow$ 50:50 $\rightarrow$ 100:0, v/v)] to afford three fractions [Fr. 7-1 (529 mg), Fr. 7-2 (570 mg), Fr. 7-3 (321 mg)]. Fraction 7-2 was identified as rutin (**19**, 570 mg). Fraction 8 (2.4 g) was subjected to reversed-phase silica gel column chromatography [100 g, MeOH–H₂O (20:80 $\rightarrow$ 30:70 $\rightarrow$ 40:60 $\rightarrow$ 50:50 $\rightarrow$ 100:0, v/v)] to give four fractions [Fr. 8-1 (562 mg), Fr. 8-2 (445 mg), Fr. 8-3 (284 mg), Fr. 8-4 (463 mg)]. Fraction 8-2 was identified as rutin (**19**, 445 mg), fraction 8-3 (284 mg) was purified by HPLC [MeOH–H₂O (45:55, v/v)] to give rutin (**19**, 7.6 mg). Fraction 9 (9.3 g) was subjected to reversed-phase silica gel column chromatography [50 g, MeOH–H₂O (20:80 $\rightarrow$ 30:70 $\rightarrow$ 40:60 $\rightarrow$ 50:50 $\rightarrow$ 60:40 $\rightarrow$ 100:0, v/v)] to afford eleven fractions [Fr. 9-1 (1.19 g), Fr. 9-2 (322 mg), Fr. 9-3 (230 mg), Fr. 9-4 (295 mg), Fr. 9-5 (511 mg), Fr. 9-6 (954 mg), Fr. 9-7 (189 mg), Fr. 9-8 (1.30 g), Fr. 9-9 (484 mg), Fr. 9-10 (981 mg), Fr. 9-11 (1.66 g)]. Fraction 9-4 (295 mg) was separated by HPLC [MeOH–H₂O (24:76, v/v)] to furnish kaempferol 3-*O*-(2,6- α -L-dirhamnopyranosyl)- β -D-glucopyranosyl-7-*O*- β -D-glucopyranoside (**18**, 138 mg). Fraction 9-5 (511 mg) was subjected to HPLC [MeOH–H₂O (24:76, v/v)] to give paeonoside (**14**, 32.5 mg), kaempferol 3-*O*-rutinosyl-7-*O*- β -D-glucopyranoside (**15**, 18.2 mg), kaempferol 3-*O*- α -L-rhamnopyranosyl(1 $\rightarrow$ 6)- β -D-galatopyranosyl-7-*O*- β -D-glucopyranoside (**16**, 71.6 mg), kaempferol 3-*O*-(2,6- α -L-dirhamnopyranosyl)- β -D-glucopyranosyl-7-*O*- β -D-glucopyranoside (**18**, 118.1 mg), and quercetin 3-*O*-rutinosyl-7-*O*- β -D-glucopyranoside (**20**, 69.2 mg). Fraction 9-8 (1.30 g) was separated by HPLC [MeOH–H₂O (24:76, v/v)] and finally purified by HPLC [MeOH–H₂O–MeCN (13:8:79, v/v/v)] to

furnish kaempferol 3-*O*-rutinoside 7-*O*- β -D-glucopyranoside (**15**, 17.1 mg), clitorin (**17**, 188 mg), manghalin (**21**, 80.3 mg), and myricetin 3-*O*- β -D-rutinoside (**22**, 63.0 mg). Fraction 9-9 (484 mg) was purified by HPLC [MeOH–H₂O (40:60, v/v)] to give rutin (**19**, 65.8 mg).

The known compounds were identified by comparison of their physical data ($[\alpha]_D$, ¹H-NMR, ¹³C-NMR, MS) with reported values.

