Available online at www.sciencedirect.com
ScienceDirect
Phytochemistry 68 (2007) 1718–1721
PHYTOCHEMISTRY
www.elsevier.com/locate/phytochem

# Secoiridoid components from *Jasminum grandiflorum*

Samir Kumar Sadhu [a,b], Md. Sojib Khan [b], Takashi Ohtsuki [a], Masami Ishibashi [a,*]

[a] *Graduate School of Pharmaceutical Sciences, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan*
[b] *Pharmacy Discipline, Life Science School, Khulna University, Khulna-9208, Bangladesh*

Received 9 February 2007; received in revised form 12 April 2007

**Abstract**

Secoiridoid glucosides, 2″-epifraxamoside and demethyl-2″-epifraxamoside, and the secoiridoid, jasminanhydride were isolated from *Jasminum grandiflorum* together with four previously known phenolics and a triterpene. Structures were elucidated by detailed spectroscopic analysis. Stereochemistry of the compounds was determined by differential NOE experiment.


*Keywords:* *Jasminum grandiflorum*; Oleaceae; Secoiridoid; 2″-Epifraxamoside; Demethyl-2″-epifraxamoside; Jasminanhydride

## 1. Introduction

*Jasminum grandiflorum* Linn. (family: Oleaceae) (local names: Jasmine or Jatiful) is a medicinal plant of Bangladesh, which has certain therapeutic properties against various psychiatric disorders, skin diseases like conjunctivitis and dermatitis, and for different types of cancer (Lis-Balchin et al., 2002; Kolanjiappan and Manoharan, 2005). Previously, iridoid-type compounds, secoiridoid glucosides, triterpenes, flavonoids, lignans, etc., were isolated from this herb (Tanahashi et al., 1999; Somanadhan et al., 1998). In our continued investigation on traditional medicinal plants of Southeast Asia, we isolated eight compounds from this herb. We report here their isolation and structure determinations together with the cell growth inhibitory activity properties, of the newly isolated compounds (**1**–**3**).

## 2. Results and discussion

The MeOH extract of the dried aerial parts of *J. grandiflorum* was partitioned successively with *n*-hexane, EtOAc, *n*-BuOH and water. Among these, the EtOAc extract was further separated as described in Section 3. Repeated column chromatography afforded three new compounds (**1**–**3**) together with four phenolics, 3,4-dihydroxy-β-methoxyphenethyl alcohol, 3,4-dihydroxyphenethyl alcohol (Takenaka et al., 2000), 3,4-dihydroxybenzoic acid or protocatechuic acid (Teng et al., 2005), 2-hydroxy-3′,4′-dihydroxyacetophenon (Tsuda et al., 1994), and a triterpene, oleanolic acid (Mahato and Kundu, 1994). The known compounds were identified by their physicochemical and spectroscopic properties and/or comparing those with the published literature data.

Compound **1** was isolated as a colorless amorphous solid, $[\alpha]_D^{24}$ −130 (MeOH), whose molecular formula $C_{25}H_{30}O_{13}$ was assigned by HR-FABMS [*m*/*z* 577.1327 $(M+K)^+$]. Its UV spectrum showed absorption maxima at 233 and 283 nm. The $^{13}C$ NMR and DEPT spectra exhibited signals for two methyls, three methylenes, thirteen methines, and seven quaternary carbons (Table 1). The chemical shifts of the quaternary carbons were two ester carbonyls at δ 168.4 and 172.6, and five olefinic carbons at δ 109.7, 130.5, 131.0, 146.6 and 146.8. Its $^1H$ NMR spectrum (Table 1) showed typical signals of an oleoside 11-methyl ester moiety (Takenaka et al., 2000) [an oxygenated olefinic proton at δ 7.51 (*s*, 3-H), an allylic acetal proton at δ 5.92 (*brs*, 1-H), an ethylidene group at δ 6.14 (*qd*, 8-H), an anomeric proton at δ 4.65 (*d*, 1′-H) and a

* Corresponding author. Tel./fax: +81 43 290 2913.
*E-mail address:* mish@chiba-u.ac.jp (M. Ishibashi).

