Structure Elucidation of Six Acylated Iridoid Glucosides from *Jasminum hemsleyi*

Takao TANAHASHI,*[,a] Atsuko SHIMADA,[a] Naotaka NAGAKURA,[a] Kenichiro INOUE,[b] Masami ONO,[c] Tetsuro FUJITA,[c] and Cheng-Chang CHEN[d]

Kobe Pharmaceutical University,[a] Higashinada-ku, Kobe 658, Japan, Gifu Pharmaceutical University,[b] Mitahora-higashi, Gifu 502, Japan, Faculty of Pharmaceutical Sciences of Kyoto University,[c] Sakyo-ku, Kyoto 606, Japan, and National Kaohsiung Normal University,[d] Kaohsiung, Taiwan, Republic of China.

Received September 2, 1994; accepted December 20, 1994

Six new iridoid glucosides, jashemslosides A—D (2—5), 6′-*O*-*trans*-*p*-coumaroylloganin (6) and 6′-*O*-*cis*-*p*-coumaroylloganin (7), were isolated from the leaves of *Jasminum hemsleyi*, together with the known glycosides, loganin, 7-dehydrologanin, jasminoside, 10-hydroxyoleoside dimethyl ester and lariciresinol-4-*O*-β-D-glucoside. The structures of the new glucosides 2—7, which contain a menthiafolic acid unit or *p*-coumaroyl group in addition to the loganin moiety, were elucidated by spectroscopic and chemical studies. Chirospecific HPLC analysis of the monoterpenic acid derivatives prepared from 2 and 3 revealed that each of the new compounds was a mixture of two inseparable diastereoisomers.

Key words *Jasminum hemsleyi*; Oleaceae; iridoid glucoside; jashemsloside; 6′-*O*-*p*-coumaroylloganin; menthiafolic acid ester

In previous papers,[1] we reported the isolation and structural elucidation of new secoiridoid glucosides from the leaves of *Fraxinus* species (Oleaceae) which grow in Taiwan. In a continuation of our phytochemical studies on the Formosan oleaceous plants, we have investigated *Jasminum hemsleyi* YAMAMOTO and isolated six novel iridoid glucosides, which are closely related to loganin (**1**). We report here the structural elucidation of the new compounds.

The MeOH extract of the fresh leaves of *J. hemsleyi* was, after removal of water-insoluble materials by filtration, partitioned between $CHCl_3$ and H_2O. The aqueous layer was further extracted with *n*-BuOH. The *n*-BuOH-soluble portion was separated by a combination of chromatographic procedures to yield six novel iridoid glucosides, named jashemslosides A—D (**2**—**5**), 6′-*O*-*trans*-*p*-coumaroylloganin (**6**) and 6′-*O*-*cis*-*p*-coumaroylloganin (**7**), along with five known compounds, which were identified as loganin (**1**), 7-dehydrologanin (**8**),[2] jasminoside (**9**),[3] 10-hydroxyoleoside dimethyl ester (**10**)[4] and lariciresinol-4-*O*-β-D-glucoside (**11**)[5] on the basis of their physical and spectroscopic data or by direct comparison with authentic samples. The structures of the new compounds **2**—**7** were determined as follows.

Jashemsloside A (**2**) showed in its high-resolution secondary ion mass spectrum (HR-SIMS) a pseudomolecular ion $[M+Na]^+$ at *m/z* 579.2398 consistent with the molecular formula $C_{27}H_{40}O_{12}$. Its ^{1}H-NMR spectrum exhibited a signal characteristic of H-3 of iridoid glucosides at δ 7.43 (d, $J=1.5$ Hz), and signals due to a secondary methyl group at δ 1.06 (d), a carbomethoxy group at δ 3.69 (s), an anomeric proton at δ 4.66 (d), an acetal proton at δ 5.30 (d) and a methine proton at δ 5.18 (td), indicating the presence of a 7-*O*-acylated loganin moiety in the molecule. Additional ^{1}H-NMR signals indicated the acylating unit at C-7 of loganin to be a menthiafolic acid[6] (**12**, (2*E*)-6-hydroxy-2,6-dimethyl-2,7-octadienoic acid) moiety. Thus, two three-proton signals at δ 1.27 and 1.83 were assigned to a tertiary methyl group (C-10″)[7] attached to a carbon bearing a hydroxyl group and a vinyl methyl group (C-9″), respectively. Three protons of a monosubstituted double bond appeared at δ 5.06, 5.23 and 5.92 as typical ABX system signals ($J=17.0$, 11.0, 1.5 Hz, H_2-8″ and H-7″). Another olefinic proton appeared at δ 6.77 as a triplet of quartets ($J=8.0$, 1.5 Hz, H-3″), indicating an *E*-configuration of the olefinic bond at C-3″.[8] All these findings suggested the structure **2** for the isolated compound. Further evidence supporting this was that the ^{13}C-NMR signals due to the loganin and menthiafolic acid moieties of **2** coincided well with those ascribable to the same parts of 7-*O*-acetylloganic acid (**13**),[9] 7-*O*-benzoylloganin (**14**)[10] and menthiafolic acid methyl ester (**15**).[6c,i] For additional structural confirmation, compound **2** was subjected to alkaline hydrolysis followed by

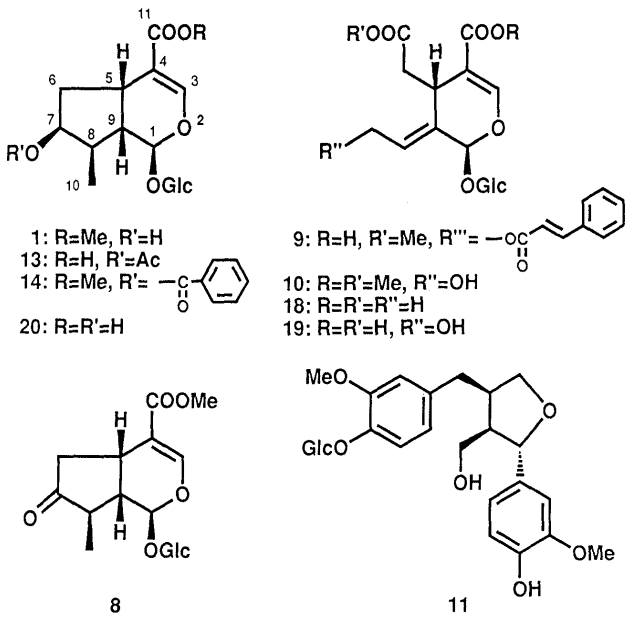

Fig. 1

* To whom correspondence should be addressed.

