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ALKALOIDS OF *STEPHANIA ERECTA* CRAIB

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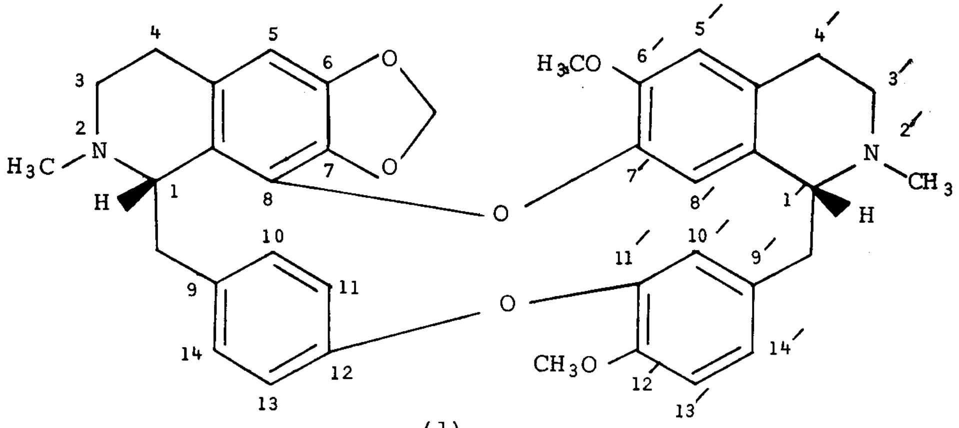
Abstract

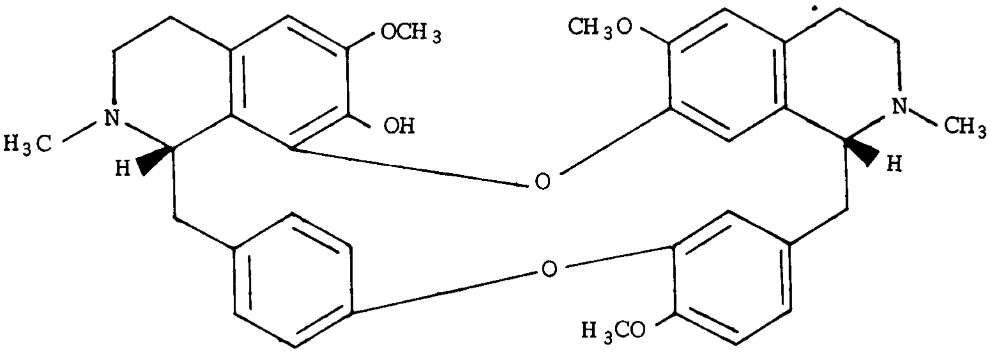
Cepharanthine (1) and homoaromoline (2) have been isolated from the tubers of Stephania erecta *Craib (Menispermaceae).*

Stephania erecta Craib is a slender herbaceous climber with a large tuber, 5-8 cm in diameter, and round membranous leaves. It is used in Thai folk remedies as a skeletal muscle relaxant, as well as an analgesic and tonic[1].

Extraction of the tubers by conventional procedures yielded a crude base which appeared to be a mixture of at least 9 components on thin layer chromatography. The two major components of the mixture were separated by chromatography on a column of silica gel. Cepharanthine[2,3] was isolated by converting the major fraction into its hydrochloride followed by crystallization and neutralization; homoaromoline[4-6] was obtained by further preparative layer chromatography of another fraction collected from the column. The properties of both cepharanthine and homoaromoline agreed with those reported previously[2-6].



(1)



(2)

Melting points were determined on an Electrothermal melting point apparatus. Nuclear magnetic resonance (n.m.r.) spectra were obtained with a Varian T 60 instrument operating at 60 MHz and a Bruker WP 80 instrument operating at 80 MHz. The low resolution mass spectra (direct insertion, source temperature 240°C, 70 eV) were measured with a Dupont 490 F GC-MS instrument. The high resolution mass spectra (direct insertion, source temperature 250°C, 70 eV) were determined with an A.E.I. MS 902 spectrometer. Ultraviolet spectra were measured on a Beckman 25 spectrophotometer and infrared spectra were obtained on a Jasco IRA-1 instrument. Optical rotations were measured with a Perkin Elmer 141 Polarimeter using a 1 dm microcell (1 ml).

A voucher specimen of the plant material (PS 489) has been deposited in the Herbarium of the Biology Department at the Prince of Songkla University, Hat Yai, Thailand.