0031-9422/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.phytochem.2007.04.029

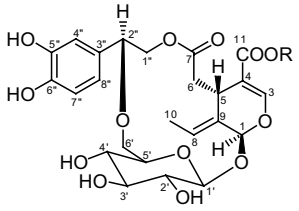
Table 1
NMR spectroscopic data of compounds **1** and **2** ($\delta$ in ppm, $J$ in Hz)

| Position | **1** | | **2** | |
|---|---|---|---|---|
| | $^{13}$C | $^{1}$H | $^{13}$C | $^{1}$H |
| 1 | 100.2 | 5.92 *br s* | 100.1 | 5.89 *br s* |
| 3 | 155.6 | 7.51 *s* | 155.3 | 7.45 *s* |
| 4 | 109.7 | | 110.3 | |
| 5 | 32.5 | 4.05 *dd* (11.9, 4.5) | 32.6 | 4.05 *dd* (11.9, 4.6) |
| 6 | 40.3 | 2.93 *dd* (13.4, 4.5) 2.49 *dd* (13.4, 11.9) | 40.4 | 2.97 *dd* (13.4, 4.6) 2.47 *dd* (13.4, 11.9) |
| 7 | 172.6 | | 172.7 | |
| 8 | 125.4 | 6.14 *qd* (7.0, 1.5) | 125.2 | 6.13 *qd* (7.0, 1.5) |
| 9 | 130.5[a] | | 130.8[a] | |
| 10 | 13.9 | 1.78 *dd* (7.0, 1.5) | 13.9 | 1.78 *dd* (7.0, 1.5) |
| 11 | 168.4 | | 170.0 | |
| 11-OMe | 51.9 | 3.72 *s* | | |
| 1' | 104.9 | 4.65 *d* (7.3) | 104.9 | 4.65 *d* (7.4) |
| 2' | 74.4 | 3.33 *m* | 74.5 | 3.33 *m* |
| 3' | 77.8 | 3.36 *m* | 77.8 | 3.37 *m* |
| 4' | 72.9 | 2.99 *dd* (9.8, 8.6) | 73.0 | 2.99 *dd* (9.8, 8.6) |
| 5' | 77.5 | 3.53 *td* (9.8, 2.1) | 77.5 | 3.53 *td* (9.8, 2.1) |
| 6' | 70.6 | 3.87 *dd* (12.2, 2.1) 3.03 *dd* (12.2, 9.8) | 70.6 | 3.88 *dd* (12.2, 2.1) 3.03 *dd* (12.2, 9.8) |
| 1'' | 68.9 | 4.52 *dd* (11.9, 1.8) 3.61 *dd* (11.9, 9.4) | 68.9 | 4.52 *dd* (11.9, 1.8) 3.61 *dd* (11.9, 9.4) |
| 2'' | 85.1 | 4.28 *dd* (9.4, 1.8) | 85.0 | 4.29 *dd* (9.4, 1.8) |
| 3'' | 131.0[a] | | 131.1[a] | |
| 4'' | 114.6 | 6.70 *d* (2.1) | 114.6 | 6.71 *d* (2.1) |
| 5'' | 146.6[b] | | 146.6[b] | |
| 6'' | 146.8[b] | | 146.8[b] | |
| 7'' | 116.5 | 6.76 *d* (8.2) | 116.5 | 6.76 *d* (8.2) |
| 8'' | 119.3 | 6.58 *dd* (8.2, 2.1) | 119.3 | 6.58 *dd* (8.2, 2.1) |

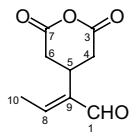
Recorded in $CD_3OD$, $^{1}$H at 500 MHz, $^{13}$C at 125 MHz.
[a,b] Interchangeable within the same column.

carbomethoxyl group at $\delta$ 3.72 (*s*, 11-OMe)] together with 1,3,4-trisubstituted aromatic ring resonances [$\delta$ 6.58 (*dd*, $J = 8.2$, 2.1 Hz, H-8″), 6.70 (*d*, $J = 2.1$ Hz, H-4″) and 6.76 (*d*, $J = 8.2$ Hz, H-7″)]. The COSY correlation between 1″-$H_2$ ($\delta$ 4.52 and 3.61) and 2″-H ($\delta$ 4.28) and the HMBC cross-peaks between 2″-H and C-4″ ($\delta$ 114.6) and C-8″ ($\delta$ 119.3), and between 1″-H and C-7 (172.6) connected the aromatic ring with oleoside methyl ester. An additional cross-peak between 6′-Hax ($\delta$ 3.03) and 2″-C (85.1) indicated the linkage of 2″-C with the hydroxyl group at 6′-C of glucose to form a 14 membered ether ring. Thus structure **1** was found to be the same as that of fraxamoside isolated from *Fraxinus americana* (Takenaka et al., 2000).