Table 1. ^{13}C-NMR Data of Loganin (**1**), Jashemslosides A—D (**2**—**5**), **16** and **17** in CD_3OD

C	1	2	3	4	5	16	17
1	97.6	97.4	98.4	97.5	97.5		
3	152.0	152.5	152.4	152.6	152.6		
4	114.0	113.2	113.8	113.4	113.4		
5	32.1	32.5	32.6	32.6	32.6		
6	42.7	40.4	43.1	40.5	40.5		
7	74.9[a)]	78.7	74.9[b)]	78.8[c)]	78.8[f)]		
8	42.1	41.0	42.4	41.1	41.1		
9	46.4	47.2	46.4	47.3	47.2		
10	13.4	13.7	13.7	13.8	13.8		
11	169.4	169.3	169.4	169.4	169.4		
COOMe	51.6	51.7	51.7	51.8	51.8		
1′, 1‴	100.0	100.1	100.3	100.3, 99.6	100.3, 99.4	99.6	99.4
2′, 2‴	74.7[a)]	74.7	74.7[b)]	74.8, 75.3	74.8, 75.2	75.3	75.2
3′, 3‴	77.9	77.9	77.9	78.1,[c)] 78.5[c)]	78.0,[f)] 78.5[f)]	78.3	78.3
4, 4‴	71.5	71.5	71.8	71.7,[d)] 71.8[d)]	71.6,[g)] 71.7[g)]	71.8	71.8
5′, 5‴	78.3	78.3	75.7	78.3,[c)] 77.7[c)]	78.3,[f)] 77.7[f)]	77.7	77.7
6′, 6‴	62.7	62.7	64.5	62.9, 62.9	62.8, 62.9	62.9	62.9
1″		169.2	169.3	169.4	169.4	170.4	170.4
2″		128.8	128.5	128.9	128.9	128.5	128.5
3″		144.0	144.2	144.4[e)]	144.4	144.4[h)]	144.5[i)]
4″		24.5	24.5	24.5	24.4	24.4	24.4
5″		41.7	41.8	41.2	39.9	41.2	40.0
6″		73.6	73.6	81.1	81.0	81.1	81.0
7″		145.9	145.9	144.3[e)]	144.4	144.2[h)]	144.4[i)]
8″		112.4	112.5	116.1	115.3	116.1	115.3
9″		12.5	12.5	12.5	12.6	12.5	12.5
10″		27.8	27.9	23.6	24.0	23.6	23.9
OMe						52.2	52.2

The spectrum of glucoside **1** was measured at 50 MHz; the others were taken at 125 MHz. *a*—*i*) Values with the same superscript are interchangeable.

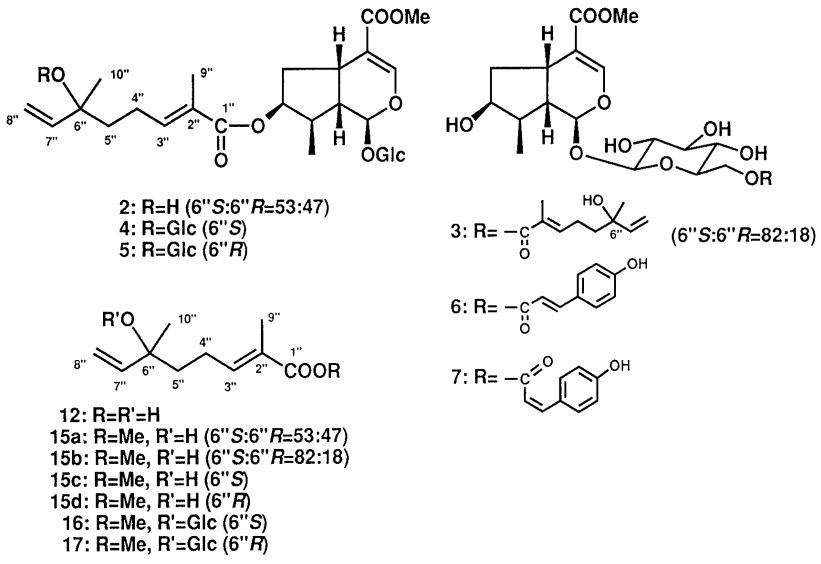

Fig. 2

methylation with CH_2N_2–Et_2O, which gave two compounds, **1** and **15a**. The spectral and physical data of **1** were in good accord with those of loganin, confirming the absolute stereostructure of the iridoid moiety in **2**. On the other hand, the IR, MS and NMR data of the latter compound **15a** were identical with those previously reported for menthiafolic acid methyl ester.[6c,i)] Accordingly, the structure of jashemsloside A was determined to be **2**, except for the absolute configuration at C-6″, which was determined by correlation with the structures of **4** and **5** (*vide infra*).

Jashemsloside B (**3**) was recognized as an isomer of **2**, $C_{27}H_{40}O_{12}$, from its mass spectrum. Its UV, IR and ^{1}H-NMR spectral features suggested a structural similarity to **2**. Alkaline hydrolysis and subsequent methylation of compound **3** gave loganin (**1**) and **15b** in a similar way to that described for **2**, suggesting that compound **3** could also be an ester of menthiafolic acid (**12**) and loganin (**1**). Comparative studies of the ^{13}C-NMR spectra of **1**, **2** and **3** indicated that the position of the ester linkage of menthiafolic acid moiety in **3** was different from that in **2**. Attachment of the acyl group to the C-6′ hydroxyl in

a glucose moiety was deduced from the appreciable downfield shift of the C-6′ signal from δ 62.7 in loganin (**1**) to δ 64.5 in **3**, whereas the signal due to C-7 of **3** was at approximately the same position as that of loganin. Accordingly, jashemsloside B (**3**) was characterized as 6′-*O*-[(2*E*)-6-hydroxy-2,6-dimethyl-2,7-octadienoyl]-loganin.

