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A MORPHINAN ALKALOID FROM *PACHYGONE DASYCARPA* LEAVES

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Abstract

Phytochemical investigation of the leaves of Thai plant, *Pachygone dasycarpa* Kurz (Menispermaceae), has led to the isolation of (-)-8-methoxysinomenine (**1**), a morphinan alkaloid, and (+)-protoquercitol (**2**), a cyclohexanepentol. Their structures were assigned after detailed analysis of ^{1}H- and ^{13}C-NMR both 1D and 2D spectra and comparison of the spectral data with published values.

Key words: *Pachygone dasycarpa*, Morphinan alkaloid, (-)-8-Methoxysinomenine

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มอร์ฟิแนนอัลคาลอยด์จากใบโพกพาย

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บทคัดย่อ

การตรวจสอบองค์ประกอบทางเคมีของใบโพกพาย (*Pachygone dasycarpa* Kurz) ซึ่งเป็นพืชสมุนไพรไทยในวงศ์เมนิสเปอร์มาซิอี สามารถแยกมอร์ฟิแนนอัลคาลอยด์ คือ (-)-8-เมทอกซีซิโนเมนีน (**1**) และ สารกลุ่มไซโคลเฮกเซนเพนทอล คือ (+)-โปรโตเควอซิทอล (**2**) การพิสูจน์สูตรโครงสร้างทางเคมีของสารใช้ข้อมูลจาก ^{1}H- NMR และ ^{13}C-NMR ทั้งระบบเอกมิติและทวิมิติ ร่วมกับการเปรียบเทียบข้อมูลจากรายงานการวิจัยในอดีต

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Introduction

Pachygone dasycarpa Kurz (Menispermaceae), a woody climber, is known locally in Thai as Pok phaai or Yaa naang chaang. In Thailand, this plant distributes throughout the Northern (Lampang and Kampaeng Phet provinces), North-eastern (Loei, Phetchabun, Udon Thani and Nakhon Ratchasima provinces) and South-western (Kanchanaburi, Ratchaburi and Prachuap Khiri Khan provinces)[1]. Thai folk medicine has used the stem for diuretic, antinephritic, antipyretic and antiedema properties[2]. In previous reports, studies of the alkaloidal content of an extract of the stem bark have resulted in the isolation of numerous bisbenzylisoquinoline alkaloids[3], an aporphine alkaloid, (-)-anonaine, and a morphinan alkaloid, (+)-14-hydroxy-isostephodeline[4].

In this paper, we describe the isolation and structural elucidation of a morphinan alkaloid, (-)-8-methoxysinomenine (**1**) and a cyclohexanepentol, (+)-protoquercitol (**2**). Compound **1** has been isolated from *Stephania sutchuenensis* in the name of aknanidine (4-*O*-demethylhasubanonine)[5], and from *S. cepharantha* in the name of cephamonine[6]. This report, however, is the first time for **1** and **2** those found in *P. dasycarpa.*

Materials and Methods

General experimental procedures

The UV spectra were obtained on a Shimadzu UV-160A UV/vis spectrophotometer, while IR spectra were measured with a JASCO FT/IR-300E spectrophotometer. The optical rotation was measured with a Perkin Elmer 241 polarimeter. The EI-MS spectra were obtained from a Fison Micromass VG Platform II mass spectrometer and NMR data were recorded from a Bruker Avance DPX-300 FT-NMR spectrometer.

Plant material

The leaves of *Pachygone dasycarpa* (Menispermaceae) were collected in Pha Taem District, Ubon Ratchathani Province and Na Doon District, Mahasarakham Province, Thailand in June to July 1998. Authentication was achieved by comparison with the herbarium specimen at the Botany Section, Technical Division, Department of Agriculture, Ministry of Agriculture and Cooperatives, Thailand. The herbarium specimen has been deposited in the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok.

Extraction and isolation

A dried and powdered leaves of *Pachygone dasycarpa* (4 kg) was macerated three times for a 3-day-period in 95% ethanol and filtered. The combined filtrate was evaporated under reduced pressure to give a brown and syrupy mass (600 gm). This mass contains precipitate of (+)-protoquercitol (**2**), which was then recrystallized to give **2** (13.0 gm) as a white crystal. The residue remained was then treated with aqueous HCl (5%), the acidic solution was basified with NH_4OH to pH 9-10 and extracted with $CHCl_3$. Evaporation of the organic solvent under reduced pressure afforded the crude alkaloid (26.1 gm). This extract was passed through a column chromatography (CC) of silica gel 60 (Merck, 70-230 mesh ASTM) and eluted with C_6H_{12}-$CHCl_3$-CH_3OH (10:35:1). Further purification was achieved by three times of CC using silica gel 60, which eluted with $CHCl_3$-C_6H_6-EtOAc-CH_3OH (4:30:8:9), $CHCl_3$-$(CH_3)_2CO$-CH_3OH (5:4:1), and C_6H_{12}-$(CH_3)_2CO$ - $CHCl_3$-CH_3OH (2:3:2:1), respectively. Finally, compound **1** was obtained as an amorphous powder (5 gm).