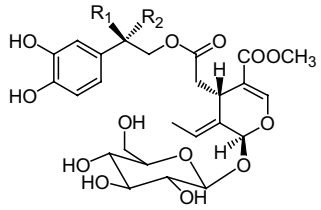
While the NMR spectroscopic data of these two compounds closely resembled each other, a significant variation was observed in the coupling constants of the methylene protons of C-1″ [$\delta$ 4.52 (*dd*, $J = 11.9$, 1.8 Hz) and 3.61 (*dd*, $J = 11.9$, 9.4 Hz) for **1**; $\delta$ 4.52 (*dd*, $J = 12.0$, 9.0 Hz) and 3.62 (*dd*, $J = 11.9$, 1.5 Hz) for fraxamoside (Takenaka et al., 2000)]. In a differential NOE experiment, irradiation of 2″-H showed a NOE in the axial methylene proton of C-6′ at $\delta$ 3.03 (*dd*, $J = 12.2$, 9.8 Hz), whereas the reference compound fraxamoside showed a NOE in the equatorial proton at $\delta$ 3.88 (*dd*, $J = 12.0$, 2.0 Hz). This data suggested an α-orientation of 2″-H. On the other hand, irradiation of 1-H $\delta$ 5.92 (*brs*) showed a NOE in 1′-H $\delta$ 4.65 (*d*, $J = 7.3$ Hz), which indicated the same configuration of this part as in fraxamoside. The difference in coupling constants of 1″-$H_2$ between the isomers of similar compounds like 2″-hydroxyoleuropeins (**4**–**5**) (Takenaka et al., 2000) and 2″-methoxyoleuropeins (**6**–**7**) (Tanahashi et al., 1999) were also compared. From



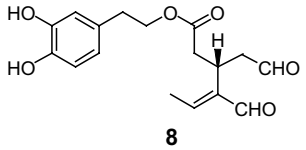
**1** R = Me
**2** R = H



**3**



**4** $R_1$ = OH $R_2$ = H
**5** $R_1$ = H $R_2$ = OH
**6** $R_1$ = OMe $R_2$ = H
**7** $R_1$ = H $R_2$ = OMe



**8**

these results, compound **1** was found to be the epimer of fraxamoside, which was named 2″-epifraxamoside.

Compound **2** was isolated as a colorless amorphous solid, $[\alpha]_D^{24}$ −130 (MeOH), and displayed a HR-FABMS peak at 563.1174 $[M+K]^+$ consistent with a molecular formula of $C_{24}H_{28}O_{13}$. The absorption maxima were observed at 226 and 282 nm in its UV spectrum similar to that of **1**. The NMR spectroscopic data of **2** (Table 1) were also very similar to that of **1** with the exception of the absence of the carbomethoxy group signal, which was also evident from the molecular weight. Similar coupling constants of the methylene protons of C-1″ [$\delta$ 4.52 (*dd*, $J = 11.9$, 1.8 Hz) and 3.61 (*dd*, $J = 11.9$, 9.4 Hz) for **2**; $\delta$ 4.52 (*dd*, $J = 11.9$, 1.8 Hz) and 3.61 (*dd*, $J = 11.9$, 9.4 Hz) for **1**] suggested the same configuration of 2″-H in **2** as that of **1**, which was also supported by the differential NOE experiment in which irradiation of 2″-H showed a NOE in the axial methylene proton of C-6′ at $\delta$ 3.03 (*dd*, $J = 12.2$, 9.8 Hz) as in **1**. The configuration of other parts of the molecule was also found to be the same as that of **1** determined by NOE. Compound **2** was a new compound named demethyl-2″-epifraxamoside.

