SHORT REPORT

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TRADITIONAL MEDICINAL PLANTS OF THAILAND. III. CONSTITUENTS OF *ZANTHOXYLUM BUDRUNGA* (RUTACEAE)*

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Abstract

Examination of the fruits of native Zanthoxylum budrunga *(Rutaceae) has yielded xanthoxylin* (1) *and the two alkaloids arborine* (2) *and dictamnine* (3).

The genus *Zanthoxylum* in the family Rutaceae is a broad genus having substantial synonymy with the genus *Fagara*. A number of alkaloid types occur in *Zanthoxylum* species. including quinolone, furoquinoline, benzophenanthridine and indoloquinazoline type[1]. In this report we describe the characterization of three compounds from the fruits of the Thai species *Zanthoxylum budrunga* Wall. obtained from a local market.

Little ethnomedical information is available for this species, except for one report of the hot aqueous extract being used orally for amenorrhoea[2]. The essential oil of the fruit was demonstrated to possess anti-inflammatory activity in the rat by the i.p. route in three test systems[3] and in humans, anti-inflammatory activity was also observed when applied topically in cases of chronic dermatitis[4].

Phytochemically, vitamin E has been detected in the seed oil[5], and *p*-menthane and trihydroxy-*p*-menthane have been isolated from the essential oil[6]. The bark has

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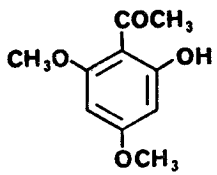
yielded an uncharacterized compound, budrungaine[7] and two alkaloids, chelerythrine and skimmianine[8].

In these, the first studies to be conducted on the fruits of *Z. budrunga*, the neutral fraction was chromatographed to afford xanthoxylin *(1)*, a new constituent of this genus, whereas the basic fraction yielded two alkaloids, arborine *(2)* and dictamnine *(3)*. The former compound is also apparently new to this genus whereas the latter is very widely distributed.



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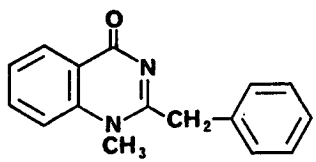

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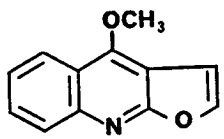

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Fruits of *Zanthoxylum budrunga* Wall. (Rutaceae) were purchased at a local market in Bangkok, and authenticated by comparison with herbarium specimens at the Botany Section, Technical Division, Department of Agriculture, Ministry of Agriculture and Cooperatives, Thailand. This material* was then air dried and coarsely powdered.

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}). ^1H-NMR spectra were recorded with a Varian T-60A instrument operating at 60MHz, with a Nicolet model TT-7 Fourier Transform attachment. 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 or with and AEI 902 double-focusing spectrometer operating at 70 eV. Optical rotations were obtained in methanol with a Perkin-Elmer 241 polarimeter.

*A voucher specimen of the plant material (NR 304) has been deposited in the Herbarium of the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand.

Extraction and Initial Fractionation: The dried and coarsely powdered plant material (1.5 kg) was macerated twice for 3 day periods with 95% ethanol (8 and 5 liters). The ethanol extracts were pooled and the solvent removed *in vacuo*. The residue was then thoroughly mixed with 5% sulphuric acid (1.5 liters), and allowed to stand overnight. After filtration, the filtrate was extracted with chloroform (4 × 500 ml), the combined chloroform extracts dried (Na_2SO_4), and the solvent removed *in vacuo* to yield a syrup (Fraction A, 230 mg).

The acidic aqueous fraction was basified (NH_4OH) and extracted with chloroform (6 × 500 ml). The pooled chloroform extract was washed with distilled water (2 × 500 ml), dried (Na_2SO_4), and the solvent removed *in vacuo* to yield a brown syrup (Fraction B, 345 mg).

Separation of Fraction A: The fraction was dissolved in chloroform (3 ml) and adsorbed onto the top of a dry silica gel (E. Merck, Darmstadt) column (2.5 × 40 cm). Elution with chloroform afforded 22 fractions (20 ml). On evaporation, fractions 1–9 yieded a yellow syrup that was a complex mixture by thin layer chromatography (TLC), while fractions 10–22 afforded a white solid, homogenous by TLC designated as ZB–1.

