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Sesquiterpene lactone glucosides and alkyl glycosides from the fruit of cumin

Tomomi Takayanagi, Toru Ishikawa, Junichi Kitajima*

Showa Pharmaceutical University, Higashi-Tamagawagakuen 3, Machida, Tokyo 194-8543, Japan

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Abstract

From the polar portion of the methanolic extract of cumin (fruit of *Cuminum cyminum* L.), two sesquiterpenoid glucosides, cuminoside A and B, and two alkyl glycosides were isolated together with five known compounds. Their structures were established as (1*S*,5*S*,6*S*,10*S*)-10-hydroxyguaia-3,7(11)-dien-12,6-olide β-D-glucopyranoside, (1*R*,5*R*,6*S*,7*S*,9*S*,10*R*,11*R*)-1,9-dihydroxyeudesm-3-en-12,6-olide 9-*O*-β-D-glucopyranoside, methyl β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside and ethane-1,2-diol 1-*O*-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside, respectively.

Keywords: Cumin; *Cuminum cyminum* fruit; Umbelliferae; Sesquiterpenoid glucoside; Alkyl glycoside; Cuminoside A, B; 10-Hydroxyguaia-3,7(11)-dien-12,6-olide β-D-glucopyranoside; 1,9-Dihydroxyeudesm-3-en-12,6-olide 9-*O*-β-D-glucopyranoside; Ethane-1,2-diol 1-*O*-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside

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1. Introduction

In a previous paper (Ishikawa et al., 2002), the isolation and characterization of 12 glucosides was reported from the methanolic extract of cumin (fruit of *Cuminum cyminum* L.; Umbelliferae), which has been used as a spice and medicine since antiquity. In continuation of our studies on the polar constituents of cumin, we undertook the isolation and structure elucidation of sesquiterpenoid glucosides, alkyl glycosides, glucides and a nucleoside.

2. Results and discussion

Commercial cumin was extracted with 70% aq. methanol, with the resulting methanol extract suspended in water and extracted with diethyl ether and ethyl acetate, successively. The aqueous layer was subjected to Amberlite XAD-II chromatography to give both water and methanol eluted fractions. These were individually applied to Sephadex LH-20, silica gel and Lobar RP-8 column chromatography. In this way, two sesquiterpenoid glucosides, cuminoside A (**1**) and cuminoside B (**2**), and two aromatic compound glucosides [benzyl β-D-glucopyranoside (**3**, Kitajima et al., 1998a) and phenethyl β-D-glucopyranoside (**4**, Miyase et al., 1988)] were isolated from the methanol eluate fraction, and three alkyl glycosides (**5**–**7**), D-mannitol (**8**) and uracil (**9**) were isolated from the water eluate fraction. Among them, **1**, **2**, **6** and **7** were new. The molecular formulae of the new compounds were suggested by the accurate mass number of $[M+H]^+$ and/or $[M+Na]^+$ ion peaks in the high-resolution positive FAB-MS.

Cuminoside A (**1**; $C_{21}H_{30}O_8$, an amorphous powder, $[\alpha]_D^{24}$ −35°) gave $[M+K]^+$, $[M+Na]^+$, $[M+H]^+$ and $[M-C_6H_{10}O_5+H]^+$ ion peaks at *m*/*z* 449, 433, 411 and 249 on the positive FAB-MS, and an $[M-H]^-$ ion peak at *m*/*z* 409 in the negative FAB-MS. Enzymatic hydrolysis of **1** gave an aglycone (**1a**; $C_{15}H_{20}O_3$, amorphous powder, $[\alpha]_D^{21}$ −32°) and D-glucose. The ^1H, ^{13}C and ^{13}C–^1H correlation spectroscopy (COSY) NMR spectral data of **1** showed the presence of three *tert*-methyls, three methylenes, three methines (one oxygenated), one oxygenated quaternary carbon, one trisubstituted double bond, one tetrasubstituted double bond and one carbonyl carbon conjugated to the double bond, in addition to the β-D-glucopyranosyl moiety. From the

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* Corresponding author. Tel.: +81-427-21-1577; fax: +81-427-21-1588.

E-mail address: kitajima@ac.shoyaku.ac.jp (J. Kitajima).