Foliasalacioside A₁ (**1**): An amorphous powder, $[\alpha]_D^{28} +24.3^\circ$ (*c* 0.65, MeOH). High-resolution positive-ion FAB-MS: Calcd for C₁₉H₃₂O₈Na (M+Na)⁺: 411.1995. Found: 411.1990. CD [MeOH, nm ($\Delta\epsilon$)]: 215 (+2.06), 328 (+0.27). UV [MeOH, nm (log ϵ)]: 238 (4.20). IR (KBr): 3420, 2932, 1653, 1489, 1387, 1078, 1036 cm⁻¹. ¹H-NMR (CD₃OD, 500 MHz) δ : 1.03, 1.11 (3H each, both s, 12, 11-H₃), 1.16 (3H, d, *J* = 6.2 Hz, 10-H₃), 1.46, 1.94 (1H each, both m, 7-H₂), 1.53 (2H, m, 8-H₂), 2.01 (1H, m, 6-H), 2.02 (1H, d, *J* = 17.9 Hz, 2-H α), 2.55 (1H, d, *J* = 17.9 Hz, 2-H β), 3.71 (1H, m, 9-H), 4.32 (1H, d, *J* = 8.2 Hz, 1'-H), 4.38, 4.54 (1H each, both dd, *J* = 1.4, 16.5 Hz, 13-H₂), 6.16 (1H, br s, 4-H). ¹³C-NMR (125 MHz, CD₃OD) δ_c : given in Table 1. Positive-ion FAB-MS: *m/z* 411 (M+Na)⁺.

Foliasalacioside A₂ (**2**): An amorphous powder, $[\alpha]_D^{26} +30.9^\circ$ (*c* 0.55, MeOH). High-resolution positive-ion FAB-MS: Calcd for C₁₉H₃₂O₈Na (M+Na)⁺: 411.1995. Found: 411.1990. CD [MeOH, nm ($\Delta\epsilon$)]: 216 (+4.23), 330 (+0.45). UV [MeOH, nm (log ϵ)]: 239 (4.09). IR (KBr): 3423, 2932, 1653, 1489, 1387, 1078, 1034 cm⁻¹. ¹H-NMR (CD₃OD, 500 MHz) δ : 1.01, 1.10 (3H each, both s, 12, 11-H₃), 1.18 (3H, d, *J* = 6.2 Hz, 10-H₃), 1.49, 1.95 (1H each, both m, 7-H₂), 1.62 (2H, m, 8-H₂), 1.94 (1H, m, 6-H), 2.01 (1H, d, *J* = 17.9 Hz, 2-H α), 2.56 (1H, d, *J* = 17.9 Hz, 2-H β), 3.88 (1H, m, 9-H), 4.18 (1H, dd, *J* = 2.0, 17.8 Hz, 13-H $\square$), 4.36 (1H, dd, *J* = 1.4, 17.8 Hz, 13-H β), 4.33 (1H, d, *J* = 8.3 Hz, 1'-H), 6.04 (1H, br s, 4-H). ¹³C-NMR (125 MHz, CD₃OD) δ_c : given in Table 1. Positive-ion FAB-MS: *m/z* 411 (M+Na)⁺.

Foliasalacioside B₁ (**3**): An amorphous powder, $[\alpha]_D^{27} +25.2^\circ$ (*c* 0.80, MeOH). High-resolution positive-ion FAB-MS: Calcd for C₂₄H₄₀O₁₁Na (M+Na)⁺: 527.2468. Found: 527.2461. CD [MeOH, nm ($\Delta\epsilon$)]: 214 (+1.92), 335 (+0.35). UV [MeOH, nm (log ϵ)]: 241 (3.98). IR (KBr): 3405, 2934, 1651, 1379, 1075, 1009 cm⁻¹. ¹H-NMR (CD₃OD, 500 MHz) δ : 1.01, 1.09 (3H each, both s, 12, 11-H₃), 1.18 (3H, d, *J* = 6.2 Hz, 10-H₃), 1.48, 1.98 (1H each, both m, 7-H₂), 1.62 (2H, m, 8-H₂), 1.97 (1H, m, 6-H), 1.97 (1H, d, *J* = 17.2 Hz, 2-H α), 2.46 (1H, d, *J* = 17.2 Hz, 2-H β), 2.05 (3H, s, 13-H₃), 3.85 (1H, m, 9-H), 4.28 (1H, d, *J* = 6.8 Hz, 1''-H), 4.31 (1H, d, *J* = 8.2 Hz, 1'-H), 5.80 (1H, s, 4-H). ¹³C-NMR (125 MHz, CD₃OD) δ_c : given in Table 1. Positive-ion FAB-MS: *m/z* 527 (M+Na)⁺. Negative-ion FAB-MS: *m/z* 503 (M-H)⁻.