Xanthoxylin (1): Fraction ZB–1 was crystallized from chloroform to yield 96 mg (6.40×10^{-5}%) of white rhomboidal plates, mp 80–81° (lit. 80.5–81°);[9] $[\alpha]_D^{24}$ 0°; ir, ν_{max} KBr) 3100, 3002, 2940, 1620, 1425, 1365, 1330, 1270, 1155, 830, and 585 cm^{-1}; uv, λ_{max} (MeOH), 320sh (log ε = 3.96), 282 (4.58), 250 min, 225sh (4.69), 207 (4.81); λ_{max} (MeOH + NaOH), 328 (3.88), 285 (4.23), 260 min, 230sh (4.64), 221 (4.67); λ_{max} (MeOH + HCl), 320sh (3.96), 282 (4.58), 250 min, 225sh (4.69) and 207 (4.81); ^{1}H–NMR (CDCl3) δ, 2.58 (3H, s, $COCH_3$), 3.78 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 5.90 (1H, d, J = 2.4 H 3–H), 6.05 (1H, d, J = 2.4 Hz, 5–H), and 14.0 (1H, s, OH); ms, *m/z* 196 (M^+, 28%), 181 (100), 166 (10), 138 (9(, 95 (10), and 69 (11). These data are in complete agreement with published values[9].

Separation of Fraction B: The fraction was dissolved in chloroform (5 ml) and adsorbed onto the top of a dry silica gel[2] column (2.5 × 40 cm). Elution with chloroform:ethanol (9:1) afforded 21 fractions (20 ml). On evaporation, fractions 1–10 yielded a solid residure which was a complex mixture by TLC, fractions 11–4, homogeneous by TLC, were designated ZB–2, and fractions 15–21, also homogeneous by TLC, were designated ZB–3.

Arborine (2): Fraction ZB–2 crystallized from chloroform to yield 23 mg (1.53×10^{-5}%) of white plates, mp 155–8° (lit. 155–156°);[11] $[\alpha]_D^{24}$0°; ir, ν_{max} (KBr) 1640, 1610, 1597, 1530, 1495, 1402, 1187, 775, 717, and 690 cm^{-1}; uv, λ_{max} (MeOH), 315sh (log ε = 3.84), 305 (3.92), 284.5 min, 277 (3.69), 269sh (3.66), 259.4 min, 230.4 (4.32), 223 min, 218sh (4.32), and 206 (4.50); λ_{max} (MeOH + $NaOCH_3$), 315sh (3.81), 305 (3.90), 284 min, 276 (3.67), 268sh (3.64), 259, min, 230 (4.30), 223 min, and, 206 (4.50); λ_{max} (MeOH + HCl), 292sh (3.78), 276.5 (3.84), 260 min, 234 (4.33), 219 min, and 206 (4.33); ^{1}H–NMR (acetone–d_6) δ, 3.77 (3H, s, N–CH_3), 4.30 (2H, s, benzylic–CH_2), 7.32 (5H, bs, benzyl phenyl group), and 7.33–8.47 (4H, m, quinazolone aromatic protons); ms, *m/z* 250 (M^+, 57%), 249 (100), 235 (8), 132 (8), 105 (34),

104 (44), 91 (42), 78 (24), and 77 (31). These data are in complete agreement with published values[10,11].

Dictamnine (3): Fraction ZB-3 was crystallized from chloroform to yield 47 mg (3.13×10^{-5}%) of white needles, mp 132.5–133° (lit. 132–133°)[13]; $[\alpha]_D^{24}$ 0°; ir, ν_{max}(KBr), 1625, 1583, 1372, 1087, 758, and 720 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ, 4.43 (3H, s, OCH_3), 7.10 (1H, d, $J = 3.5$ Hz, β-furan proton), 7.67 (1H, d, $J = 3.5$ Hz, α-furan proton), and 7.25–8.40 (4H, m, 5–H, 6–H, 7–H, and 8–H); ms, m/z 199 M^+, 100%), 185 (11), 184 (88), 156 (47), 130 (13), 128 (29), 101 (23) and 76 (22). These data are in complete agreement with values obtained from an authentic sample, and with published values[12,13].

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บทคัดย่อ

จากการตรวจสอบลูกระมาศ *(Zanthoxylum budrunga)* พบว่าลูกระมาศมีสาร xanthoxylin *(1)* และอัลกาลอยด์ 2 ชนิด คือ arborine *(2)* และ dictamnine *(3)*