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analysis of heteronuclear multiple-bond correlation (HMBC) spectral data (see Experimental), the aglycone was considered to be 10-hydroxyguaia-3,7(11)-dien-12,6-olide, whose glucosyl group was thought to be at C-10. The stereochemistry of **1** was solved by a detailed analysis of the ^{1}H NMR and NOESY spectra. As NOE interactions between H-6/H-2ax and H-9ax were observed in the NOESY spectrum (Fig. 1), the configuration of H-6 was concluded to be axial, and H-1 and H-5 should thus be as shown. Furthermore, observed NOE interactions between H_3-14/H-2ax and H-2eq (Fig. 2), and the ^{1}H signal of H-8ax, which was found downfield at δ 3.45 due to the influence of an axial-hydroxyl group at C-10, suggested the 10-methyl to be equatorial. The absolute configuration at C-10 of **1** was concluded to be *S* by its α- and β-carbon glycosylation shift values which showed an obvious difference between the values of macrocliniside G (Fig. 1; **10**, Miyase et al., 1985; Ishikawa et al., 2003) which has the 10*R* configuration (Table 1). It was also supported by the positive optical rotation of **10** ($[\alpha]_D$ +39.8°) i.e. opposite to those of **1** and **1a**. From these data, **1** was concluded to be (1*S*,5*S*,6*S*,10*S*)-10-hydroxyguaia-3,7(11)-dien-12,6-olide β-D-glucopyranoside as described in Fig. 2.

Cuminoside B (**2**; $C_{21}H_{32}O_9$, an amorphous powder, $[\alpha]_D^{21}$ −14°) gave $[M+H]^+$ and $[M-C_6H_{10}O_5+H]^+$ ion peaks at *m*/*z* 429 and 267 in the positive FAB-MS, and an $[M+H]^+$ ion peak at *m*/*z* 427 in the negative FAB-MS. Enzymatic hydrolysis of **2** gave an aglycone (**2a**; $C_{15}H_{22}O_4$, amorphous powder, $[\alpha]_D^{21}$ −18°) and D-glucose, and the ^{1}H, ^{13}C and ^{13}C–^{1}H COSY NMR spectral data (Tables 2 and 3) showed the presence of one β-D-glucopyranosyl, two *tert*-methyls, one *sec*-methyl, two methylenes, six methines (three of which were oxygenated), one quaternary carbon, one trisubstituted double bond and one carbonyl group. From the analysis of the HMBC correlation data (see Experimental), **2a** appeared to be 1,9-dihydroxyeudesm-3-en-12,6-olide, with the attachment of the glucosyl unit at C-9. In the NOESY spectrum **2**, NOE interactions between the signals of H_3-14/H-1, H-2ax, H-6, H-7 and H-9, and between H-7/H-9 were observed (Fig. 1), and the configuration of 10-methyl, H-2, H-6, H-7 and H-9 should be in the same β-configuration. Furthermore, NOE interactions between H-5/H-8ax, and between H_3-13/H-8ax and H-8eq were observed in its NOESY spectrum (Fig. 1), and the configuration of C-11 methyl and H-5 was suggested to be in the opposite α-configuration to 10-methyl. So, **2** was confirmed to be a 9-*O*-β-D-glucopyranoside of 1β,9β-dihydroxyeudesm-3-en-12,6-olide. Further, the glucosylation shift values (Δδ) of the α- and β-carbon [C-8 (β-pro-*R*);−1.2, C-9 (α); +8.8, C-10 (β-pro-*S*);−1.0] and the chemical shift of the anomeric carbon (*δ* 105.50) were in agreement with that of secondary *S*-alcohol (Kasai et al., 1977; Tori et al., 1977; Kitajima et al., 2000), and the absolute configuration at C-9 should be *S*. From these facts, **2** was concluded to be (1*R*,5*R*,6*S*,7*S*,9*S*,10*S*,11*R*)-1,9-dihydroxyeudesm-3-ene-12,6-olide 9-*O*-β-D-glucopyranoside as described in Fig. 2.

