

COMMUNICATION V

Dicentrine: the Major Alkaloid of *Cyclea laxiflora* Miers.

Key words: *Cyclea laxiflora*, dicentrine, alkaloid.

ABSTRAK

Sebatian alkaloid bagi Cyclea laxiflora Miers. telah diasingkan dan dikenalpasti sebagai disentrina berdasarkan data spektrum dan fizik.

ABSTRACT

The major alkaloid of Cyclea laxiflora Miers. was isolated and identified as dicentrine from its spectral and physical data.

INTRODUCTION

Cyclea laxiflora Miers (Menispermaceae) is a slender woody climber found in the limestone hills of Langkawi Island located at the northern tip of Peninsular Malaysia. The tubers of this plant are sold by dealers for traditional medicine; it is claimed that these roots are a remedy for sinus trouble and fever (Burkill, 1936). As part of our interest in the chemical constituents of medicinal plants, we have now investigated the alkaloid of this plant.

MATERIALS AND METHODS

The roots of *C. laxiflora* were collected from the limestone hill near Tanjung Aru on Langkawi Island, off Peninsular Malaysia. A voucher specimen No UPM 4666 has been deposited at the herbarium of the Biology Department, Universiti Pertanian Malaysia.

Melting points were determined on a Kofler hot stage and are uncorrected. Infrared and ultraviolet spectra were recorded on Beckmann Acculab 3 and Hitachi 200-2 spectrometers, respectively. ^1H and ^{13}C NMR spectra were measured at 80 and 20.1 MHz, respectively on a Bruker WP 80 spectrometer. Mass spectra were recorded on AE1-MS 12 instrument at 70 eV.

Extraction

The fresh roots were cleaned to remove soil, grated to small pieces of roughly 1×0.5 mm cross-section and steeped in methanol for 24 hours. The methanol extract was then drained off and fresh methanol was introduced. This procedure was repeated until the final extract gave a negative Meyers test for alkaloids.

The methanol extracts were combined and evaporated *in vacuo* to give 10 g of a brown gum which was partitioned between chloroform and 1 M H_2SO_4 . The aqueous acidic solution was then basified with Na_2CO_3 and extracted with chloroform to give 4 g of crude base.

Isolation of Dicentrine

The crude base was subjected to column chromatography using silica gel (mesh 230-400). The column was eluted with chloroform/methanol mixtures (5% increment of methanol on each addition of 500 ml of eluent until a 35% methanol concentration was reached, followed by 10% increments of methanol from then on). A set of 55 fractions (each 50 ml) was collected; the major constituent was found to be present in fractions 13, 14 and 15. These fractions were combined and recrystallized from methanol to give 500 mg of colourless prisms, m.p. 168-169°C (lit. 169°C, Southon and Buckingham, 1989).

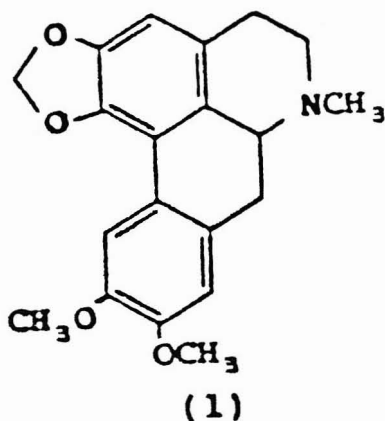
λ_{max} MeOH: 306 nm (log ϵ 4.20), 284 nm (log ϵ 4.18), 220 nm (log ϵ 4.52), (Craig and Roy 1965); ν_{max} (CHCl_3 film): 2980-2920, 1615, 1595, 1520, 1470, 1400, 1105, 870 cm^{-1} ; ^1H NMR (80 MHz, CDCl_3) δ : 7.67 (s, 1H), 6.78 (s, 1H), 6.51 (s, 1H), 6.00 (dd, 11.7, 1.3 MHz, 2H), 3.92 (s, 6H $2 \times \text{OCH}_3$), 3.21-2.93 (m, 5H), 2.79-2.61 (m, 2H), 2.55 (s, 3H, N-CH_3); ^{13}C NMR (20.1 MHz, CDCl_3) δ : 148.2 (C-9), 147.6 (C-2), 146.5 (C-10), 141.7 (C-1), 128.3 (C-7a), 126.5 (C-11c), 126.3 (C-11b), 123.5 (C-11a), 110.6 (C-11), 106.6 (C-3), 62.3 (C-6a), 53.5 (C-5), 43.83 (N- CH_3), 34.2 (C-7), 29.2 (C-4); MS m/z (%): 339(70), 338(100),

322(25), 307(20), 296(30), 265(20).

