Available online at www.sciencedirect.com

ScienceDirect

South African Journal of Botany 72 (2006) 555 – 558

SOUTH AFRICAN JOURNAL OF BOTANY

www.elsevier.com/locate/sajb

Benzo[*c*]phenanthridine alkaloids from stem bark of the Forest Knobwood, *Zanthoxylum davyi* (Rutaceae)

P.K. Tarus [a,b], P.H. Coombes [a,*], N.R. Crouch [a,c], D.A. Mulholland [a,d]

[a] *School of Chemistry, University of KwaZulu-Natal, Howard College Campus, Durban 4041, South Africa*
[b] *Department of Chemistry, Kenyatta University, PO Box 43844, Nairobi, Kenya*
[c] *Ethnobotany Unit, South African National Biodiversity Institute, PO Box 52099, Berea Road 4007, South Africa*
[d] *School of Biomedical and Molecular Sciences, University of Surrey, Guildford, Surrey, GU2 7XH, UK*

Received 18 October 2005; accepted 9 March 2006

Abstract

The stem bark of the southern African ethnomedicinal tree *Zanthoxylum davyi* (Rutaceae) has yielded five benzo[*c*]phenanthridine alkaloids, chelerythrine, dihydrochelerythrine, bocconoline, 6-hydroxydihydrochelerythrine and 6-methoxy-7-demethyldihydrochelerythrine, together with 4-methoxy-1-methyl-2(1*H*)-quinolinone and the uncommon lignan *meso*-sesamin. The chemotaxonomic and ethnopharmacological relevance of these compounds is discussed, particularly that of the well-documented antimicrobial and anti-inflammatory chelerythrine.

Keywords: 6-Hydroxydihydrochelerythrine; 6-Methoxy-7-demethyldihydrochelerythrine; Benzo[*c*]phenanthridine alkaloids; Rutaceae; *Zanthoxylum davyi*

1. Introduction

Zanthoxylum davyi (I.Verd.) Waterm. (syn. *Fagara davyi* I. Verd.) (Rutaceae), or Forest Knobwood, is a medium to tall tree (8–30 m) found commonly in montane and coastal scarp forests of KwaZulu-Natal and the Transkei, extending northwards through Mpumalanga, Swaziland and Zimbabwe (Coates Palgrave, 2002). The trunk and main branches usually bear large knobs tipped with spines; the leaves and unripe fruits are distinctly lemon-scented. Until fairly recently, this species was included in *Fagara* L. (Waterman, 1975). In common with other African *Zanthoxylum* species such as *Z. capense* (Thunb.) Harv., *Z. gilletii* (De Wild.) Waterm. and *Z. chalybeum* Engl., *Z. davyi* is employed in the treatment of snakebite (Mpondo in Transkei, Vhavenda in Limpopo) and severe coughs and colds (Zulu, Vhavenda) (Watt and Breyer-Brandwijk, 1962; Gelfand et al., 1985; Mabogo, 1990; Beentje, 1994; Kokwaro and Johns, 1998). Its spines are used by the Vhavenda for infected wounds, the leaves for chest pains, the stem bark to treat boils, pleurisy and toothache, and root preparations for mouth ulcers, sore throats and as an aphrodisiac (Mabogo, 1990). Root-bark decoctions are used by the Zulu as a tonic both for man and animals (Watt and Breyer-Brandwijk, 1962) and to treat toothache. The plant is known as *nungumabele* to the Xhosa (*C. Kromhout 36*, PRE), *umnumgwane omkhulu* to the Zulu (Pooley, 1994) and *munungu* to the Vhavenda (*G. Hemm 672*, PRE).

Z. davyi has not previously been investigated phytochemically. Accordingly, the current investigation sought to profile the bark chemistry and determine whether the constituents could reasonably be related to the documented ethnopharmacology.

2. Materials and methods

2.1. Plant materials

Stem bark (1.55 kg) of *Z. davyi* (I. Verd.) Waterm. was collected in March 2003 from the Buffelskloof Private Nature Reserve in Mpumalanga, South Africa, and a voucher (*N. Crouch 989*, NH) lodged for verification purposes.