Alkyl glycoside **5** ($C_8H_{16}O_6$, a colorless syrup, $[\alpha]_D^{23}$ −27°) was identified as ethyl β-D-glucopyranoside

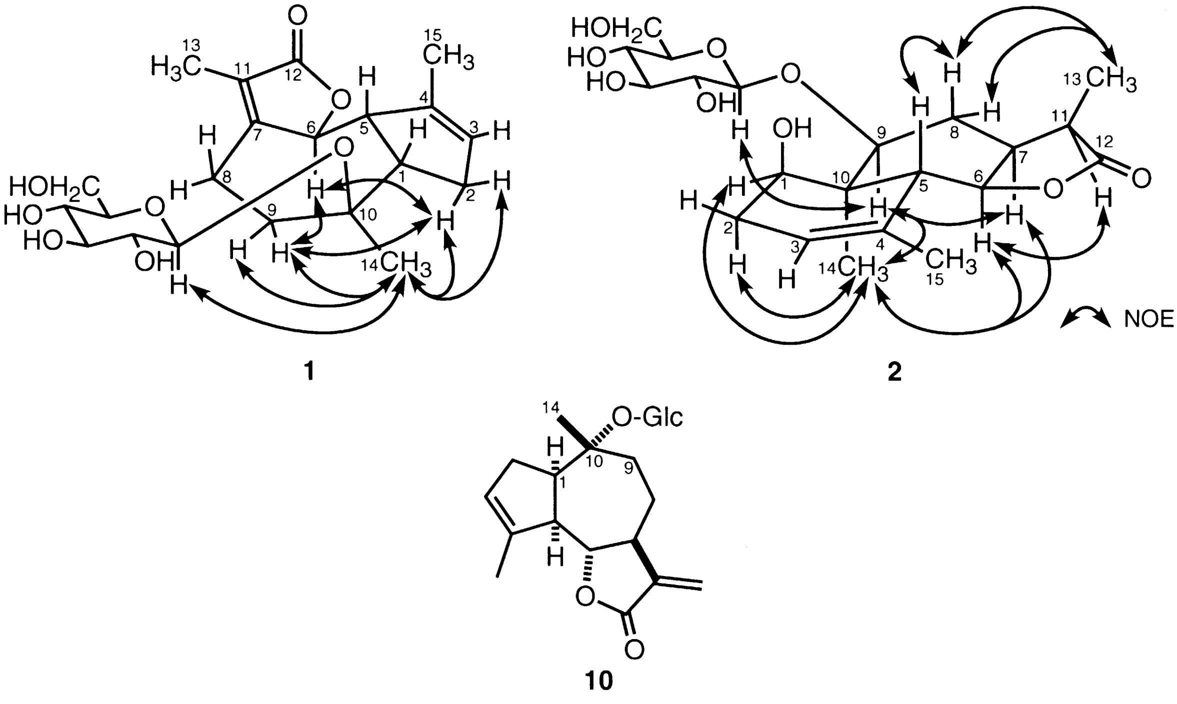

Fig. 1. Important NOE correlations for **1** and **2**, and the structure of **10**.

