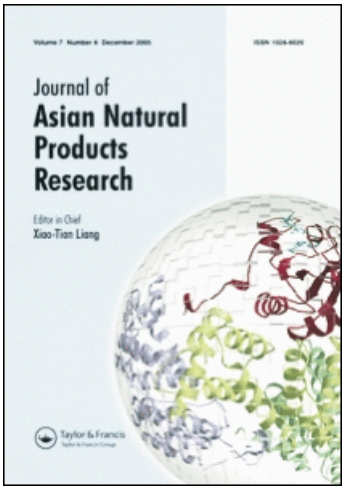

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Note: A new iridoid diglycoside from *Clerodendrum chinense*

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Note

A new iridoid diglycoside from *Clerodendrum chinense*

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A new iridoid diglucoside, 5-*O*-β-glucopyranosyl-harpagide, has been isolated from the aerial part of *Clerodendrum chinense* together with three known iridoid glucosides and six known cyclohexylethanoids. Their structures have been determined by analyses of spectroscopic data.

Keywords: *Clerodendrum chinense*; *Clerodendrum fragrans*; Verbenaceae; Iridoid glucoside; 5-*O*-β-Glucopyranosyl-harpagide; Cyclohexylethanoid

1. Introduction

Clerodendrum chinense (Osbeck) Mabb. [Syn. *C. fragrans* (Vent.) Willd.; Verbenaceae; Thai name: Nang-Yam] is a shrub, native to tropical regions of Asia. The leaves are used in Thai traditional medicine, as an anti-pyretic as well as an anti-inflammatory. In our continuing studies on Thai medicinal plants [1,2], the constituents of this plant have been investigated. The present paper deals with the isolation and determination of a new iridoid diglucoside (**4**), three known iridoid glucosides (**1**–**3**), and six known cyclohexylethanoids (**5**–**10**) from the aerial part of this plant.

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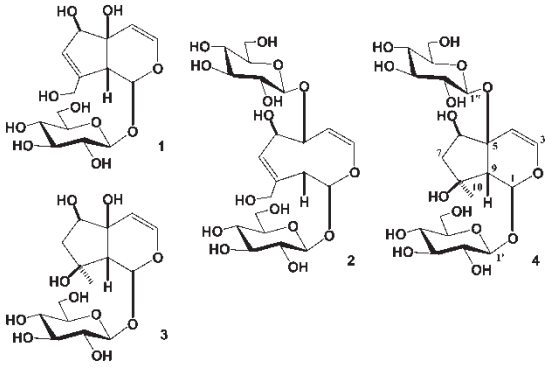

2. Results and discussion

Ten compounds were isolated from the methanolic extract of the aerial part of *C. chinense*. Nine compounds were identified as known compounds, monomelittoside (**1**), melittoside (**2**), harpagide (**3**), racemic rengyolone (**5**), racemic dihydrorengyolone (**6**), rengyoxide (**7**), rengyoside B (**8**), cornoside (**9**) and dihydrocornoside (**10**) by comparison of physical data with literature values and from spectroscopic evidence [1,3–6].

Compound **4** was obtained as an amorphous powder. Its molecular formula was determined as $C_{21}H_{34}O_{15}$ by HR-FAB mass spectrometry. ^{13}C NMR spectral data reveal two β-glucopyranosyl units and a cyclopentanopyran ring, corresponding to a C-9 iridoid skeleton. DEPT experiments indicate that compound **4** has one methyl (δ 25.1), one methylene (δ 46.6), five methines (δ 57.2, 76.7, 93.0, 104.5, 143.6), and two quaternary carbons (δ 78.4, 80.1) in the aglycone moiety. The methine signals at δ 143.6 (C-3) and δ 104.5 (C-4) suggest that C-4 is unsubstituted [7]. Inspection of the ^1H NMR spectrum reveals signals at δ 5.75 (d, $J = 1.5$ Hz), 6.39 (d, $J = 6.6$ Hz), 5.15 (d, $J = 6.6$ Hz), 3.93 (dd, $J = 3.8$, 3.2 Hz) and 2.76 (d, $J = 1.5$ Hz), which were assignable to the methine protons H-1, H-3, H-4, H-6 and H-9, respectively. The methyl singlet at δ 1.25 belongs to H-10. Chemical shifts at δ 4.71 (d, $J = 7.8$ Hz) and 4.59 (d, $J = 7.8$ Hz) are assigned to the signals of two anomeric protons of two β-glucopyranosyl moieties. Assignment of the proton signals is based on the result of HSQC. The ^1H and ^{13}C NMR spectral data are very similar to those of harpagide (**3**), except for a set of additional signals arising from a β-glucopyranosyl moiety in compound **4**. The additional unit was assigned to be at C-5 of the cyclopentanopyran ring because of the downfield shift of C-5 (+7.2 ppm) together with the upfield shifts of C-4 (−4.3 ppm), C-6 (−1.2 ppm) and C-9 (−2.8 ppm) [3]. Also, the chemical shift of the anomeric carbon at δ 97.5 (C-1″) agrees with the tertiary alcoholic β-glucopyranoside [8], linked at C-5. Consequently, compound **4** was elucidated as 5-*O*-β-glucopyranosyl-harpagide.