Fresh tubers (13 kg) were blended with methanol (6.4 l), then chloroform (2.1 l) and ammonia (d.0.88,0.43 l) were added. After allowing to stand for 2 days at room temperature, the mixture was filtered and the solid residue was extracted 5 more times with methanol/chloroform/aq. ammonia (d.0.88) (15:5:1). The combined extract was concentrated under reduced pressure to 700 ml then poured into glacial acetic acid (1,250 ml). The mixture was filtered and the aqueous solution was basified with ammonia to precipitate the alkaloids, which were then taken up in chloroform (4×300 ml). The combined chloroform extract was evaporated under reduced pressure to yield the crude base as a brown gum (52 g, 0.4%). Thin layer chromatography of this product on silica gel using chloroform/methanol (9:1) as the mobile phase revealed the presence of 9 spots which were visible under U.V. light.

Portion of the crude base (26 g) was chromatographed on a column of silica gel (820 g) which was eluted with petroleum ether, then chloroform and finally chloroform containing increasing amount of methanol. The first fractions collected gave a negative Mayer's test and were discarded. The second series of fractions contained mainly one component, which was converted into its hydrochloride by dissolving in methanol saturated with hydrogen chloride (150 ml) then evaporating to dryness. Crystallization of the residue from acetone gave a small yellow needles of cepharanthine hydrochloride (3.65 g, 14%), m.p.261-265° (d). A portion of the hydrochloride (0.936 g) was converted into the free base which crystallized from a mixture of acetone-benzene to give colourless needles of cepharanthine (1), m.p. 143-145° C, undepressed on admixture with an authentic sample kindly provided by Professor M. Kozuka, [Lit^3 m.p. 140-145°], $[\alpha]_D^{20}$ + 289.1° (c.1.5, $CHCl_3$) {Lit^2 $[\alpha]_D^{22}$ + 292° (c.1.0, $CHCl_3$)}. λ_{max}^{MeOH}nm, (logε) : 211 (4.45), 282 (3.61). N.m.r.($CDCl_3$) δ : 2.10-4.38 (m, 14H, alicyclic H); 2.58 (s, 3H, 2-NCH_3); 2.66 (s, 3H, 2'-NCH_3); 3.66 (s, 3H, 6'-OCH_3); 3.87 (s, 3H, 12'-OCH_3); 5.53 (s, 2H, -O-CH_2-O-); 6.15-7.56 (m, 10H, ArH). (Found : M^+606.2738. Calc. for $C_{37}H_{38}N_2O_6$: 606.2728). Mass spectrum m/e : 606 (M^+, 85%), 605 (54), 380 (29), 379 (100), 378 (11), 366 (13), 365 (25), 192 (13), 190 (90), 189 (19), 175 (13), 174 (57), 159 (12), 146 (28).

The third, fourth, fifth and sixth series of fractions collected gave intractable mixtures.

The seventh series of fractions gave a brown product (2.85 g), a portion (2.0 g) of which was subjected to preparative layer chromatography on silica gel using chloroform/methanol (94:6) as the mobile phase. The band with R_f 0.35-0.47 was extracted with chloroform/methanol (1:1) and evaporated to dryness. This residue was further purified by preparative layer chromatography using chloroform/methanol (92:8) as the mobile phase. Extraction of the major band with chloroform/methanol afforded a pale yellow powder (0.33 g) which crystallized from ethanol to give small pale yellow needles of homoaromoline (2), m.p. 240-242°C (d) [Lit^{6}238-240°C (d)], $[\alpha]_D^{20}$ + 434.1° (c.0.7,$CHCl_3$) {Lit^7 $[\alpha]_D^{21}$ + 425.3° ($CHCl_3$)}. λ_{max}^{MeOH}nm, (logε) : 209 (4.78), 283 (3.86). N.m.r. ($CDCl_3$) δ : 2.17-4.33 (m, 14H, alicyclic H); 2.47 (s, 3H, 2-NCH_3); 2.53 (s, 3H, 2'-NCH_3); 3.58 (s, 3H, 6'-OCH_3); 3.77 (s, 3H, 6-OCH_3); 3.86 (s, 3H, 12'-OCH_3); 5.51 (s, H, OH); 6.13-7.43 (m, 10H, ArH). (Found : M^+608.2879. Calc. for $C_{37}H_{40}N_2O_6$: 608.2885). Mass spectrum m/e : 608 (M^+, 76%), 607 (36), 382 (31), 381 (100), 380 (10), 368 (10), 367 (38), 365 (17), 192 (40), 191 (81), 190 (21), 176 (17), 175 (19), 174 (48), 168 (19).

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บทคัดย่อ

จากการสกัดหัวของต้นโกฐหัวบัว *(Stephania erecta Craib)* พบว่าประกอบด้วยสาร cepharanthine (1) และ homoaromoline (2)