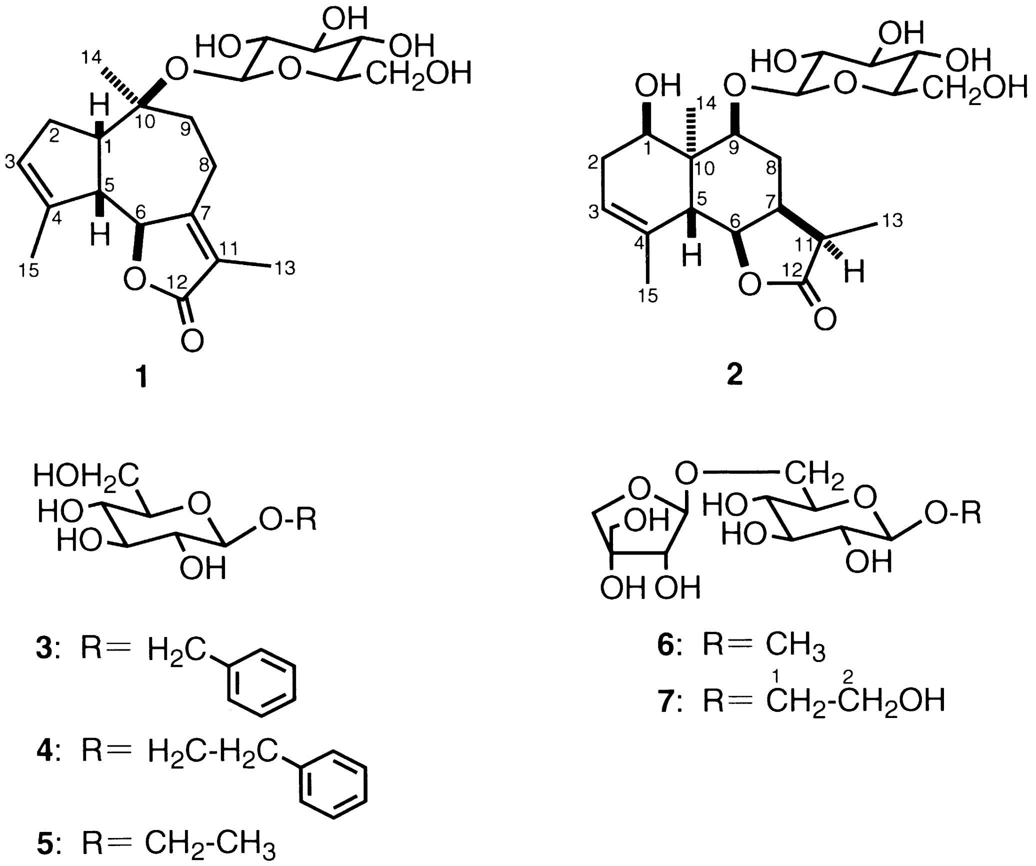

Fig. 2. Structures of **1**–**7**.

Table 1
Glycosylation values [$\Delta\delta$ (δ glucoside−δ aglycone)] of **1** and **10** in pyridine-d_5

	1	**10**
C-10	−7.5 (α)	+7.7 (α)
C-1	−3.7 (β-pro-*S*)	−1.6 (β-pro-*R*)
C-9	+0.2 (β-pro-*R*)	−4.7 (β-pro-*S*)
C-14	−5.5	−2.1

(Kitajima et al., 1998b) by comparison with the authentic compound.

Alkyl glycoside **6** ($C_{12}H_{22}O_{10}$, a colorless syrup, $[\alpha]_D^{21}$ −71°) gave $[M+K]^+$, $[M+Na]^+$ and $[M+H]^+$ ion peaks at *m/z* 365, 349 and 327 in the positive FAB-MS, and the ^1H and ^{13}C NMR spectral data showed the presence of one β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl group. By comparison of its NMR spectral data (Table 4) and $[M]_D$ value with that of methyl β-D-glucopyranoside (**11**) {$[M]_D$ value of **6**—$[M]_D$ value of **11** = −169°}, **6** was identified as a β-D-apiofuranoside of **11** (Kitajima et al., 1998b). Thus, **6** was characterized as methyl β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside.

Alkyl glycoside **7** ($C_{13}H_{24}O_{11}$, a colorless syrup, $[\alpha]_D^{21}$ −47°) gave $[M+Na]^+$ and $[M+H]^+$ ion peaks at *m/z* 379 and 357 in the positive FAB-MS. By comparison of its ^1H and ^{13}C NMR spectral data with those of **6** (Table 4), and $[M]_D$ value with that of **5** ($[M]_D$ value of **7**—$[M]_D$ value of **5** = −113°), the aglycone of **7** was suggested to be ethane-1,2-diol, and the structure of the sugar moiety was β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside. Therefore, **7** was characterized as ethane-1,2-diol 1-*O*-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside. Though **6** and **7** are very simple compounds, they are both new.

3. Experimental

3.1. General

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. FAB-MS were recorded with a JEOL HX-110 spectrometer using glycerol as a matrix. ^1H and ^{13}C NMR spectra were taken on a JEOL A-500 spectrometer with tetramethylsilane as an internal standard, and chemical shifts were recorded in δ values. ^{13}C–^1H COSY, HMBC, NOESY and 1-D NOESY