Jashemslosides C (**4**) and D (**5**) had the same molecular formula of $C_{33}H_{50}O_{17}$. The ^{1}H- and ^{13}C-NMR spectral features of **4** and **5** showed them to be closely related to jashemsloside A (**2**), but to differ in that **4** and **5** exhibited a set of additional signals due to a β-D-glucosyl unit. In the ^{13}C-NMR spectra of **2**, **4** and **5**, the signals attributable to a loganin moiety resonated at nearly identical frequencies, while the signals assignable to the carbons around C-6″ of a menthiafolic acid moiety showed significant differences. The downfield shifts of C-6″ and C-8″ as well as the upfield shifts of C-5″, C-7″ and C-10″ of **4** and **5**, when compared with the corresponding signals of **2**, indicated the attachment of another glucose unit at C-6″ of the menthiafolic acid moiety in both glucosides. In each case the anomeric configuration of the glucosyl linkage was determined to be β from the coupling constant (d, J=8.0 Hz) of the anomeric proton. In addition, the chemical shifts of the anomeric carbons (**4**: δ 99.6; **5**: δ 99.4) were in good agreement with those of β-D-glucose linked to a tertiary alcohol.[11]

Detailed inspection of the ^{13}C-NMR spectra suggested that **4** and **5** differed from each other only in the absolute configuration of C-6″. Slight but significant differences between **4** and **5** in the glycosidation shifts observed for C-5″, 6″ and 8″ were comparable to those previously reported for the glycosides of (*S*)-(+)-linalool and (*R*)-(−)-linalool.[12] The C-5″ glycosidation shifts observed in **4** (−0.5 ppm) and **5** (−1.8 ppm) were indicative of 6″*S* and 6″*R* configurations, respectively. To confirm this, the following series of reactions were carried out: jashemsloside C (**4**) was subjected to Zemplen reaction to give **16** and loganin (**1**), while jashemsloside D (**5**) yielded **17** and **1**. The ^{1}H- and ^{13}C-NMR spectra of **16** and **17** demonstrated clearly the presence of a β-D-glucosyl moiety in addition to a menthiafolic acid methyl ester. Enzymatic hydrolysis of compounds **16** and **17** with β-glucosidase liberated **15c** and **15d**, respectively. Both products revealed spectral features identical with those of menthiafolic acid methyl ester,[6c,i] but the signs of their specific optical rotations were opposite. An *S* configuration at C-6″ of **15c** was deduced from the agreement of the positive sign of its $[\alpha]_D$ (+19.4°) with those of similar compounds, such as (*S*)-(+)-linalool ($[\alpha]_D$ +21.6°) or (2*E*,6*S*)-(+)-6-hydroxy-2,6-dimethyl-2,7-octadienoic acid ($[\alpha]_D$ +19.3°),[6f] thereby requiring **15d** ($[\alpha]_D$ −18.2°) to have 6″*R* configuration. Accordingly, the absolute stereostructures of jashemslosides C and D were established to be as shown in **4** and **5**, respectively.

Since the optically pure reference substances **15c** and **15d** were obtained, we studied the absolute stereochemistry at C-6″ of jashemslosides A (**2**) and B (**3**). The optical rotation of the monoterpenic acid derivative **15a**, which was derived from **2**, was nearly zero. This implied that compound **15a** was a mixture of (+)-menthiafolic acid methyl ester (**15c**) and its (−)-enantiomer (**15d**), and so the glucoside **2** consisted of two C-6″ epimers. In order to evaluate the optical purity of **15a**, we employed chirospecific HPLC analysis of the enantiomers **15c** and **15d**. Ordinary-phase HPLC with CHIRALCEL OB as a column and *n*-hexane–2-propanol as an eluent resulted in sufficient enantio-resolution of both monoterpenic acid derivatives. Chiral HPLC analysis showed **15a** to be a mixture of **15c** and **15d** in the ratio of 53:47. As in the case of **15a**, **15b** derived from **3** was found to be an enantiomeric mixture with a different proportion (**15c**:**15d**=82:18). These results led us to conclude that each of jashemslosides A (**2**) and B (**3**) is an inseparable mixture of (6″*S*)- and (6″*R*)-diastereoisomers, although they seemed to be single compounds from the NMR and HPLC (octadecyl silica (ODS), MeOH–H_2O) analyses.

Glucosides **6** and **7** were found to be geometric isomers with the molecular formula $C_{26}H_{32}O_{12}$. These compounds were separated by preparative HPLC on an ODS column with MeOH–H_2O, but on evaporation of the solvent at 40 °C, each fraction again gave a mixture of **6** and **7**, indicating an equilibrium between the two compounds. Careful and rapid evaporation of MeOH at lower temperature (< 10 °C) followed by freeze-drying enabled their purification.

The ^{1}H- and ^{13}C-NMR spectra of **6** and **7** exhibited all the characteristic signals of 6′-*O*-acylated loganin derivatives such as jashemsloside B (**3**). Furthermore, the ^{1}H-NMR spectrum exhibited additional signals corresponding to *trans*- or *cis*-*p*-coumaroyl moieties; a pair of doublets due to olefinic protons (**6**: δ 6.34, 7.62, J=16.0 Hz; **7**: δ 5.77, 6.87, J=13.0 Hz) and an aromatic AA′BB′ spin system (**6**: δ 6.80, 7.44; **7**: δ 6.75, 7.65). The presence of the *p*-coumaroyl moiety was also supported by the UV maxima (**6**: 300 sh, 314 nm; **7**: 298 sh, 311 nm) and IR bands (**6**: 1698, 1638, 1608, 1518, 832 cm^{-1}; **7**: 1698, 1634, 1610, 1518 cm^{-1}). Thus, compounds **6** and **7** were identified as 6′-*O*-*trans*-*p*-coumaroylloganin and 6′-*O*-*cis*-*p*-coumaroylloganin, respectively.

Oleoside (**18**)- and 10-hydroxyoleoside (**19**)-type secoiridoid glucosides such as jasminoside (**9**) are characteristic constituents of oleaceous plants. However, excepting loganic acid (**20**),[13] loganin derivatives have never been found in plants belonging to this family, although loganin (**1**) is an established precursor for these types of secoiridoid glucosides.[14] This constitutes the first report of the isolation from the family Oleaceae of loganin (**1**) and loganin derivatives esterified with a monoterpenic acid or *p*-coumaric acid.