2.2. Extraction and fractionation

The air-dried, milled stem bark was extracted successively for 24 h in a Soxhlet apparatus with 3 l each of hexane,

---

* Corresponding author.
E-mail address: coombesp@ukzn.ac.za (P.H. Coombes).

0254-6299/$ - see front matter © 2006 SAAB. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.sajb.2006.03.014

dichloromethane, ethyl acetate and methanol. Compounds were isolated by vacuum and gravity column (silica gel, Merck 7734 and 9385) and preparative thin layer chromatography (aluminium-backed analytical plates, Merck 1.05554) using varying proportions of dichloromethane and methanol. The ethyl acetate extract (8.47 g) yielded compound 1, chelerythrine (8.1 mg), compound 2, dihydrochelerythrine (17.0 mg), compound 3, bocconoline (16.5 mg), compound 4, 6-hydroxydihydrochelerythrine (6.8 mg), compound 5, 6-methoxy-7-demethyldihydrochelerythrine (14.3 mg), compound 6, *meso*-sesamin (12.9 mg), compound 7, 4-methoxy-1-methyl-2(1*H*)-quinolinone (20.4 mg), compound 8, sinapaldehyde (14.1 mg), and compound 9, lupeol (18.2 mg).

2.3. Structure determinations

^{1}H and ^{13}C NMR spectra were recorded at room temperature on a Varian Unity Inova 400 MHz spectrometer. Structures were assigned by analysis of the ^{1}H, ^{13}C and 2D NMR spectra and by comparison with literature values. Accordingly, compound 1 was identified as chelerythrine (Krane et al., 1984) (Fig. 1), compound 2 as dihydrochelerythrine (Oechslin et al., 1991), compound 3 as bocconoline, compound 4 as 6-hydroxydihydrochelerythrine (Sečkářová et al., 2002), compound 5 as 6-methoxy-7-demethyldihydrochelerythrine, compound 6 as *meso*-sesamin (Cheplogoi, 2001), compound 7 as 4-methoxy-1-methyl-2(1*H*)-quinolinone (Tsai et al., 2000), and compounds 8 and 9 as the ubiquitous extractives sinapaldehyde (Ismail, 2003) and lupeol (Reynolds et al., 1986), respectively. The fully assigned ^{13}C NMR data for bocconoline (compound 3), and ^{1}H and ^{13}C NMR data for 6-methoxy-7-demethyldihydrochelerythrine (compound 5) have not been reported previously and are presented here for the first time:

Bocconoline. ^{13}C NMR (100 MHz, CDCl$_3$) δ 152.2 (C-8), 148.5 (C-3), 147.6 (C-2), 146.4 (C-7), 137.8 (C-4b), 131.0 (C-12a), 127.0 (C-4a), 125.8 (C-6a), 125.1 (C-10a), 124.3 (C-12), 123.5 (C-10b), 119.8 (C-11), 118.9 (C-10), 111.8 (C-9), 104.7 (C-1), 101.2 (–O$\underline{C}H_2$O–), 99.8 (C-4), 61.9 (6-$\underline{C}H_2$OH), 61.2 (7-$\underline{C}H_3$O–), 59.7 (C-6), 55.8 (8-$\underline{C}H_3$O–), 42.9 (N-$\underline{C}H_3$).