Foliasalacioside B₂ (**4**): An amorphous powder, $[\alpha]_D^{26} +30.5^\circ$ (*c* 0.60, MeOH). High-resolution positive-ion FAB-MS: Calcd for C₂₄H₄₀O₁₁Na (M+Na)⁺: 527.2468. Found: 527.2473. CD [MeOH, nm ($\Delta\epsilon$)]: 214 (+1.26), 327 (+0.19). UV [MeOH, nm (log ϵ)]: 240 (3.92). IR (KBr): 3397, 2930, 1655, 1379, 1075, 1040 cm⁻¹. ¹H-NMR (CD₃OD, 500 MHz) δ : 1.01, 1.09 (3H each, both s, 12, 11-H₃), 1.18 (3H, d, *J* = 6.1 Hz, 10-H₃), 1.41, 1.96 (1H each, both m, 7-H₂), 1.61 (2H, m, 8-H₂), 1.97 (1H, d, *J* = 17.4 Hz, 2-H α), 2.47 (1H, d, *J* = 17.4 Hz, 2-H β), 1.98 (1H, m, 6-H), 2.05 (3H, s, 13-H₃), 3.83 (1H, m, 9-H), 4.31 (1H, d, *J* = 7.1 Hz, 1'-H), 4.96 (1H, d, *J* = 1.5 Hz, 1''-H), 5.81 (1H, s, 4-H). ¹³C-NMR (125 MHz, CD₃OD) δ_c : given in Table 1. Positive-ion FAB-MS: *m/z* 527 (M+Na)⁺. Negative-ion FAB-MS: *m/z* 503 (M-H)⁻.

Foliasalacioside C (**5**): An amorphous powder, $[\alpha]_D^{23} -20.4^\circ$ (*c* 0.24, MeOH). High-resolution positive-

ion FAB-MS: Calcd for $C_{24}H_{40}O_{11}Na$ ($M+Na$)⁺: 527.2468. Found: 527.2470. IR (KBr): 3379, 2928, 1705, 1660, 1456, 1379, 1084, 1044 cm^{-1} . 1H -NMR (CD_3OD , 500 MHz) δ : 1.16 (6H, s, 11, 12- H_3), 1.20 (3H, d, J = 6.1 Hz, 10- H_3), 1.61 (2H, m, 8- H_2), 1.74 (3H, s, 13- H_3), 2.09, 2.31 (1H each, both m, 7- H_2), 2.34 (2H, t, J = 6.7 Hz, 4- H_2), 2.52 (2H, t, J = 6.7 Hz, 3- H_2), 3.90 (1H, m, H-9), 4.33 (1H, d, J = 6.7 Hz, 1'-H), 4.34 (1H, d, J = 8.0 Hz, 1'-H). ^{13}C -NMR (125 MHz, CD_3OD) δ_c : given in Table 1. Positive-ion FAB-MS: m/z 527 ($M+Na$)⁺. Negative-ion FAB-MS: m/z 503 ($M-H$)⁻.