Experimental

UV spectra were recorded on a Shimadzu UV-240 spectrophotometer and IR spectra on a Shimadzu FTIR-8200 or a Hitachi 270-30 infrared spectrophotometer. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. MS and HR-MS were obtained with a Hitachi M-4100 mass spectrometer. For SIMS, glycerol was used as the matrix. The NMR experiments were performed with Varian VXR-500, Varian Gemini-300 and Varian XL-200 spectrometers, with tetramethylsilane as an internal standard. HPLC was performed using a Waters system (600E Multisolvent Delivery System, 490 Programmable Multiwavelength Detector, 741 Datamodule). Column chromatograpy was carried out with Silica gel 60 (70—230 mesh, Nacalai Tesque). Thin-layer chromatography was performed on a precoated Kieselgel

$60F_{254}$ plate (Merck) and spots were visualized under UV light.

Isolation of Glucosides The leaves of *J. hemsleyi* were collected in Heng-Chun Tropical Botanical Garden, Taiwan in November 1986. A voucher specimen (IT-9002) has been deposited in the Herbarium of Gifu Pharmaceutical University, Gifu 502, Japan. Fresh leaves of *J. hemsleyi* (1.17 kg) were extracted with hot MeOH. After concentration, the extract (110.4 g) was dissolved in H_2O and filtered through a Celite layer. The filtrate and washings were combined and extracted with $CHCl_3$ and *n*-BuOH successively. The *n*-BuOH layer was concentrated to give a viscous residue (27.9 g), which was chromatographed on a silica gel column. Elution with $CHCl_3$–MeOH mixtures of the indicated MeOH content gave 8 fractions, I (7%, 738 mg), II (7%, 691 mg), III (7—10%, 3.05 g), IV (10—15%, 1.48 g), V (15%, 2.38 g), VI (15%, 1.81 g), VII (15—18%, 5.30 g) and VIII (18—40%, 4.61 g), respectively. Each fraction was further purified by a combination of column chromatography with AcOEt–C_6H_6–EtOH, preparative TLC (AcOEt–C_6H_6–EtOH, 4 : 1 : 1) and preparative HPLC (μBondasphere 5μC8-100 Å or μBondasphere 5μC18-100 Å, MeOH–H_2O, 1 : 1). Fraction I gave **2** (89.8 mg), **3** (23.2 mg), 7-dehydrologanin (12.8 mg), A (6.1 mg), **6** (28.8 mg), **7** (8.6 mg) and B (7.0 mg). Fraction II: **3**: (2.0 mg), **6** (8.3 mg), **7** (3.2 mg), C (13.3 mg), 10-hydroxyoleoside dimethyl ester (8.4 mg); fr. III: **1** (264.0 mg), **3** (2.0 mg), 10-hydroxyoleoside dimethyl ester (4.7 mg), lariciresinol-4-*O*-*β*-D-glucoside (63.2 mg), jasminoside (51.8 mg); fr. IV: **4** (115.9 mg), **5** (29.7 mg); fr. V: **4** (50.9 mg), **5** (43.6 mg). A, B and C are unidentified ionone-type glycosides. Studies on the structures of these compounds are in progress.

Jashemsloside A (2) Powder, $[\alpha]_D^{28}$ −36.1° (c=1.05, MeOH). UV λ_{max}^{MeOH} nm (log ε): 225 (4.32). IR ν_{max}^{KBr} cm^{-1}: 3432, 1708, 1640. ^{1}H-NMR (CD_3OD) δ: 1.06 (3H, d, J=6.5 Hz, H_3-10), 1.27 (3H, s, H_3-10″), 1.62 (2H, m, H_2-5″), 1.76 (1H, ddd, J=14.5, 8.0, 5.0 Hz, H-6), 1.83 (3H, d, J=1.5 Hz, H_3-9″), 2.08 (1H, td, J=8.5, 5.0 Hz, H-9), 2.15 (1H, m, H-8), 2.23 (2H, m, H_2-4″), 2.28 (1H, ddd, J=14.5, 8.0, 1.5 Hz, H-6), 3.11 (1H, br q, J=8.0 Hz, H-5), 3.19 (1H, dd, J=9.0, 8.0 Hz, H-2′), 3.37 (1H, t, J=9.0 Hz, H-3′), 3.66 (1H, dd, J=12.0, 6.0 Hz, H-6′), 3.69 (3H, s, COOMe), 3.90 (1H, dd, J=12.0, 2.0 Hz, H-6′), 4.66 (1H, d, J=8.0 Hz, H-1′), 5.06 (1H, dd, J=11.0, 1.5 Hz, H-8″), 5.18 (1H, td, J=5.0, 1.5 Hz, H-7), 5.23 (1H, dd, J=17.0, 1.5 Hz, H-8″), 5.30 (1H, d, J=5.0 Hz, H-1), 5.92 (1H, dd, J=17.0, 11.0 Hz, H-7″), 6.77 (1H, tq, J=8.0, 1.5 Hz, H-3″), 7.43 (1H, d, J=1.5 Hz, H-3). ^{13}C-NMR: see Table 1. HR-SIMS m/z: 579.2398 $(M+Na)^+$. Calcd for $C_{27}H_{40}NaO_{12}$: 579.2419.

Jashemsloside B (3) Powder, $[\alpha]_D^{24}$ −36.9° (c=1.09, MeOH). UV λ_{max}^{MeOH} nm (log ε): 225 (4.26). IR ν_{max}^{KBr} cm^{-1}: 3448, 1710, 1638. ^{1}H-NMR (CD_3OD) δ: 1.05 (3H, d, J=7.0 Hz, H_3-10), 1.26 (3H, s, H_3-10″), 1.50 (1H, ddd, J=14.0, 8.5, 4.5 Hz, H-6), 1.59 (2H, m, H_2-5″), 1.82 (3H, br s, H_3-9″), 1.83 (1H, m, H-8), 1.95 (1H, td, J=9.0, 5.5 Hz, H-9), 2.22 (2H, m, H_2-4″), 2.25 (1H, ddd, J=14.0, 7.5, 1.5 Hz, H-6), 3.11 (1H, br q, J=8.0 Hz, H-5), 3.20 (1H, dd, J=9.0, 8.0 Hz, H-2′), 3.34 (1H, t, J=9.0 Hz, H-4′), 3.38 (1H, t, J=9.0 Hz, H-3′), 3.52 (1H, ddd, J=9.0, 6.5, 2.5 Hz, H-5′), 3.69 (3H, s, COOMe), 4.01 (1H, br t, J=4.5 Hz, H-7), 4.28 (1H, dd, J=12.0, 6.5 Hz, H-6′), 4.48 (1H, dd, J=12.0, 2.5 Hz, H-6′), 4.64 (1H, d, J=8.0 Hz, H-1′), 5.05 (1H, dd, J=11.0, 1.5 Hz, H-8″), 5.05 (1H, d, J=5.5 Hz, H-1), 5.22 (1H, dd, J=17.5, 1.5 Hz, H-8″), 5.90 (1H, dd, J=17.5, 11.0 Hz, H-7″), 6.78 (1H, tq, J=7.0, 1.5 Hz, H-3″), 7.42 (1H, d, J=1.0 Hz, H-3). ^{13}C-NMR: see Table 1. HR-SIMS m/z: 579.2416 $(M+Na)^+$. Calcd for $C_{27}H_{40}NaO_{12}$: 579.2419.