Compound **3** was obtained as a colorless amorphous solid. The HR-FABMS exhibited $[M+H]^+$ peak at 183.0660, indicating a molecular formula of $C_9H_{10}O_4$ for **3**. The UV spectrum showed absorption maxima only at 232 nm. The $^{13}C$ NMR and DEPT spectra showed seven signals for one methyl, one methylene, three methines, and two quaternary carbons (Table 2), implying that two signals overlapped due to symmetry. In the $^1H$ NMR spectrum, signals for an aldehyde proton at $\delta$ 9.28 (*d*, $J = 2.0$ Hz, 1-H) and an ethylidene group at $\delta$ 6.79 (*q*, $J = 7.2$ Hz, 8-H) were observed. The COSY correlation indicated the bridge between 4-$H_2$/5-H/6-$H_2$ and the HMBC cross-peaks between 5-H and C-1, C-8 and C-9 connected the side-chain. Again, the cross-peak between 5-H and C-3/C-7, and the molecular weight of compound suggested the anhydride ring structure of **3**. Compound **3** was a new secoiridoid named jasminanhydride. Considering its biosynthetic pathway, we found that oleacein (**8**) (Somanadhan et al., 1998) was previously isolated from this plant, whose ester linkage might break down to form 3,4-dihydroxyphenethyl alcohol and a dialdehyde secoiridoid. The dialdehyde secoiridoid recently isolated from olive oil (Christophoridou et al., 2005), could form the anhydride **3** after oxidation of aldehyde group at C-3 to a carboxylic acid and subsequent dehydration.

Compounds **1**–**3** were checked for growth inhibitory activity against human cervical carcinoma HeLa cells and colon carcinoma SW480 cells. However, none of them were active.

Oleosides with oxygenated substituent at C-2″ of the 2-(3,4-dihydroxyphenyl) ethyl alcohol moiety, 2″-methoxyoleuropeins (**6** and **7**), were isolated previously from *J. grandiflorum* (Tanahashi et al., 1999), while 2″-hydroxyoleuropeins (**4** and **5**) were isolated from *F. americana* (Oleaceae) together with fraxamoside, a novel secoiridoid glucoside containing 14-membered ether ring between C-2″ and C-6′ (Takenaka et al., 2000). In the present work, we isolated two latter type of compounds 2″-epifraxamoside (**1**) and demethyl-2″-epifraxamoside (**2**) from *J. grandiflorum* that indicated the similar biosynthetic pathway within plants of the same family.

## 3. Experimental

### 3.1. General

UV spectra were recorded on a Shimadzu UVmini 1240 spectrometer. Optical rotations were measured with a Jasco P-1020 polarimeter. EIMS was measured on a Jeol GC-Mate, FABMS on a Jeol JMS-AX500 and HR-FABMS using a Jeol HX-110A spectrometer. NMR spectra were recorded on a Jeol JNM-GSX500A spectrometer with a deuterated solvent, whose chemical shift was used as an internal standard.

### 3.2. Plant material

The aerial parts of *J. grandiflorum* were collected from Jessore, Bangladesh, in July 2005. After complete drying it was subjected to grinding. A voucher specimen (CU-NPC-P-2005-002) has been deposited in the Laboratory

Table 2
NMR spectroscopic data and HMBC and COSY correlations of compound **3** ($\delta$ in ppm, $J$ in Hz)

| Position | $^{13}C$ | $^1H$ | HMBC | COSY |
|---|---|---|---|---|
| 1 | 197.0 | 9.28 *d* (2.0) | 31.6, 145.0, 156.1 | 3.56–3.61 (w) |
| 3 | 175.7 | | | |
| 4 | 37.8 | ax2.69 *dd* (15.7, 9.0) eq2.62 *dd* (15.7, 6.0) | 31.6, 37.8, 145.0, 175.7 | 3.56–3.61 |
| 5 | 31.6 | 3.56–3.61 *m* | 37.8, 145.0, 156.1, 175.7, 197.0 | 2.62, 2.69 |
| 6 | 37.8 | ax2.69 *dd* (15.7, 9.0) eq2.62 *dd* (15.7, 6.0) | 31.6, 37.8, 145.0, 175.7 | 3.56–3.61 |
| 7 | 175.7 | | | |
| 8 | 156.1 | 6.79 *q* (7.2) | 15.4, 31.6, 145.0, 197.0 | 2.07 |
| 9 | 145.0 | | | |
| 10 | 15.4 | 2.07 *d* (7.2) | 145.0, 156.1, 31.6 (w), 37.8 (w) | 6.79 |

Recorded in $CD_3OD$, $^1H$ at 500 MHz, $^{13}C$ at 125 MHz; w: weak signal.

of Natural Products Chemistry, Graduate School of Pharmaceutical Sciences, Chiba University, Japan.