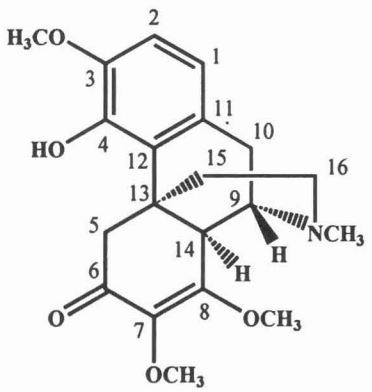
(-)-8-Methoxysinomenine (**1**) Amorphous powdered, m.p. 183-186°, $[\alpha]^{20}_D$ -32.6 (c = 0.09). IR ν_{max}: 3402, 1668, 1609, 1483, 1439, 1277, 1236, 1137, 1048 cm^{-1}. UV λ_{max}^{MeOH}: 209 sh (4.39), 275 (3.93). EI-MS *m/z* (rel. int.): 359 (M^+ 39), 344 (61), 328 (100), 316 (14), 222 (42), 178 (30), 146 (25). ^{1}H- and ^{13}C-NMR: Table **1**.

(+)-Protoquercitol (**2**) Colorless prism, m.p. 228-230°, $[\alpha]^{20}_D$ +235-237. IR ν_{max}: 3320 (st., br.) 1070, 1050 cm^{-1}. EI-MS *m/z* (rel. int.): 165 (M^+ +1, 1), 128(10), 102(8), 99(23), 86(24), 74(53), 73(100), ^{13}C-NMR (D_2O) δ 33.3 (C-6), 68.6 (C-5), 68.9 (C-1), 71.0 (C-3), 72.3 (C-4), 74.6 (C-2).

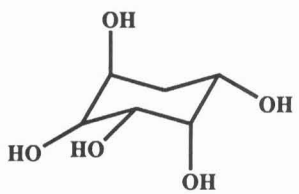
Results and Discussion

The brown and syrupy mass form the leaves of *Pachygone dasycarpa* was decanted and recrystallized to yield (+)-protoquercitol (**2**) which was identified by spectroscopic techniques and comparison with the published values in previous report[7,8]. Our 300 MHz ^{1}H-NMR spectrum of this cyclitol was essentially the same as that previously reported at 220 MHz[7]. The ^{13}C-NMR spectrum of **2** was reported recently[8], but two of the six carbon resonances could not be assigned unambiguously. We have found that ^{1}H-^{13}C shift-correlated 2-D NMR spectroscopy showed clearly that the multiplet at δ 3.59 ppm assigned

doublets at δ 3.85 for H-5 was attached to the carbon resonating at δ 68.6. Thus, we have been able to assign all six resonances. The alkaloidal crude extract was repeatedly subjected to silica gel column chromatography to give (-)-8-methoxysinomenine (**1**) as an amorphous powder. The molecular formula $C_{20}H_{25}NO_5$ was established by EI-MS. The IR spectrum exhibited the presence of α, β-unsaturated carbonyl moiety (1668, 1609 cm^{-1}). The ^{1}H-NMR spectrum showed the presence of *N*-methyl group (δ 2.47), three methoxy groups (δ 3.39, 3.81, 4.02), a set of coupled aromatic protons (δ 6.55, 6.65, each d, J = 8.3 Hz), and characteristic methylene protons (δ 2.34, 4.23, each d, J = 15.6 Hz). The completed structural assignment of **1**, however, was performed by comparison of the ^{1}H- and ^{13}C-NMR data of the same compound which was isolated from other plants, including *Stephania sutchuenensis* in the name of aknanidine (4-*O*-demethylhasubanonine)[5], and *S. cepharantha* in the name of cephamonine[6] and also those of sinomenine which was isolated from *S. cepharantha*[6]. Further biological evaluations of these isolates should be recommended to perform.



1



2

Table 1 The ^{1}H-and ^{13}C-NMR data of **1** in $CDCl_3$

C	δ_C (ppm)	δ_H (ppm), *J* (Hz)	C	δ_C (ppm)	δ_H (ppm), *J* (Hz)
1	118.29	6.55 (d, 8.3)	11	130.71	-
2	108.90	6.65 (d, 8.3)	12	122.21	-
3	144.83	-	13	38.04	-
4	144.25	-	14	49.18	3.12 (d, 2.7)
5	48.08	2.34 (d, 15.6)	15	35.41	1.88 (ddd, 12.6, 12.4, 4.6)
		4.23 (d, 15.6)			1.93 (ddd, 12.6, 2.7, 1.7)
6	194.46	-	16	47.08	2.63 (ddd, 12.4, 12, 2.7)
7	137.72	-			2.67 (ddd, 12, 4.6, 1.7)
8	161.46	-	$N-CH_3$	42.30	2.47 (s)
9	53.10	3.60 (dd, 5.4, 2.7)	$3-OCH_3$	56.00	3.81 (s)
10	24.09	2.87 (dd, 18.3, 5.4)	$7-OCH_3$	60.53	3.39 (s)
		2.92 (d, 18.3)	$8-OCH_3$	60.63	4.02 (s)

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