6-Methoxy-7-demethyldihydrochelerythrine. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (1H, *s*, H-4), 7.67 (1H, *d*, *J* 8.6 Hz, H-11), 7.47 (1H, *d*, *J* 8.6 Hz, H-10), 7.43 (1H, *d*, *J* 8.6 Hz, H-12), 7.15 (1H, *s*, H-1), 6.84 (1H, *d*, *J* 8.6 Hz, H-9), 6.59 (1H, *s*, H-6), 6.10 (1H, *d*, *J* 1.2 Hz, –OC$\underline{H_a}$O–), 6.09 (1H, *d*, *J* 1.2 Hz, –OC$\underline{H_b}$O–), 3.71 (3H, *s*, 8-OC$\underline{H_3}$), 3.03 (3H, *s*, N-C$\underline{H_3}$), 2.40 (3H, *s*, 6-OC$\underline{H_3}$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 152.2 (C-8), 148.0 (C-2), 147.5 (C-3), 146.3 (C-7), 138.4 (C-4b), 131.2 (C-12a), 126.9 (C-4a), 126.1 (C-6a), 125.5 (C-10a), 123.2 (C-12), 123.0 (C-10b), 119.8 (C-11), 118.7 (C-10), 112.3 (C-9), 104.5 (C-1), 101.1 (–O$\underline{C}H_2$O–), 100.8 (C-4), 77.4 (C-6), 60.4 (6-$\underline{C}H_3$O–), 55.6 (8-$\underline{C}H_3$O–), 40.8 (N-$\underline{C}H_3$).

3. Discussion

Chelerythrine and dihydrochelerythrine are both widespread in the Papaveraceae, Rutaceae and Fumariaceae, with chelerythrine being found additionally in the Sapindaceae. 4-Methoxy-1-methyl-2(1*H*)-quinolinone is reported as restricted to, but widespread within, the Rutaceae (Dictionary of Natural Products on CD-ROM, 2005). First isolated from *Bocconia cordata* Willd. (Papaveraceae) (Tani and Takao, 1962), bocconoline is relatively common, with reports from six species

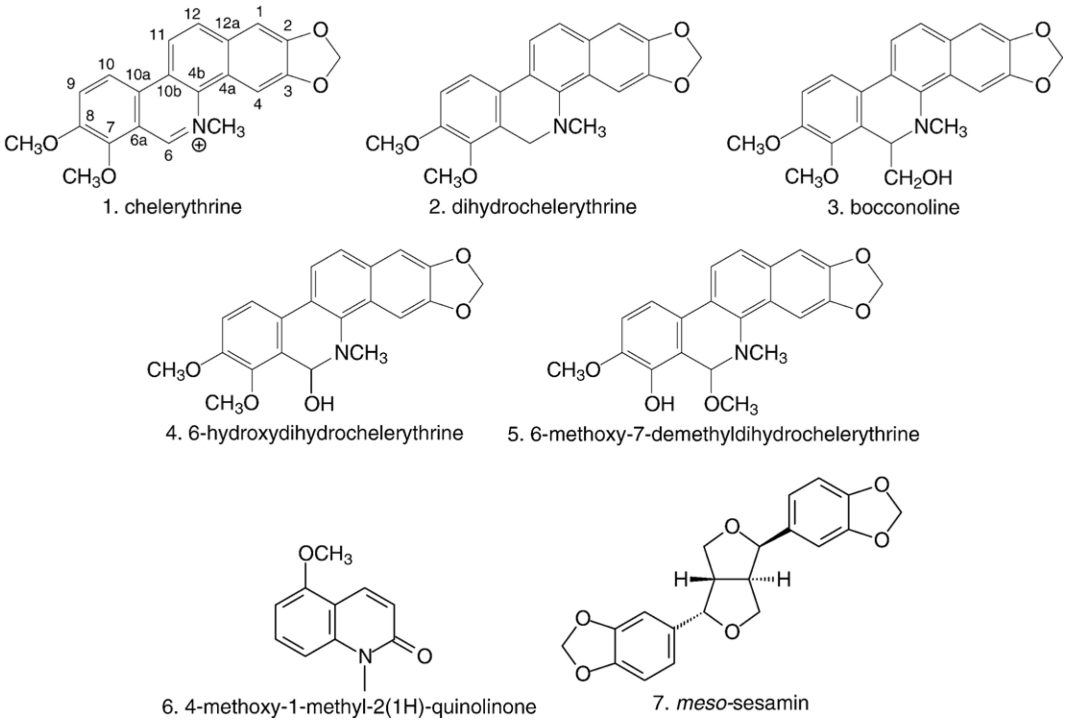

Fig. 1. Isolates of the stem bark of *Zanthoxylum davyi*.