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Phenanthroindolizidine alkaloids from *Vincetoxicum pumilum*

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1. Subject and source

Vincetoxicum pumilum Decne. [syn. *Alexitoxicon pumilum* (Decne.) Pobed., *Antitoxicum pumilum* (Decne.) Pobed., *Cynanchum pumilum* (Decne.) Bornm.] (Apocynaceae–Asclepiadoideae) is a perennial herb endemic to Central Asia (Jalili and Jamzad, 1999). The plant (roots and aerial parts) was collected in Deh-Ghaibi near Mashhad, Iran. A voucher specimen (accession number 35007) was deposited in herbarium FUMH (Ferdowsi University Mashhad Herbarium).

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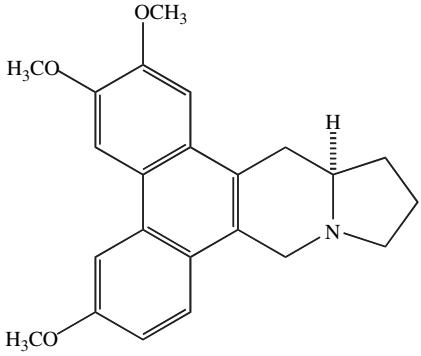
2. Previous work

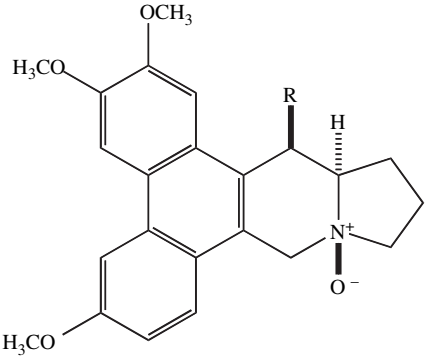
There are no literature reports of phytochemical investigations of *V. pumilum*.

3. Present study

Dried and milled roots (310 g) and aerial parts (568 g) were repeatedly extracted with a 1:1 mixture of methanol and dichloromethane. The extracts were evaporated and the residues (27 g from the roots and 59 g from the aerial parts) were suspended in water at pH 2–3, extracted with diethyl ether, the solutions alkalized with aqueous ammonia, and re-extracted with diethyl ether. The resulting alkaloid fraction of the root extract (560 mg) was fractionated by LC [75 × 2 cm column of Matrex silica gel 60A (35–70 μm), CH_2Cl_2–CH_3OH–28% aqueous NH_3 (93:6:1 followed by 90:10:1)] and HPLC [25 × 2.1 cm column of LiChrosorb Si60 (5 μm), CH_2Cl_2–saturated methanolic NH_3 (97:3) and CH_2Cl_2–CH_3OH–28% aqueous NH_3 (92.5:6.5:1)] to give 70 mg of (−)-13aα-antofine (**1**), 2 mg of (−)-10β,13aα-antofine *N*-oxide (**2**) and 3 mg of (−)-14β-hydroxy-10β,13aα-antofine *N*-oxide (**3**). Similarly, fractionation of the alkaloid fraction from the aerial parts (800 mg) by HPLC as above gave 7 mg of **1**, 3 mg of **2**, and 2 mg of **3**.



1.



2. R = H
3. R = OH

The compounds were identified by comparison of their ^1H and ^{13}C NMR spectra with literature data (Stærk et al., 2000, 2002). Compound **1**: $[\alpha]_D^{25}$ −118° (*c* 0.3, $CHCl_3$), lit. −124° (Stærk et al., 2002); compound **2**: $[\alpha]_D^{25}$ −56° (*c* 0.3, $CHCl_3$), lit. −37° (Stærk et al., 2000); compound **3**: CD spectrum (CH_3OH) showed positive Cotton effects at 211 nm and 233 nm and a negative Cotton effect at 268 nm, in agreement with the literature (Stærk et al., 2000).

4. Chemotaxonomic significance

The genus *Vincetoxicum* Wolf [*Cynanchum* sect. Vincetoxicum (Wolf) Tsiang & P. T. Li] has traditionally been classified within the cosmopolitan family Asclepiadaceae. However, the traditionally defined Asclepiadaceae have long been regarded as an apomorphic derivative of the Apocynaceae. Recently, a unified classification of Apocynaceae s. l. has been provided on the basis of extensive morphological studies as well as cladistic interpretation of molecular data (Endress and Bruyns, 2000; Endress and Stevens, 2001; Potgieter and Albert, 2001). Apocynaceae s. l. thus include Asclepiadaceae and Periplocaceae, reduced to a subfamily status (Endress and Bruyns, 2000). Most recent studies focus on subtribal classification within the Asclepiadoideae (Liede, 1999; Liede and Kunze, 2002; Liede and Meve, 2001, 2002; Liede and Täuber, 2002; Rapini et al., 2003). Although taxonomic interpretations of *Vincetoxicum* Wolf and *Cynanchum* L. and their relationships are complex, the former genus appears to be more related to *Tylophora* R. Br. rather than to the latter (Liede, 1996; Liede and Kunze, 2002; Yamashiro et al., 2004). *Vincetoxicum* and *Tylophora* produce phenanthroindolizidine alkaloids (Govindachari, 1967; Bick and Sinchai, 1981; Ali and Bhutani, 1989; Capo and Saa, 1989; Li et al., 1989; Lavault et al., 1994; Abe et al., 1995, 1998; Stærk et al., 2000, 2002; Huang et al., 2002; Zhen et al., 2002), absent from the Old World *Cynanchum* s. s. (sections *Cynanchum* and *Rhodostegiella*). The presence of phenanthroindolizidine alkaloids in *V. pumilum* is thus consistent with the most recent views (Liede, 1996; Yamashiro et al., 2004) on taxonomy of the phylogenetically complex Asclepiadeae. The phenanthroindolizidine alkaloids such as antofine are also of interest, because they exhibit potent antitumor activity by a mode of action different from known antitumor drugs (Gao et al., 2004).

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