Table 2
^{1}H NMR chemical shifts of **1**, **1a**, **2** and **2a**

	1	**1a**	**2**	**2a**
H-1	2.85 *ddd* (7.0, 7.0, 10.0)	2.69 *ddd* (7.0, 7.0, 11.0)	4.36 *dd* (3.0, 3.0)	4.21 *dd* (3.0, 3.0)
H-2*ax*	2.27 *br dd* (10.0, 14.5)	2.31 *br dd* (11.0, 15.5)	2.34 *br d* (18.0)	2.34 *br d* (18.0)
eq	2.13 *br dd* (7.0, 14.5)	2.18 *br dd* (7.0, 15.5)	2.25 *ddd* (3.0, 3.0, 18.0)	2.25 *br d* (18.0)
H-3	5.53 *br s*	5.57 *br s*	5.41 *br s*	5.42 *br s*
H-5	2.79 *dd* (7.0, 10.0)	2.57 *dd* (7.0, 10.5)	3.09 *d* (9.0)	3.06 *d* (9.0)
H-6*ax*	4.87 *d* (10.0)	4.92 *d* (10.5)	4.48 *dd* (6.0, 9.0)	4.56 *dd* (7.0, 9.0)
H-7*ax*	–	–	2.49 *dddd* (3.0, 6.0, 9.0, 14.0)	2.58 *dddd* (3.0, 6.0, 8.5, 13.0)
H-8*ax*	3.45 *br dd* (14.5, 14.5)	3.28 *br dd* (14.5, 14.5)	1.63 *ddd* (10.0, 14.0, 14.0)	1.57 *ddd* (10.0, 13.0, 13.0)
eq	2.29 *br d* (14.5)	2.34 *br d* (14.5)	2.26 *ddd* (3.0, 7.0, 14.0)	1.99 *ddd* (3.0, 7.0, 13.0)
H-9*ax*	2.08 *ddd* (3.5, 14.5, 14.5)	2.12 *ddd* (3.5, 14.5, 14.5)	4.09 *dd* (7.0, 10.0)	3.96 *dd* (7.0, 10.0)
eq	1.91 *ddd* (3.5, 3.5, 14.5)	1.75 *ddd* (3.5, 3.5, 14.5)	–	–
H-11*ax*	–	–	2.85 *dq* (7.5, 9.0)	2.95 *dq* (7.5, 8.5)
H_3-13	1.65 *s*	1.71 *s*	0.97 *d* (7.5)	1.16 *d* (7.5)
H_3-14	1.46 *s*	1.39 *s*	0.84 *s*	0.83 *s*
H_3-15	1.97 *s*	2.02 *s*	1.91 *s*	1.95 *s*
Glc H-1	5.04 *d* (7.5)		5.09 *d* (8.0)	
Glc H-2	3.93 *dd* (7.5, 8.5)		4.02 *dd* (8.0, 9.0)	
Glc H-3	4.22 *dd* (8.5, 8.5)		4.27 *dd* (9.0, 9.0)	
Glc H-4	4.20 *dd* (8.5, 8.5)		4.24 *dd* (9.0, 9.0)	
Glc H-5	3.93 *m*		4.02 *m*	
Glc H-6a	4.35 *dd* (6.0, 11.5)		4.40 *dd* (6.0, 11.5)	
b	4.54 *dd* (2.5, 11.5)		4.57 *dd* (2.5, 11.5)	

δ in ppm from TMS [coupling constants (J) in Hz are given in parentheses].

Table 3
^{13}C NMR chemical shifts of **1**, **1a**, **2** and **2a**

	1	**1a**	**2**	**2a**
C-1	54.02 (−3.7)	57.71	70.07	71.48
C-2	33.12	33.26	31.63	31.36
C-3	126.07	126.49	120.66	120.43
C-4	145.68	145.55	133.38	133.44
C-5	53.01	53.81	40.60	39.89
C-6	84.49	84.51	79.50	79.85
C-7	164.95	164.77	35.54	35.67
C-8	22.38	22.72	29.46 (−1.2)	30.69
C-9	32.01 (+0.2)	31.79	84.43 (+8.8)	75.59
C-10	78.54 (+7.5)	71.04	41.44 (−1.0)	40.45
C-11	121.18	121.57	37.81	37.85
C-12	174.44	174.33	178.83	178.95
C-13	8.27	8.38	10.27	10.49
C-14	27.01 (−5.5)	32.54	22.14	21.46
C-15	18.37	18.34	22.48	22.51
Glc-1	98.17		105.50	
Glc-2	75.18		75.30	
Glc-3	79.12		78.83	
Glc-4	71.83		71.69	
Glc-5	78.21		78.81	
Glc-6	62.98		62.79	

spectra were obtained with the usual pulse sequence, and data processing was performed with standard JEOL software. CC was carried out under TLC monitoring using Kieselgel 60 (70–230 mesh, Merck), Sephadex LH-20 (25–100 μm, Pharmacia), Lobar RP-8 column (Merck) and Amberlite XAD-II (Organo). TLC was performed on silica gel (Merck 5721) and compounds were detected with *p*-anisaldehyde-H_2SO_4 reagent. HPLC separation was carried out with Symmetryprep C_{18} 7 μm (Waters; column size, 7.8 × 300 mm; ODS), and carbohydrate analysis (Waters; column size, 3.9 × 300 mm; CHA) columns.