3. Experimental

3.1 General experimental procedures

NMR spectra were recorded in CD_3OD or C_5D_5N using a Jeol JNM α-400 spectrometer. MS spectra were obtained on a Jeol JMS-SX 102 spectrometer. Optical rotations

were measured with a Union PM-1 digital polarimeter. Preparative HPLC was carried out on an ODS column (20 × 150 mm i.d., YMC) with a Tosoh refractive index detector; flow rate of 6 ml min^{-1}. For column chromatography, Diaion HP-20 (Mitsubishi Chem. Ind. Co. Ltd), silica gel 60 (Merck), and YMC-gel ODS (50 μm, YMC) were used. The solvent systems were: (I) EtOAc–MeOH–H_2O (40:10:1), (II) EtOAc–MeOH–H_2O (70:30:3), (III) EtOAc–MeOH–H_2O (6:4:1), (IV) 10–40% aq. MeOH, (V) 2% aq. MeCN, (VI) 1% aq. MeCN, and (VII) 5% aq. MeCN. The spray reagent used was 10% H_2SO_4 in 50% EtOH.

3.2 Plant material

The aerial part of *Clerodendrum chinense* (Osbeck) Mabb. was collected from Petchaburi Province, Thailand, in August 2001. The identity of the plant was confirmed by Professor Vichiara Jirawongse, Faculty of Pharmaceutical Sciences, Khon Kaen University. Voucher specimens are kept in the Herbarium of the Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand.

3.3 Extraction and isolation

The dried aerial part (1.5 kg) of *Clerodendrum chinense* was extracted three times with hot MeOH (8 l each extraction, 70°C). The solvent was then concentrated *in vacuo* to give a greenish powder (131.0 g). This residue was subsequently suspended in H_2O (1.0 l) and defatted with Et_2O, (4 ×, 1.0 l each time). The aqueous layer was applied to a column of Diaion HP-20, and eluted with H_2O, MeOH and Me_2CO, successively. The fraction eluted with MeOH (19.2 g) was concentrated to dryness, and subjected to column chromatography on silica gel using solvent systems I, II and III. Seven fractions were collected. Fraction 2 (2.1 g) was applied to an RP-18 column, using solvent system IV, to provide seven fractions. Fraction 2-1 was purified by preparative HPLC-ODS with solvent system V to afford compounds **5** (13 mg), **6** (69 mg), and **7** (51 mg). Fraction 3 (4.3 g) was subjected to a RP-18 column, using solvent system IV, to afford eight fractions. Fraction 3-1 was followed by preparative HPLC-ODS with solvent system VI to provide compounds **8** (8 mg), **9** (103 mg) and **10** (14 mg). Fraction 4 (2.2 g) was applied to an RP-18 column, employing solvent system IV, to yield eight fractions. Fraction 4-2 was purified by preparative HPLC-ODS to give compound **1** (56 mg). Fractions 4-3-5 were combined and then subjected to preparative HPLC-ODS with solvent system VII to afford compounds **3** (43 mg) and **4** (7 mg). Similarly, fraction 5 (1.8 g) was subjected to a RP-18 column, using solvent system IV. Fraction 5-3 was purified by HPLC-ODS with solvent system VII to give compound **2** (223 mg).

3.4 5-O-β-Glucopyranosyl-harpagide (4)

Amorphous powder; $[\alpha]_D^{21}$ −33.1° (MeOH, *c* 0.45); ^{1}H NMR (CD_3OD) δ (ppm): 6.39 (1H, d, $J = 6.6$ Hz, H-3), 5.75 (1H, d, $J = 1.5$ Hz, H-1), 5.15 (1H, d, $J = 6.6$ Hz, H-4), 4.71 (1H, d, $J = 7.8$ Hz, H-1′), 4.59 (1H, $J = 7.8$ Hz, H-1″), 3.93 (1H, dd, $J = 3.8$, 3.2 Hz, H-6), 3.88 (1H, dd, $J = 12.0$, 2.0 Hz, H-6′a), 3.78 (1H, dd, $J = 12.6$, 2.2 Hz, H-6″a), 3.70 (1H, dd, $J = 12.6$, 4.6 Hz, H-6″b), 3.66 (1H, dd, $J = 12.0$, 5.6 Hz, H-6′b), 2.76 (1H, d, $J = 1.5$ Hz, H-9), 1.85 (2H, br s, H-7), 1.25 (3H, s, H-10); ^{13}C NMR

Table 1. ^{13}C NMR spectral data of compound **4** in CD_3OD (100 MHz).

C		*C*	
1	93.0 (CH)	1′	99.2 (CH)
3	143.6 (CH)	2′	74.8 (CH)
4	104.5 (CH)	3′	78.4 (CH)
5	80.1 (C)	4′	71.7 (CH)
6	76.7 (CH)	5′	77.1 (CH)
7	46.6 (CH_2)	6′	62.8 (CH_2)
8	78.4 (C)	1″	97.5 (CH)
9	57.2 (CH)	2″	75.2 (CH)
10	25.1 (CH_3)	3″	78.1 (CH)
		4″	70.7 (CH)
		5″	78.0 (CH)
		6″	61.9 (CH_2)

(CD_3OD): see table 1. Negative HR-FAB-MS, *m/z* 525.1819 $[M - H]^-$ (calcd. for $C_{21}H_{33}O_{15}$, 525.1819).

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