SHORT REPORT

J. Sci. Soc. Thailand, 11 (1985) 47 - 50

TRADITIONAL MEDICINAL PLANTS OF THAILAND VI. ISOLATION OF CRYPTOMERIDIOL FROM *BLUMEA BALSAMIFERA*[1]

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(Received 20 November 1984)

Abstract

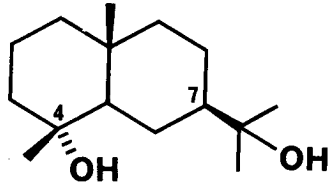
The leaves of Blumea balsamifera *(Compositae) have yielded the antispasmodic principle cryptomeridiol* **(1).**

Blumea balsamifera DC (Compositae) has been reported to have quite wide use in the Chinese and Thai systems of traditional medicine. Preparations of the plant have been used as a carminative, as a mild stimulant, as a vermifuge, as a preventive medicament, as an abortifacient and as a topical application for septic ulcers in the ancient Chinese medical literature[2]. In Thailand, the dried leaves are cut into small pieces and smoked as a cigarette to relieve sinusitis pain. An infusion of the leaves is used as a stomachic, carminative, diaphoretic, expectorant and emmenagogue. A decoction from the fresh leaves alone or in combination with other plants is used as a bath for women after giving birth.

The phytochemistry of *Blumea* has been of interest of many years. Following initial studies on the essential oil[3], aliphatic hydrocarbons[4], monoterpenes[3-9], sesquiterpenes[4,9], triterpenes and steroids[2,5,10-12], a diester of coniferyl alcohol[13], some polyacetylene and thiophene derivatives[13,14], xanthoxylin[2], eranthin and 5,3',4'-trihydroxy-3,6,7-trimethoxy flavone[15-17], two dihydroquercetin derivatives[18], a number of unidentified flavonoids[2,15], and some coumarins[2] have been obtained from *Blumea* species.

In a previous report[18] we described the isolation and structure elucidation of two new flavonoids from *Blumea balsamifera*. Here we describe the characterization of the antispasmodic principle cryptomeridiol **(1)** from the leaves of this plant.

The leaf material of *Blumea balsamifera* DC (compositae) was purchased from a local herbal drug store in Bangkok. Authentication was achieved by comparison with herbarium specimens at the Botany Section, Technical Division, Department of Agriculture, Ministry of Agriculture and Cooperatives, Thailand.*



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Experimental Procedures

Melting points were determined on a Kofler hotplate and are uncorrected. The ultraviolet spectra were recorded with a Beckman model DB-G spectrophotometer. The infrared spectra were determined with a Perkin-Elmer model 283 or a Beckman model IR-18A spectrophotometer; absorption bands are reported in wavenumbers (cm^{-1}). ^{1}H-NMR spectra were recorded with a Varian T-60A instrument operating at 60 MHz, with a Nicolet model TT-7 Fourier Transform attachment. ^{13}C-NMR, spectral data were obtained at 20.15 MHz, through the assistance of Dr. V.M. Chari on a Bruker WP-80 instrument. Tetramethylsilane was used as an internal standard and chemical shifts are reported in δ (ppm). Mass spectra were obtained with a Varian MAT-112S double-focusing spectrometer operating at 70 eV. Optical rotations were obtained in chloroform with a Perkin-Elmer 241 polarimeter.

Extraction and Initial Fractionation:

The dried and powdered plant material (4.5 kg) was macerated twice for five day periods with 95% ethanol (20 and 15 liters). After pooling the ethanol extracts the alcohol was removed *in vacuo* and the residue suspended in 10% aqueous ethanol (3 liters). Following filtration, the solution was treated with 10% aqueous lead acetate solution until there was no further precipitation. The filtrate was extracted with chloroform (3 x 7 liters) and the combined chloroform extracts dried (Na_2SO_4) and evaporated *in vacuo* to yield a brown syrup (13.5 g). On stirring with chloroform a pale yellow

precipitate formed which was removed by filtration to afforded a solid (Fraction A, 977 mg). The isolation of two new dihydroquercetin derivatives from this fraction was described previously[18]. The filtrate was evaporated *in vacuo* to afford a yellow syrup (Fraction B, 12 g).

Separation of Fraction B:

Fraction B was divided into 24 batches and each batch chromatographed on a dried silica gel column (40 x 2.5 cm) and eluted with ether (8.5 liters). Thin-layer chromatography was used as a guide for the separation and like fractions were combined and evaporated *in vacuo* to afford three major fractions. The most polar of these (2.4 g) was divided into 12 batches and each batch was chromatographed on a dry silica gel column (30 x 1.5 cm) eluting with chloroform:ethanol (95:5, 500 ml). Five ml fractions were collected and like fractions were combined. Crystallization of the more polar fractions afforded feathery white crystals (445 mg, 0.01% yield) of cryptomeridiol **(1)**, mp 140-142°(lit. 141-142°), $[\alpha]_D^{24}$ -53° ($CHCl_3$); ir, νmax (KBr) 3385, 3330, 2980, 2950, 2940, 2915, 2880, 2865, 1480, 1470, 1455, 1385, 1370, 1340, 1265, 1230, 1200, 1185, 1125, 1095, 1025, 925 and 915 cm^{-1}; ^{1}H-nmr, ($CDCl_3$ δ) 0.86 (3H, s, 10-CH_3), 1.12 (3H, s, 4-CH_3) and 1.20 (6H, s, 11-$(CH_3)_2$); ^{13}C-nmr, ($CDCl_3$, δ) 18.6 (C-15), 20.1 (C-2), 21.5 (C-8), 22.5 (C-6 or C-14), 22.6 (C-14 or C-6), 27.1 (C-12 or C-13), 27.3 (C-13 or C-12), 34.5 (C-10), 41.1 (C-1), 43.5 (C-3), 44.6 (C-9), 49.9 (C-7), 54.8 (C-5), 72.3 (C-4), and 72.9 (C-11); ms, *m/z* : 240 (M^+, 0.5%), 207 (6), 204 (3), 189 (7), 182 (10), 16(11), 164 (35), 150 (9) 149 (76), 135 (12), 123 (29), 122 (13), 121 (15), 109 (40) 108 (29), 107 (15), 96 (21), 95 (28), 93 (22) 81 (39), 71 (47) 67 (27), 59 (100) and 55 (34). These data are in complete agreement with those reported previously[19] for cryptomeridiol **(1)** and with an authentic sample.

Cryptomeridiol is the active principle of Proximol^R a renal antispasmodic product from the desert weed *Cymbopogon proximus* Stapf. (Gramineae[19]). The compound is quite widely distributed occurring in other members of the Compositae, the Cupressaceae[19], the Euphorbiaceae[20], the Magnoliaceae, the Taxodiaceae, the Winteraceae, and the Zingiberaceae[19].

Acknowledgements

One of the authors (R.P.B.) wishes to thank the American Foundation for Pharmaceutical Education for its support in the form of a graduate fellowship and to the Graduate College, University of Illinois at Chicago, Health Sciences Center, Chicago for its support in the form of Dorothea H. Fleming Student Research Fellowship. Part of this work was conducted while one of us (G.A.C.) was the recipient of a fellowship from the Alexander von Humboldt Foundation which was held at the Institut fur Pharmazeutische Biologie der Universitat Munchen.

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* A voucher specimen (no. NR 310) of the plant material has been deposited in the Herbarium of the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand.

บทคัดย่อ

ใบหนาด *(Blumea balsamifera)* วงศ์ Compositae ให้สาร cryptomeridiol **(1)** ที่ออกฤทธิ์แก้อาการเกร็ง