Jashemsloside C (4) Powder, $[\alpha]_D^{26}$ −35.4° (c=0.93, MeOH). UV λ_{max}^{MeOH} nm (log ε): 225 (4.32). IR ν_{max}^{KBr} cm^{-1}: 3464, 1710, 1642. ^{1}H-NMR (CD_3OD) δ: 1.06 (3H, d, J=7.0 Hz, H_3-10), 1.41 (3H, s, H_3-10″), 1.71 (2H, m, H_2-5″), 1.76 (1H, ddd, J=15.0, 8.0, 5.0 Hz, H-6), 1.83 (3H, br s, H_3-9″), 2.10 (1H, td, J=8.0, 4.5 Hz, H-9), 2.14 (1H, m, H-8), 2.28 (1H, ddd, J=15.0, 8.0, 1.0 Hz, H-6), 2.32 (2H, m, H_2-4″), 3.11 (1H, br q, J=8.0 Hz, H-5), 3.17 (1H, dd, J=9.0, 8.0 Hz, H-2‴), 3.20 (1H, dd, J=9.0, 8.0 Hz, H-2′), 3.63 (1H, dd, J=12.0, 5.5 Hz, H-6‴), 3.66 (1H, dd, J=12.0, 6.0 Hz, H-6′), 3.69 (3H, s, COOMe), 3.81 (1H, dd, J=12.0, 2.0 Hz, H-6‴), 3.90 (1H, dd, J=12.0, 2.0 Hz, H-6′), 4.37 (1H, d, J=8.0 Hz, H-1‴), 4.66 (1H, d, J=8.0 Hz, H-1′), 5.18 (1H, td, J=5.0, 1.0 Hz, H-7), 5.22 (1H, dd, J=11.0, 1.0 Hz, H-8″), 5.28 (1H, dd, J=18.0, 1.0 Hz, H-8″), 5.31 (1H, d, J=4.5 Hz, H-1), 5.95 (1H, dd, J=18.0, 11.0 Hz, H-7″), 6.78 (1H, tq, J=7.5, 1.5 Hz, H-3″), 7.43 (1H, br s, H-3). ^{13}C-NMR: see Table 1. HR-SIMS m/z: 741.2950 $(M+Na)^+$. Calcd for $C_{33}H_{50}NaO_{17}$: 741.2947.

Jashemsloside D (5) Powder, $[\alpha]_D^{26}$ −30.9° (c=1.20, MeOH). UV λ_{max}^{MeOH} nm (log ε): 225 (4.31). IR ν_{max}^{KBr} cm^{-1}: 3424, 1710, 1642. ^{1}H-NMR (CD_3OD) δ: 1.06 (3H, d, J=6.5 Hz, H_3-10), 1.36 (3H, s, H_3-10″), 1.71—1.79 (3H, m, H-6, H_2-5″), 1.84 (3H, br s, H_3-9″), 2.10 (1H, td, J=8.5, 5.0 Hz, H-9), 2.14 (1H, m, H-8), 2.28 (1H, ddd, J=15.0, 8.0, 1.5 Hz, H-6), 2.35 (2H, m, H_2-4″), 3.11 (1H, br q, J=8.0 Hz, H-5), 3.17 (1H, dd, J=9.0, 8.0 Hz, H-2‴), 3.20 (1H, dd, J=9.0, 8.0 Hz, H-2′), 3.65 (1H, dd, J=12.0, 5.5 Hz, H-6‴), 3.66 (1H, dd, J=12.0, 6.0 Hz, H-6′), 3.69 (3H, s, COOMe), 3.79 (1H, dd, J=12.0, 2.0 Hz, H-6‴), 3.90 (1H, dd, J=12.0, 2.0 Hz, H-6′), 4.34 (1H, d, J=8.0 Hz, H-1‴), 4.66 (1H, d, J=8.0 Hz, H-1′), 5.18 (1H, m, H-7), 5.18 (1H, dd, J=11.0, 1.0 Hz, H-8″), 5.24 (1H, dd, J=17.5, 1.0 Hz, H-8″), 5.31 (1H, d, J=5.0 Hz, H-1), 6.10 (1H, dd, J=17.5, 11.0 Hz, H-7″), 6.79 (1H, tq, J=7.5, 1.5 Hz, H-3″), 7.43 (1H, d, J=1.0 Hz, H-3). ^{13}C-NMR: see Table 1. HR-SIMS m/z: 719.3147 $(M+H)^+$. Calcd for $C_{33}H_{51}O_{17}$: 719.3128, 741.2934 $(M+Na)^+$. Calcd for $C_{33}H_{50}NaO_{17}$: 741.2947.