### 3.3. Extraction and isolation

The grinded dried aerial parts of *J. grandiflorum* (272 g) were extracted with MeOH (1.9 l) for 17 days at room temperature. The concentrated filtrate from the extraction was passed through a Diaion HP 20 column (48 × 240 mm) with MeOH and acetone eluent. An almost chlorophyll-free MeOH eluate was evaporated to dryness in vacuo to afford an extract (13.33 g). The latter was then suspended in MeOH–$H_2O$ (1:9 v/v, 250 ml) and successively partitioned with *n*-hexane (200 ml × 4), EtOAc (200 ml × 5) and *n*-BuOH (100 ml × 2). Based on TLC profiles, the EtOAc extract (4.67 g) was applied to a silica gel PSQ 100B column (45 × 330 mm) with *n*-hexane-acetone eluent to give fractions 1A–I. The polar fraction 1H, eluted with acetone and MeOH (433 mg) was subjected to ODS flash CC (25 × 175 mm) using MeOH–$H_2O$ (1:2, v/v) as eluent. One of the fractions from this column was applied to reversed phase HPLC (Develosil C30-UG-5; 8 × 250 mm; MeOH–$H_2O$ (2:1, v/v); RI detection) to afford **2** (7 mg). Fraction 1G (286 mg), the *n*-hexane–acetone (1:3, v/v) eluted fraction, was subjected to the same HPLC conditions, with fraction of interest further purified by Sephadex LH-20 CC (18 × 300 mm) with MeOH, **1** (12 mg) being isolated. The *n*-hexane–acetone (1:1 → 2:3, v/v) eluted fraction 1E (340 mg) was at first applied to reversed phase HPLC (YMC pak ODS-AM; 10 × 250 mm; MeOH–$H_2O$ (1:1, v/v); RI detection) to give a fraction (56 mg), which was subsequently purified by Sephadex LH-20 CC (18 × 600 mm) using MeOH as eluent to afford **3** (17 mg), a 1:1 mixture of **3** and 3,4-dihydroxy-β-methoxyphenethyl alcohol (5 mg), as well as 3,4-dihydroxyphenethyl alcohol (4 mg) and 3,4-dihydroxybenzoic acid (17 mg). 3,4-Dihydroxy benzoic acid (23 mg) was also obtained from the *n*-hexane–acetone (1:1, v/v) eluted fraction 1D (139 mg) following subsequent reversed phase HPLC (Senshu pak ODS-5251-S; 20 × 250 mm; MeOH–$H_2O$ (1:1, v/v); $UV_{280}$ detection) together with 2-hydroxy-3′,4′-dihydroxyacetophenon (8 mg). Application of fraction 1B (65 mg), the *n*-hexane–acetone (5:2, v/v) eluted fraction, to reversed phase HPLC (Develosil C30-UG-5; 8 × 250 mm; MeCN–$H_2O$ (19:1, v/v); RI detection) afforded oleanolic acid (10 mg).

### 3.4. 2″-Epifraxamoside (*1*)

Colorless amorphous solid, $[\alpha]_D^{24}$ −130 (c 1.0, MeOH); $[\alpha]_D^{24}$ −137 (c 0.12, MeOH) for fraxamoside (Takenaka et al., 2000); UV $\lambda_{max}^{MeOH}$ nm (ε): 233 (18000), 283 (4800); UV $\lambda_{max}^{MeOH}$ nm (log ε): 233 (4.14), 282 (3.45) for fraxamoside (Takenaka et al., 2000); For $^1H$ and $^{13}C$ NMR spectroscopic data, see Table 1; FABMS (NBA) *m/z*: 538 $[M]^+$, 539 $[M+H]^+$, 577 $[M+K]^+$; HR-FABMS (NBA/PEG) *m/z*: 577.1327 (calculated for $C_{25}H_{30}O_{13}K$, 577.1323).