3.2. *Extraction and separation*

Commercial cumin (the fruit of *C. cyminums* L.; purchased from Asaoka Spices Ltd., Lot. No. 99012001; 2 kg) was extracted with 70% aq methanol (10 l × 4), with the extract (281.1 g) partitioned into ether–water and ethyl acetate–water fractions, respectively. The aqueous portion (152.3 g) was applied to an Amberlite XAD-II column ($H_2O \rightarrow MeOH$) to give a water eluate (87.1 g) and methanol eluate (65.2 g) fractions.

The methanol eluate fraction was subjected to Sephadex LH-20 [MeOH–H_2O (9:1)] to give four fractions (frs. A–D). Fraction B (17.95 g) was subjected to silica gel chromatography [$CHCl_3$–MeOH–H_2O (17:3:0.2→4:1:0.1→7:3:0.5→MeOH)] to give 13 fractions (frs. B_1–B_{13}). Fraction B_2 (0.50 g) was passed through a Lobar RP-8 column [MeCN–H_2O (3:17→3:7)] to give nine fractions (frs. $B_{2\text{-}1}$–$B_{2\text{-}9}$), and fr. $B_{2\text{-}6}$ was subjected to silica gel CC [$CHCl_3$–MeOH (19:1)] to give **1** (50 mg). Fraction B_3 (0.50 g) was passed through a Lobar RP-8 column [MeCN–H_2O (3:17→3:7)] to give 15 fractions (frs. $B_{3\text{-}1}$–$B_{3\text{-}15}$), and fr. $B_{3\text{-}9}$ was subjected to HPLC [ODS, MeOH–H_2O (7:33)] to give **4** (8 mg). Fraction B_4 (2.00 g) was passed through a Lobar RP-8 column [MeCN–H_2O (3:17)] to

Table 4
^{13}C NMR chemical shifts of **5**–**7**

	5	6	7
C-1	64.94	56.73	72.63
C-2	15.52	–	62.00
Glc-1	104.45	105.56	104.96
Glc-2	75.21	75.01	75.15
Glc-3	78.60	78.54	78.48
Glc-4	71.68	71.86	71.88
Glc-5	78.50	77.21	77.07
Glc-6	62.80	68.98	69.05
Api-1		111.19	111.16
Api-2		77.85	77.80
Api-3		80.49	80.48
Api-4		75.04	75.07
Api-5		65.53	65.57

δ in ppm from TMS.

give 11 fractions (frs. $B_{4\text{-}1}$–$B_{4\text{-}11}$), and fr. $B_{4\text{-}5}$ was subjected to HPLC [ODS, MeCN–H_2O (1:9)] to give **3** (101 mg). Fraction $B_{4\text{-}9}$ was subjected to HPLC [ODS, MeCN–H_2O (3:17)] to give **2** (12 mg). An aliquot part of the water eluate fraction (51.4 g) was subjected to Sephadex LH-20 chromatography [MeOH–H_2O (4:1)] to give three fractions (frs. E–G). Fraction F (46.56 g) was applied to a silica gel column [$CHCl_3$–MeOH–H_2O (4:1:0.1→7:3:0.5→6:4:0.5→1:1:0.1)→MeOH] to give 21 fractions (frs. F_1–F_{21}). Fraction F_5 (0.10 g) was passed through a RP-8 column (H_2O) to give eight fractions (frs. $F_{5\text{-}1}$–$F_{5\text{-}8}$), and fr. $F_{5\text{-}5}$ and $F_{5\text{-}7}$ were subjected to HPLC [CHA, MeCN–H_2O (97:3)] to give **9** (3 mg) and **5** (4 mg), respectively. Fraction F_{12} (2.30 g) was subjected to a Lobar RP-8 column (H_2O) and HPLC [CHA, MeCN–H_2O (9:1)] to give **6** (4 mg). Fraction F_{14} (2.30 g) was subjected to a Lobar RP-8 column (H_2O) to give seven fractions (frs. $F_{14\text{-}1}$–$F_{14\text{-}7}$), and fr. F14-6 was subjected to HPLC [CHA, MeCN–H_2O (14:1)] to give **8** (25 mg). Fraction $F_{14\text{-}8}$ was subjected to HPLC [CHA, MeCN–H_2O (9:1)] to give **7** (6 mg).

The following compounds were identified by comparison with authentic compounds: benzyl β-D-glucopyranoside (**3**), phenethyl β-D-glucopyranoside (**4**), ethyl β-D-glucopyranoside (**5**), D-mannitol (**8**) and uracil (**10**).