6′-*O*-*trans*-*p*-Coumaroylloganin (6) Powder, $[\alpha]_D^{25}$ −32.0° (c=1.0, MeOH). UV λ_{max}^{MeOH} nm (log ε): 231 (4.29), 300 sh (4.25), 314 (4.31). IR ν_{max}^{KBr} cm^{-1}: 3464, 1698, 1638, 1608, 1518, 832. ^{1}H-NMR (CD_3OD) δ: 1.03 (3H, d, J=7.0 Hz, H_3-10), 1.45 (1H, ddd, J=14.0, 9.0, 5.0 Hz, H-6), 1.83 (1H, m, H-8), 1.93 (1H, td, J=9.0, 5.5 Hz, H-9), 2.17 (1H, ddd, J=14.0, 7.5, 1.5 Hz, H-6), 3.08 (1H, br q, J=8.0 Hz, H-5), 3.23 (1H, br t, J=8.5 Hz, H-2′), 3.36 (1H, t, J=9.0 Hz, H-4′), 3.40 (1H, t, J=9.0 Hz, H-3′), 3.56 (1H, ddd, J=9.0, 6.5, 2.5 Hz, H-5′), 3.66 (3H, s, COOMe), 3.98 (1H, br t, J=5.0 Hz, H-7), 4.42 (1H, dd, J=12.0, 6.5 Hz, H-6′), 4.47 (1H, dd, J=12.0, 2.5 Hz, H-6′), 4.66 (1H, d, J=8.0 Hz, H-1′), 5.05 (1H, d, J=5.0 Hz, H-1), 6.34 (1H, d, J=16.0 Hz, H-α), 6.80 (2H, AA′BB′ pattern, J=8.5 Hz, H-3″, 5″), 7.39 (1H, d, J=1.5 Hz, H-3), 7.44 (2H, AA′BB′ pattern, J=8.5 Hz, H-2″, 6″), 7.62 (1H, d, J=16.0 Hz, H-β). ^{13}C-NMR (CD_3OD) δ: 13.8 (C-10), 32.7 (C-5), 42.5 (C-8), 43.0 (C-6), 46.4 (C-9), 51.7 (OMe), 64.4 (C-6′), 71.9 (C-4′), 74.7* (C-2′), 75.0* (C-7), 75.7 (C-5′), 78.0 (C-3′), 98.5 (C-1), 100.5 (C-1′), 113.8 (C-4), 115.0 (C-α), 116.9 (C-3″, 5″), 127.1 (C-1″), 131.3 (C-2″, 6″), 146.9 (C-β), 152.4 (C-3), 161.5 (C-4″), 169.0 (CO), 169.5 (C-11). * Assignments are interchangeable. HR-SIMS m/z: 537.1969 $(M+H)^+$. Calcd for $C_{26}H_{33}O_{12}$: 537.1973, 559.1832 $(M+Na)^+$. Calcd for $C_{26}H_{32}NaO_{12}$: 559.1793.

6′-*O*-*cis*-*p*-Coumaroylloganin (7) Powder, $[\alpha]_D^{25}$ −58.0° (c=1.0, MeOH). UV λ_{max}^{MeOH} nm (log ε): 229 (4.33), 298 sh (4.15), 311 (4.20). IR ν_{max}^{KBr} cm^{-1}: 3456, 1698, 1634, 1610, 1518. ^{1}H-NMR (CD_3OD) δ: 1.02 (3H, d, J=7.0 Hz, H_3-10), 1.46 (1H, ddd, J=14.0, 9.0, 5.0 Hz, H-6), 1.81 (1H, m, H-8), 1.94 (1H, td, J=9.0, 5.0 Hz, H-9), 2.19 (1H, ddd, J=14.0, 8.0, 1.5 Hz, H-6), 3.08 (1H, br q, J=8.0 Hz, H-5), 3.21 (1H, dd, J=9.0, 8.0 Hz, H-2′), 3.34 (1H, m, H-4′), 3.38 (1H, t, J=9.0 Hz, H-3′), 3.51 (1H, ddd, J=9.5, 6.5, 2.0 Hz, H-5′), 3.68 (3H, s, COOMe), 3.93 (1H, td, J=5.0, 1.5 Hz, H-7), 4.33 (1H, dd, J=12.0, 6.5 Hz, H-6′), 4.46 (1H, dd, J=12.0, 2.0 Hz, H-6′), 4.62 (1H, d, J=8.0 Hz, H-1′), 5.01 (1H, d, J=5.0 Hz, H-1), 5.77 (1H, d, J=13.0 Hz, H-α), 6.75 (2H, AA′BB′ pattern, J=8.5 Hz, H-3″, 5″), 6.87 (1H, d, J=13.0 Hz, H-β), 7.39 (1H, d, J=1.5 Hz, H-3), 7.65 (2H, AA′BB′ pattern, J=8.5 Hz, H-2″, 6″). ^{13}C-NMR (CD_3OD) δ: 13.7 (C-10), 32.6 (C-5), 42.5 (C-8), 43.0 (C-6), 46.5 (C-9), 51.7 (OMe), 64.3 (C-6′), 71.8 (C-4′), 74.7* (C-2′), 75.0* (C-7), 75.6 (C-5′), 77.9 (C-3′), 98.5 (C-1), 100.4 (C-1′), 113.8 (C-4), 115.0 (C-α), 116.2 (C-3″, 5″), 127.6 (C-1″), 133.9 (C-2″, 6″), 145.5 (C-β), 152.4 (C-3), 160.3 (C-4″), 168.0 (CO), 169.5 (C-11). HR-SIMS m/z: 559.1805 $(M+Na)^+$. Calcd for $C_{26}H_{32}NaO_{12}$: 559. 1793.

10-Hydroxyoleoside Dimethyl Ester (10) Powder, $[\alpha]_D^{23}$ −157.5° (c=0.4, MeOH). UV λ_{max}^{MeOH} nm (log ε): 234 (4.05). IR ν_{max}^{KBr} cm^{-1}: 3428, 1712, 1636. ^{1}H-NMR (CD_3OD) δ: 2.50 (1H, dd, J=15.0, 9.0 Hz, H-6), 2.77 (1H, dd, J=15.0, 4.3 Hz, H-6), 3.65 (3H, s, COOMe), 3.71 (3H, s, COOMe), 3.96 (1H, dd, J=9.5, 4.3 Hz, H-5), 4.18 (1H, ddd, J=13.0, 6.0, 1.5 Hz, H-10), 4.33 (1H, dd, J=13.0, 6.0 Hz, H-10), 4.78 (1H, d, J=8.0 Hz, H-1′), 5.96 (1H, br s, H-1), 6.16 (1H, t, J=6.0 Hz, H-8), 7.54 (1H, s, H-3).