### 3.5. Demethyl-2″-epifraxamoside (*2*)

Colorless amorphous solid, $[\alpha]_D^{24}$ −130 (c 0.28, MeOH); UV $\lambda_{max}^{MeOH}$ nm (ε): 226 (16000), 282 (5000); For $^1H$ and $^{13}C$ NMR spectroscopic data, see Table 1; FABMS (NBA) *m/z*: 524 $[M]^+$, 525 $[M+H]^+$, 563 $[M+K]^+$; HR-FABMS (NBA/PEG) *m/z*: 563.1174 (calculated for $C_{24}H_{28}O_{13}K$, 563.1167).

### 3.6. Jasminanhydride (*3*)

Colorless amorphous solid, UV $\lambda_{max}^{MeOH}$ nm (ε): 232 (6600); For $^1H$ and $^{13}C$ NMR spectroscopic data, see Table 2; EIMS *m/z* (%): 182 ($M^+$, 12), 172 (12), 154 (28), 141 (23), 136 (13), 126 (100), 123 (46), 113 (32), 108 (25), 95 (62); FABMS (NBA) *m/z*: 183 $[M+H]^+$; HR-FABMS (NBA/PEG) *m/z*: 183.0660 (calculated for $C_9H_{11}O_4$, 183.0657).

## Acknowledgement

This work was partly supported by a Grant-in-Aid from Tokyo Biochemical Research Foundation (TBRF), Japan.

## References

Christophoridou, S., Dais, P., Tseng, L.H., Spraul, M., 2005. Separation and identification of phenolic compounds in olive oil by coupling high performance liquid chromatography with postcolumn solid phase extraction to nuclear magnetic resonance spectroscopy. Journal of Agricultural and Food Chemistry 53, 4667–4679.

Kolanjiappan, K., Manoharan, S., 2005. Chemopreventive efficacy and anti-lipid peroxidative potential of *Jasminum grandiflorum* Linn. on 7,12-dimethylbenz(*a*)anthracene-induced rat mammary carcinogenesis. Fundamental and Clinical Pharmacology 19, 687–693.

Lis-Balchin, M., Hart, S., Wan Hang Lo, B., 2002. Jasmine absolute (*Jasminum grandiflora* L.) and its mode of action on guinea-pig ileum in vitro. Phytotherapy Research 16, 437–439.

Mahato, S.B., Kundu, A.P., 1994. $^{13}C$ NMR spectra of pentacyclic triperpenoids-a compilation and some salient features. Phytochemistry 37, 1517–1575.

Somanadhan, B., Smitt, U.W., George, V., Pushpangadan, P., Rajasekharan, S., Duus, J., Nyman, U., Olsen, C.E., Jaroszewski, J.W., 1998. Angiotensin converting enzyme (ACE) inhibitors from *Jasminum azoricum* and *Jasminum grandiflorum*. Planta Medica 64, 246–250.

Takenaka, Y., Tanahashi, T., Shintaku, M., Sakai, T., Nagakura, N., Parida, 2000. Secoiridoid glucosides from *Fraxinus Americana*. Phytochemistry 55, 275–284.

Tanahashi, T., Sakai, T., Takenaka, Y., Nagakura, N., Chen, C.C., 1999. Structure elucidation of two secoiridoid glucosides from *Jasminum officinale* L. var. *grandiflorum* (L.) Kobuski. Chemical and Pharmaceutical Bulletin 47, 1582–1586.

Teng, R.W., Wang, D.Z., Wu, Y.S., Lu, Y., Zheng, Q.T., Yang, C.R., 2005. NMR assignments and single-crystal X-ray diffraction analysis of deoxyloganic acid. Magnetic Resonance in Chemistry 43, 92–96.

Tsuda, T., Watanabe, M., Ohshima, K., Yamamoto, A., Kawakishi, S., Osawa, T., 1994. Antioxidative components isolated from the seed of Tamarind (*Tamarindus indica* L.). Journal of Agricultural and Food Chemistry 42, 2671–2674.