3.3. *Cuminoside A [(1S,5S,6S,10S)-10-hydroxyguaia-3,7(11)-dien-12,6-olide β-D-glucopyranoside] (**1**)*

Amorphous powder, $[\alpha]_D^{24}$ −35° ($c=2.3$, MeOH). Positive FAB-MS *m/z*: 821 $[2M+H]^+$, 449 $[M+K]^+$, 433.1842 $[M+Na]^+$ (calc. for $C_{21}H_{30}NaO_8$; 433.1839), 411.2012 $[M+H]^+$ (calc. for $C_{21}H_{31}O_8$; 411.2019), 249 $[M-C_6H_{10}O_5+H]^+$ (base), 231 $[M\text{-}C_6H_{12}O_6+H]^+$. negative FAB-MS *m/z*: 409 $[M-H]^-$. ^{1}H NMR (pyridine-d_5, 500 MHz) δ: Table 2. ^{13}C NMR (pyridine-d_5, 125 MHz) δ: Table 3. HMBC correlations: H-1/C-2, C-5, C-6, C-9, C-10, C-14; H_2-2/C-3, C-4, C-5; H-3/C-1, C-2, C-4, C-5, C-15; H-5/C-1, C-2, C-3, C-4, C-6, C-7, C-15; H-6/C-4, C-5, C-7, C-11; H-8/C-7, C-9; H-9ax/C-1, C-7, C-8; H-9eq/C-1, C-7, C-8, C-10, C-14; H_3-13/C-7, C-11, C-12; H_3-14/C-1, C-9, C-10; H_3-15/C-3, C-4, C-5; Glc H-1/C-10.

3.4. *Enzymatic hydrolysis of **1***

A mixture of **1** (16 mg) and β-glucosidase (5 mg, Toyobo Co. Ltd., lot 52275) in water (5 ml) was shaken in a water bath at 37 °C for 14 d. The mixture was concentrated in vacuo to dryness and the residue was applied to a silica gel column [$CHCl_3$–MeOH (25:1) and $CHCl_3$–MeOH–H_2O (6:4:0.5)] to afford an aglycone **1a** (5 mg) and a sugar fraction. The sugar fraction was passed through Sephadex LH-20 (MeOH) to give a syrup, and HPLC [carbohydrate analysis (Waters), detector; JASCO RI-930 detector and JASCO OR-990 chiral detector, soln.; MeCN–H_2O (17:3), 2 ml/min; t_R 4.50 min (same location as that of D-glucose)] showed the presence of D-glucose.

3.5. *(1S,5S,6S,10S)-10-Hydroxyguaia-3,7(**11**)-dien-12,6-olide (**1a**)*

Amorphous powder, $[\alpha]_D^{21}$ −32° ($c=0.4$, MeOH). ^{1}H NMR (pyridine-d_5, 500 MHz) δ: Table 2. ^{13}C NMR (pyridine-d_5, 125 MHz) δ: Table 3.

3.6. *Cuminoside B [(1R,5R,6S,7S,9S,10S,11R)-1,9-dihydroxyeudesm-3-en-12,6-olide 9-O-β-D-glucopyranoside] (2)*

Amorphous powder, $[\alpha]_D^{21}$ −14° ($c=1.1$, MeOH). Positive FAB-MS *m/z*: 467 $[M+K]^+$, 451.1951 $[M+Na]^+$ (calc. for $C_{21}H_{32}NaO_9$; 451.1943), 429.2106 $[M+H]^+$ (calc. for $C_{21}H_{33}O_9$; 429.2124), 267 $[M-C_6H_{10}O_5+H]^+$ (base), 249 $[M-C_6H_{12}O_6+H]^+$. Negative FAB-MS *m/z*: 427 $[M-H]^-$. ^{1}H NMR (pyridine-d_5, 500 MHz) δ: Table 2. ^{13}C NMR (pyridine-d_5, 125 MHz) δ: Table 3. HMBC correlations: H-1eq/C-3; H-3/C-1, C-5, C-15; H-5ax/C-3, C-4, C-6, C-10, C-14, C-15; H-6ax/C-4, C-5, C-7, C-8; H-7ax/C-8, C-11, C-12; H-8ax/C-6, C-7, C-9, C-11; H-8eq/C-6, C-7, C-9, C-10; H-9ax/C-1, C-5, C-8, C-10, C-14, Glc C-1; H-11ax/C-7, C-8, C-12, C-13; H_3-13/C-7, C-11, C-12; H_3-14/C-1, C-5, C-9, C-10; H_3-15/C-3, C-4, C-5; Glc H-1/C-9.