Foliasalacioside D (**6**): An amorphous powder, $[\alpha]_D^{26}$ -17.7° (c 0.29, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{24}H_{40}O_{11}Na$ ($M+Na$)⁺: 527.2468. Found: 527.2474. UV [MeOH, nm (log ϵ)]: 247 (3.86). IR (KBr): 3339, 2928, 1653, 1074, 1036 cm^{-1} . 1H -NMR (CD_3OD , 500 MHz) δ : 1.20 (6H, s, 11, 12- H_3), 1.22 (3H, d, J = 6.1 Hz, 10- H_3), 1.65 (2H, m, 8- H_2), 1.76 (3H, s, 13- H_3), 1.81 (2H, t, J = 6.8 Hz, 2- H_2), 2.31, 2.54 (1H each, both m, 7- H_2), 2.44 (2H, t, J = 6.8 Hz, 3- H_2), 3.93 (1H, m, 9-H), 4.34 (1H, d, J = 7.6 Hz, 1'-H), 4.98 (1H, d, J = 1.4 Hz, 1''-H). ^{13}C -NMR (125 MHz, CD_3OD) δ_c : given in Table 1. Positive-ion FAB-MS: m/z 527 ($M+Na$)⁺. Negative-ion FAB-MS: m/z 503 ($M-H$)⁻.

Acid Hydrolysis of 1–6

Solutions of **1**, **2** (each 0.5 mg) and **3–6** (each 1.0 mg) in 1 M HCl (1.0 mL) were heated under reflux for 3 h. After cooling, each reaction mixture was neutralized with Amberlite IRA-400 (OH^- form) and filtrated, and the solution was partitioned with EtOAc to give two layers. The aqueous layer was evaporated and then subjected to HPLC analysis using Kaseisorb LC NH_2 -60-5 column (4.6 mm $\times$ 250 mm i.d., Tokyo Kasei Co., Ltd., Tokyo, Japan) and an optical rotation detector (Shodex OR-2, Showa Denko Co., Ltd., Tokyo, Japan). D-Glucose (from **1–6**) and L-arabinose (from **3–6**) were confirmed by comparison of the retention times with the authentic samples (Wako Pure Chemicals Ltd., Osaka, Japan) [mobile phase: MeCN– H_2O (85:15, v/v), flow rate: 0.8 mL/min, t_R : 10.2 min (L-arabinose, positive optical rotation); t_R : 12.8 min (D-glucose, positive optical rotation)].

Enzymatic Hydrolysis of 1 and 2 with β -Glucosidase

Solutions of **1** and **2** (12.6, 3.8 mg, respectively) in H_2O (1.0 mL) were treated with β -glucosidase (16.0, 6.1 mg, respectively) and the solution was stirred at 37 $^\circ C$ for 20 h. Work-up of the reaction mixture as described above to furnish foliasalaciol A (**1a**, 5.7 mg, 77.7% from **1** and 2.0 mg, 90.5% from **2**).

Foliasalaciol A (**1a**): Colorless oil; $[\alpha]_D^{27}$ $+69.2^\circ$ (c 0.25, MeOH); High-resolution positive-ion EI-MS: Calcd for $C_{13}H_{22}O_3$: 226.1569. Found: 226.1564. IR (film) 3415, 2965, 2932, 2874, 1651, 1372, 1121 cm^{-1} ; 1H -NMR ($CDCl_3$, 500 MHz) δ : 1.02, 1.09 (3H each, both s, 12, 11- H_3), 1.21 (3H, d, J = 6.1 Hz, 10- H_3), 1.54, 1.87 (1H each, both m, 7- H_2), 1.51 (2H, m, 8- H_2), 2.08, 2.47 (1H each, both d, J = 17.5 Hz, 2- H_2), 1.96 (1H, m, 6-H), 3.82 (1H, m, 9-H), 4.25 (1H, dd, J = 1.5, 16.8 Hz, 13- H_a), 4.35 (1H, dd, J = 1.4, 16.8 Hz, 13- H_b), 6.08 (1H, br s, 4-H); ^{13}C -NMR (125 MHz, CD_3OD) δ_c : given in Table 1. Positive-ion FAB-MS: m/z 527 ($M+Na$)⁺. Negative-ion FAB-MS: m/z 503 ($M-H$)⁻. ^{13}C NMR data, see Table 1; Positive-ion EI-MS (%): m/z 226 (M^+ , 9), 209 (14), 208 (66), 193 (16), 179 (42), 135 (89), 109 (100).