RESULTS AND DISCUSSION

The major alkaloid isolated from the fresh root of *C. laxiflora* crystallized as a colourless prism (m.p. 168-169°) from methanol after purification of the crude basic fraction by column and thin layer chromatography. The mass spectrum gave M^+ at m/z 339 consistent with the molecular formula $C_{20}H_{21}NO_4$. The proton NMR spectrum showed three one-proton singlet peaks at δ 7.67, 6.78 and 6.51 corresponding to H-11, H-8 and H-3 respectively of an aporphine alkaloid. The two protons double-doublet at δ 6.0 is consistent with a methylenedioxy substituent on C1 - C2 and a six-proton singlet peak at δ 3.92 attributed to two methoxyl groups on C-9 and C-10. The *N*-methyl protons appeared at δ 2.55. Other signals which appeared as multipliers at δ 3.21 to 2.93 and 2.79 to 2.61 ppm integrated for five protons and two protons, respectively (Lu *et al.* 1972). The assignment of the structure was further supported by the ^{13}C NMR spectrum which agreed with the reported value (Marsaioli *et al.* 1979; Hara *et al.* 1986) for dicentrine (1).

Previously, berbamine had been isolated from *C. barbata* (Dahmen *et al.* 1977) and the seven *Cyclea* species used in Chinese traditional medicine have also been found to contain bisbenzylisoquinolines (Zhu *et al.* 1983). Aporphine alkaloids do not appear to have been found in *Cyclea* species before.



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REFERENCES

- BURKILL, I.H. 1936. *A Dictionary of the Economic Products of the Malay Peninsula*, 2 vols. Crown Agents for the Colonies, London. (reprint 1966, Ministry of Agriculture and Cooperatives, Kuala Lumpur).
- CRAIG, J.C. and S.K. ROY. 1965. Optical Rotatory Dispersion and Absolute Configuration II, Aporphine Alkaloids. *Tetrahedron* **21**:395.
- DAHMEN, K., P. PACHALY and F. ZYMALKOWSKI. 1977. Alkaloids from the Thai Drug, Krung Kha Moa, (*Cyclea barbata*, Menispermaceae). V. Isolation and Structural Elucidation of Further Bisbenzylisoquinoline Alkaloids. *Arch. Pharm.* **310**:95.
- HARA, H., F. HASHIMOTO, O. HOSHINO and B. UMEZAWA. 1986. Studies on Tetrahydroisoquinolines XXVIII. Syntheses of (\pm)-*N*-methyllaurotetanine, (\pm)-cassythicine, (\pm)-9-hydroxy-1,2,3,10-tetramethoxyaporphine, (\pm)-dicentrine and (\pm)-thalicsimidine. *Chem. Pharm. Bull.* **34**:1946-1949.
- LU, S.T., S.J. WANG, P.H. LAI, C.M. LING and L.C. LIN. 1972. Alkaloids of Formosan Lauraceous Plants. XV: Alkaloids of *Lindera oldhamii*, Heinsl. *Yakugaku Zasshi.* **92**: 910-917 (CA:77, 101949m).
- MARSAIOLI, A. J., F. A. M. REIS, A. F. MAGALHAES and E.A. RUVEDA. 1979. ^{13}C NMR Analysis of Aporphine Alkaloids. *Phytochemistry* **18**: 535-545.
- SOUTHON, I.W. and J. BUCKINGHAM. 1989. *Dictionary of Alkaloids*. London: Chapman and Hall. 333p.
- ZHU, Z., Y. FENG, L. HE and Y. WANG. 1983. Study on Utilization of Medicinal Plant Resources of the Genus *Cyclea* of Menispermaceae in China. *Yaoxue xuebau.* **18**:535-540 (CA: 100, 25973r).

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