3.7. *Enzymatic hydrolysis of **2***

A mixture of **2** (8 mg) and β-glucosidase (5 mg) in water (5 ml) was shaken in a water bath at 37 °C for 7 d. The mixture was treated in the same way as described for **1** to afford an aglycone **2a** (3 mg) and a sugar fraction. From the sugar fraction, D-glucose was detected as described for **1**.

3.8. (1R,5R,6S,7S,9S,10S,11R)-1,9-Dihydroxyeudesm-3-en-12,6-olide (**2a**)

Amorphous powder, $[\alpha]_D^{21}$ −18° (c=0.3, MeOH). ^{1}H NMR (pyridine-d_5, 500 MHz) δ: Table 2. ^{13}C NMR (pyridine-d_5, 125 MHz) δ: Table 3.

3.9. Methyl β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside (**6**)

Colorless syrup, $[\alpha]_D^{21}$ −81° (c=0.4, MeOH). Positive FAB-MS *m*/*z*: 365 $[M+K]^+$, 349.1098 $[M+Na]^+$ (calc. for $C_{12}H_{22}NaO_{10}$; 349.1111), 327.1311 $[M+H]^+$ (base, calc. for $C_{12}H_{23}O_{10}$; 327.1291). ^{1}H NMR (pyridine-d_5, 500 MHz) δ: 3.60 (3H, *s*, $-OCH_3$), 4.68 (1H, *d*, J=7.5, Glc H-1), 4.01 (1H, *dd*, J=7.5, 8.0 Hz, Glc H-2), 4.21 (1H, *dd*, J=8.0, 8.0 Hz, Glc H-3), 4.03 (1H, *dd*, J=8.0, 8.0 Hz, Glc H-4), 4.07 (1H, *m*, Glc H-5), 4.19 (1H, *dd*, J=6.0, 11.0 Hz, Glc H-6a), 4.75 (1H, *dd*, J=2.0, 11.0 Hz, Glc H-6b), 5.81 (1H, *d*, J=2.5, Api H-1), 4.78 (1H, *d*, J=2.5, Api H-2), 4.37 (1H, *d*, J=9.5, Api H-4a), 4.60 (1H, *d*, J=9.5, Api H-4b), 4.16 (1H, *d*, J=11.5, Api H-5a), 4.18 (1H, *d*, J=11.5, Api H-4b). ^{13}C NMR (pyridine-d_5, 125 MHz) δ: Table 4.

3.10. Ethane-1,2-diol 1-O-β-D-apiofuranosyl-(1→6)-β-D-Glucopyranoside (**7**)

Colorless syrup, $[\alpha]_D^{21}$ −47° (c=0.7, MeOH). Positive FAB-MS *m*/*z*: 379 $[M+Na]^+$, 357.1389 $[M+H]^+$ (base, calc. for $C_{13}H_{25}O_{11}$; 357.1397). ^{1}H NMR (pyridine-d_5, 500 MHz) δ: 4.02 (2H, *m*, H-2), 4.04, 4.28 (each 1H, *ddd*, J=3.5, 6.0, 10.0 Hz, H_2-1), 4.89 (1H, *d*, J=7.5, Glc H-1), 4.04 (1H, *dd*, J=7.5, 9.0 Hz, Glc H-2), 4.21 (1H, *dd*, J=9.0, 9.0 Hz, Glc H-3), 4.02 (1H, *dd*, J=9.0, 9.0 Hz, Glc H-4), 4.08 (1H, *m*, Glc H-5), 4.14 (1H, *dd*, J=6.5, 11.0 Hz, Glc H-6a), 4.74 (1H, *dd*, J=2.0, 11.0 Hz, Glc H-6b), 5.77 (1H, *d*, J=2.5, Api H-1), 4.78 (1H, *d*, J=2.5, Api H-2), 4.36 (1H, *d*, J=9.0, Api H-4a), 4.60 (1H, *d*, J=9.0, Api H-4b), 4.15 (1H, *d*, J=11.5, Api H-5a), 4.18 (1H, *d*, J=11.5, Api H-4b). ^{13}C NMR (pyridine-d_5, 125 MHz) δ: Table 4.

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