Preparation of the (R)-MTPA Ester and (S)-MTPA Esters from Foliasalaciol A (**1a**)

A solution of **1a** (2.9 mg) in dry CHCl_3 (1.0 mL) was reacted with (*R*)-2-methoxy-2-trifluoromethylphenylacetic acid [(*R*)-MTPA, 40.7 mg] in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC·HCl, 44.0 mg) and 4-dimethylaminopyridine (4-DMAP, 15.5 mg), and the resulting mixture was stirred at room temperature for 10 h. The reaction mixture was poured into ice-water and extracted with EtOAc. The EtOAc extract was washed successively with 5% HCl, NaHCO_3 -saturated H_2O and brine and dried over Na_2SO_4 and filtered. Removal of the solvent from the filtrate under reduced pressure. The residue was subjected to normal-phase silica gel column chromatography [500 mg, *n*-hexane-EtOAc (10: 1 $\rightarrow$ 3:1 $\rightarrow$ 1:1) to furnish **1b** (2.9 mg, 34.3%). Using a similar procedure, (*S*)-MTPA ester [**1c**, 2.9 mg, 45.2%] was obtained from **1a** (2.2 mg) with (*S*)-MTPA (30.9 mg), EDC·HCl (38.2 mg) and 4-DMAP (12.0 mg).

Compound 1b. Colorless oil; ^1H -NMR (CDCl_3 , 500 MHz) δ : 0.95, 0.98 (3H each, both s, 12, 11- H_3), 1.28 (3H, d, $J = 6.4$ Hz, 10- H_3), 1.39, 1.75 (1H each, both m, 7- H_2), 1.70 (2H m, 8- H_2), 1.80 (1H, m, 6-H), 2.04, 2.30 (1H each, both d, $J = 17.4$ Hz, 2- H_2), 3.48, 3.54 (3H each, both s, - OCH_3), 4.78, 4.89 (1H each, both br d, $J = ca.$ 16, 13- H_2), 5.04 (1H, m, 9-H), 5.88 (1H, s, 4-H), 7.40 (3H, m, Ph-H), 7.43 (3H m, Ph-H), 7.50 (4H, m, Ph-H).

Compound 1c. Colorless oil; ^1H -NMR (CDCl_3 , 500 MHz) δ : 0.88 (6H, s, 12, 11- H_3), 1.35 (3H, d, $J = 6.4$ Hz, 10- H_3), 1.27, 1.58 (1H each, both m, 7- H_2), 1.64 (2H m, 8- H_2), 1.71 (1H, dd, m, 6-H), 1.98, 2.19 (1H each, both d, $J = 17.4$ Hz, 2- H_2), 3.55, 3.57 (3H each, both s, - OCH_3), 4.70 (1H, dd, $J = 1.2, 15.0$ Hz, 13- H_a), 4.83 (1H, dd, $J = 1.6, 15.0$ Hz, 13- H_b), 5.04 (1H, m, 9-H), 5.85 (1H, s, 4-H), 7.38 (3H, m, Ph-H), 7.43 (3H m, Ph-H), 7.50 (4H, m, Ph-H).

Enzymatic Hydrolysis of 3 and 4 with Nariginase

Solutions of **3** and **4** (5.5, 5.1 mg, respectively) in 0.2 M acetate buffer (pH 3.8) (1.0 mL) were treated with nariginase (10.5 and 12.2 mg, respectively) and the solution was stirred at 40 °C for 4 day. After cooling, the reaction mixture was extracted with EtOAc. The EtOAc solvent was removed under reduced pressure and the residue was purified by HPLC [$\text{MeOH-H}_2\text{O}$ (50:50, v/v)] to give blumenyl C (1.3 mg, 54.9% from **3** and 2.0 mg, 91.3% from **4**).

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