Lariciresinol-4-*O*-*β*-D-glucoside (11) Needles, mp 113—115 °C (H_2O), $[\alpha]_D^{22}$ −17.0° (c=1.0, MeOH) [lit.[5] $[\alpha]_D^{23}$ −19.3° (MeOH)]. UV λ_{max}^{MeOH} nm (log ε): 227 (4.17), 279 (3.74). IR ν_{max}^{KBr} cm^{-1}: 3432, 1600, 1518. ^{1}H-NMR (CD_3OD) δ: 2.37 (1H, br quintet, J=7.0 Hz, H-8′), 2.54 (1H, dd, J=13.5, 11.0 Hz, H-7), 2.75 (1H, m, H-8), 2.97 (1H, dd, J=13.5, 5.0 Hz, H-7), 3.64 (1H, dd, J=11.0, 6.5 Hz, H-9′), 3.68 (1H, dd, J=12.0, 6.0 Hz, H-6″), 3.71 (1H, dd, J=8.5, 6.0 Hz, H-9), 3.82 (1H, dd, J=11.0, 8.0 Hz, H-9′), 3.84 and 3.85 (6H, each s, 2×OMe), 3.87 (1H, br d, J=12.0 Hz, H-6″), 3.98 (1H, dd, J=8.5, 6.5 Hz, H-9), 4.75 (1H, d, J=7.0 Hz, H-7′), 6.75 (1H, d, J=8.5 Hz, H-5′), 6.76 (1H, dd, J=8.5, 2.0 Hz, H-6′), 6.77 (1H, dd, J=8.5, 2.0 Hz, H-6), 6.89 (1H, d, J=2.0 Hz, H-2), 6.90 (1H, d, J=2.0 Hz, H-2′), 7.09 (1H, d, J=8.5 Hz, H-5). HR-SIMS m/z: 545.2005 $(M+Na)^+$. Calcd for $C_{26}H_{34}NaO_{11}$: 545.2000.

Zemplen Reaction of 4 and 5 A solution of **4** (47.7 mg) in dry MeOH (1 ml) and 0.1 M NaOMe (1 ml) was heated for 7.5 h under reflux. The reaction mixture was neutralized with Amberlite IR-120 (H^+-form) and concentrated *in vacuo*. The resulting residue (48.8 mg) was subjected to preparative HPLC (μBondasphere 5μC8-100 Å, MeOH–H_2O, 1 : 1) to give **1** (11.7 mg) and **16** (14.0 mg). Compound **1** was identical with an authentic sample of loganin. Compound **16**. Syrup, $[\alpha]_D^{26}$ −19.4° (c=3.87, MeOH). UV λ_{max}^{MeOH} nm (log ε): 218 (4.08). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460, 1712, 1642, 1440, 1286, 816. ^{1}H-NMR (CD_3OD) δ: 1.40 (3H, s, H_3-10″), 1.70 (2H, m, H_2-5″), 1.81 (3H, d, J=1.5 Hz, H_3-9″), 2.29 (2H, m, H_2-4″), 3.16 (1H, dd, J=9.0, 8.0 Hz, H-2‴), 3.18 (1H, ddd, J=9.0, 5.5, 2.0 Hz, H-5‴), 3.27 (1H, t, J=9.0 Hz, H-4‴), 3.32 (1H, t, J=9.0 Hz, H-3‴), 3.63 (1H, dd, J=12.0, 5.5 Hz, H-6‴), 3.71 (3H, s, COOMe), 3.81 (1H, dd, J=12.0, 2.0 Hz, H-6‴), 4.36 (1H, d, J=8.0 Hz, H-1‴), 5.22 (1H, dd, J=11.0, 1.0 Hz, H-8″), 5.28 (1H, dd, J=18.0, 1.0 Hz, H-8″), 5.95 (1H, dd, J=18.0, 11.0 Hz, H-7″), 6.77 (1H, tq, J=7.5, 1.5 Hz, H-3″). ^{13}C-NMR: see Table 1. HR-SIMS m/z: 383.1674 $(M+Na)^+$. Calcd for $C_{17}H_{28}NaO_8$: 383.1683. Compound **5** (39.5 mg) was treated and purified in the same way as described above to afford loganin (10.4 mg) and **17** (12.7 mg). Compound **17**. Syrup, $[\alpha]_D^{26}$ −10.7° (c=2.84, MeOH). UV λ_{max}^{MeOH} nm (log ε): 218 (4.13). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3406, 1707, 1647, 1437, 1286, 931. ^{1}H-NMR (CD_3OD) δ: 1.35 (3H, s, H_3-10″), 1.73 (2H, m, H_2-5″), 1.82 (3H, d, J=1.5 Hz, H_3-9″), 2.32 (2H, m, H_2-4″), 3.15 (1H, ddd, J=9.0, 5.5, 2.5 Hz, H-5‴), 3.16 (1H, dd, J=9.0, 8.0 Hz, H-2‴), 3.28 (1H, t, J=9.0 Hz, H-4‴), 3.33 (1H, t, J=9.0 Hz, H-3‴), 3.63 (1H, dd, J=12.0, 5.5 Hz, H-6‴), 3.71 (3H, s, COOMe), 3.79 (1H, dd, J=12.0, 2.5 Hz, H-6‴), 4.33 (1H, d, J=8.0 Hz, H-1‴), 5.17 (1H, dd, J=11.0, 1.0 Hz, H-8″), 5.23 (1H, dd, J=18.0, 1.0 Hz, H-8″), 6.10 (1H, dd, J=18.0, 11.0 Hz, H-7″), 6.78 (1H, tq, J=7.0, 1.5 Hz, H-3″). ^{13}C-NMR: see Table 1. HR-SIMS m/z: 383.1686 $(M+Na)^+$. Calcd for $C_{17}H_{28}NaO_8$: 383.1683.

Enzymic Hydrolysis of 16 and 17 β-Glucosidase (Sigma) (7.6 mg) was added to an acetate buffer solution (0.2 M, pH 5.0) (4 ml) of **16** (28.3 mg) and the mixture was incubated at 37 °C for 3 h. Then, further β-glucosidase (43.3 mg) was added portionwise to the mixture within 45 h. The completeness of the hydrolysis was monitored by HPLC (μBondasphere 5μC8-100 Å, MeOH–H_2O, 1 : 1). The solution was extracted with EtOAc and concentration of the EtOAc layers afforded a residue (14.8 mg), which was purified by preparative HPLC (μBondasphere 5μC8-100 Å, MeOH–H_2O, 1 : 1) to give **15c** (7.4 mg). Compound **15c**. Syrup, $[\alpha]_D^{29}$ +19.4° (c=0.42, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1707, 1648, 1437, 1281, 997, 927. ^{1}H-NMR ($CDCl_3$) δ: 1.31 (3H, s, H_3-10″), 1.65 (2H, m, H_2-5″), 1.83 (3H, d, J=1.5 Hz, H_3-9″), 2.22 (2H, m, H_2-4″), 3.73 (3H, s, COOMe), 5.10 (1H, dd, J=11.0, 1.0 Hz, H-8″), 5.24 (1H, dd, J=17.0, 1.0 Hz, H-8″), 5.92 (1H, dd, J=17.0, 11.0 Hz, H-7″), 6.76 (1H, tq, J=8.0, 1.5 Hz, H-3″). EIMS (70 eV) m/z: 198 (M^+), 180 ($M^+ - H_2O$), 166, 165, 148, 138, 121, 97, 71 (base peak). Compound **17** (19.4 mg) was hydrolyzed and purified in the same way as described above to afford **15d** (4.7 mg), $[\alpha]_D^{25}$ −18.2° (c=0.33, $CHCl_3$). The ^{1}H-NMR, IR and EI mass spectral data for the compound were identical with those of **15a** derived from **16**.

Alkaline Hydrolysis of 2 and 3 Followed by Methylation A solution of **2** (19.3 mg) in dioxane (1 ml) and 10% KOH (1 ml) was stirred for 8 h under ice-cooling in a nitrogen atmosphere. After neutralization with Amberlite IR-120 (H^+-form), the reaction mixture was concentrated *in vacuo*. The resulting residue (13.5 mg) was submitted to preparative HPLC (μBondasphere 5μC8-100 Å, MeOH–H_2O, 2 : 3—1 : 1), giving rise to loganic acid (6.4 mg) and menthiafolic acid (3.1 mg). Treatment of each compound with CH_2N_2–Et_2O yielded loganin (**1**) and menthiafolic acid methyl ester (**15a**), respectively. HPLC analysis [column, CHIRALCEL OB (4.6 mm i.d. × 250 mm, Diacel Chemical Industries, Ltd.); mobile phase, *n*-hexane–2-propanol (19 : 1); flow rate, 0.6 ml/min; detection, 230 nm; retention time, *S*-form (18.4 min), *R*-form (20.7 min)] demonstrated **15a** to be a mixture of 6″*S*- and 6″*R*-enantiomers with a ratio of 53 : 47. Compound **3** was treated in the same way as described above to yield **1** and **15b** (*S* : *R* = 82 : 18).

Acknowledgement The excellent technical assistance of Misses C. Fukunaga, S. Watanabe, M. Haze, and Y. Yamamuka is gratefully acknowledged. Thanks are also due to Dr. M. Sugiura (Kobe Pharmaceutical University) for ^{1}H- and ^{13}C-NMR spectra, and to Dr. K. Saiki (Kobe Pharmaceutical University) for mass spectral measurements.

References and Notes

1) *a*) Tanahashi T., Watanabe H., Itoh A., Nagakura N., Inoue K., Ono M., Fujita T., Chen C.-C., *Phytochemistry*, **31**, 2143 (1992); *b*) Tanahashi T., Watanabe H., Itoh A., Nagakura N., Inoue K., Ono M., Fujita T., Morita M., Chen C.-C., *ibid.*, **32**, 133 (1993); *c*) Tanahashi T., Shimada A., Nagakura N., Inoue K., Kuwajima H., Takaishi K., Chen C.-C., *ibid.*, **33**, 397 (1993); *d*) Tanahashi T., Shimada A., Nagakura N., Inoue K., Kuwajima H., Takaishi K., Chen C.-C., He Z.-D., Yang C.-R., *Chem. Pharm. Bull.*, **41**, 1649 (1993).
2) Coscia C. J., Guarnaccia R., Botta L., *Biochemistry*, **8**, 5036 (1969).
3) Inoue K., Tanahashi T., Inouye H., Murai F., Tagawa M., *Phytochemistry*, **21**, 359 (1982).
4) Kikuchi M., Yamauchi Y., *Yakugaku Zasshi*, **104**, 390 (1984).
5) Sugiyama M., Kikuchi M., *Heterocycles*, **36**, 117 (1993).
6) *a*) Battersby A. R., Barnett A. R., Knowles G. D., Parsons P. G., *J. Chem. Soc., Chem. Commun.*, **1968**, 1277; *b*) Junior P., *Planta Med.*, **55**, 83 (1989); *c*) Okada Y., Koyama K., Takahashi K., Okuyama T., Shibata S., *ibid.*, **40**, 185 (1980); *d*) Nicoletti M., Serafini M., Tomassini L., Bianco A., Passacantilli P., *ibid.*, **53**, 295 (1987); *e*) Hase T., Iwagawa T., Munesada K., *Phytochemistry*, **21**, 1435 (1982); *f*) Takido M., Fukuhara K., Yamanouchi S., Takahashi S., *ibid.*, **22**, 223 (1983); *g*) Konoshima T., Kozuka M., Sawada T., Kimura T., *Chem. Pharm. Bull.*, **35**, 46 (1987); *h*) Takeda T., Nakamura T., Takashima S., Yano O., Ogihara Y., *ibid.*, **41**, 2132 (1993); *i*) Marco J. A., Sanz-Cervera J. F., Sancenon F., Jakupovic J., Rustaiyan A., Mohamadi F., *Phytochemistry*, **34**, 1061 (1993).
7) The numbering of references 6*e*—*h* is used for the menthiafolic acid moiety of the compounds in this report.
8) Nair M. D., Adams R., *J. Am. Chem. Soc.*, **83**, 922 (1961).
9) Nakamoto K., Ohtsuka H., Yamasaki, K., *Phytochemistry*, **27**, 1856 (1988).
10) Itoh, A., Tanahashi T., Nagakura N., *Phytochemistry*, **33**, 161 (1993).
11) Kasai R., Suzuo M., Asakawa J., Tanaka O., *Tetrahedron Lett.*, **1977**, 175.
12) Voirin S., Baumes R., Bayonove C., M'Bairaroua O., Tapiero C., *Carbohydr. Res.*, **207**, 39 (1990).
13) Damtoft S., Franzyk H., Jensen S. R., *Phytochemistry*, **35**, 705 (1994).
14) Inouye H., Ueda S., Inoue K., Takeda Y., *Chem. Pharm. Bull.*, **22**, 676 (1974).