

## ALKALOIDS OF *Convolvulus subhirsutus* FROM UZBEKISTAN

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*Convolvine, convolamine, convolidine, phyllalbine, and the new alkaloid phyllalbine N-oxide and the aminoalcohol nortropine were isolated from the total alkaloids of Convolvulus subhirsutus and for the first time from this plant.*

**Key words:** *Convolvulus subhirsutus*, alkaloids, isolation, phyllalbine N-oxide, nortropine.

Several tropane derivatives [1], mainly convolvine and convolamine [2], have been isolated previously from the aerial part and roots of *Convolvulus subhirsutus* growing in Kazakhstan.

The plant growing in Uzbekistan has not been investigated. We studied the aerial part of *C. subhirsutus* [3] collected in Tashkent district at the start of flowering. The quantitative content of total alkaloids was 0.36% of the air-dried mass of the aerial part. The total alkaloids obtained by extraction of the aerial part were divided into phenolic and nonphenolic parts. Separation of the phenolic fraction over a column of  $\text{Al}_2\text{O}_3$  isolated two alkaloids with mp 209-210°C and 214-215°C, which turned out to be phyllalbine and convolidine, respectively [4, 5]. The total bases of the nonphenolic part were separated by citrate—phosphate buffer at pH 6.8 to afford a fraction consisting of crude convolvine. The fraction obtained by work up with a buffer at pH 5.6 isolated convolamine with an impurity of convolvine.

Alkaloids in a basic aqueous solution were extracted with  $\text{CHCl}_3$  to produce a solution containing polar alkaloids that were very soluble in water but nonextractable by organic solvents. The aqueous solution was evaporated to dryness. The solid was chromatographed over a column of  $\text{Al}_2\text{O}_3$ . An amorphous base **1** was isolated from the first  $\text{CHCl}_3:\text{CH}_3\text{OH}$  eluents. The IR spectrum of **1** exhibited absorption bands for active H at 3552-3451  $\text{cm}^{-1}$ ; an aromatic ring, 1703, 1640, 1601, 874, 759; and stretching and deformation vibrations of  $\text{CH}_3-$ ,  $\text{CH}_2-$ , and  $\text{CH}-$  groups, 2962, 2838, 1439, 1323. The PMR spectrum of **1** showed signals for an  $\text{N}-\text{CH}_3$  group as a 3H singlet at 3.24 ppm and an aromatic methoxyl as a 3H singlet at 3.84. The range 1.75-2.25 ppm contained a broad 8H peak from four methylene protons. This was probably from protons of the tropane ring in positions C2, C4, C6, and C7. A 1H signal appeared at 5.14 ppm for the C3 proton, which is diagnostic for tropane alkaloids esterified at the C3 hydroxyl. Signals for aromatic protons (3H) were found in the range 6.75-7.55 ppm.

The spectral properties indicated that the isolated alkaloid was a tropane base esterified at the C3 hydroxyl by a methoxy-substituted aromatic acid. Comparison of the spectral properties of **1** with those of phyllalbine showed that their structures were similar. However, the  $\text{N}-\text{CH}_3$  signal in the PMR spectrum of **1** was shifted to weak field by 1 ppm compared with that of phyllalbine. This indicated that there was an electronegative group on the N atom that was causing such a large shift. Reduction of **1** with zinc in dilute HCl produced phyllalbine. Therefore, **1** was phyllalbine N-oxide.

Continued separation of total alkaloids from the next  $\text{CHCl}_3:\text{CH}_3\text{OH}$  fractions isolated amorphous base **2** with  $R_f$  0.1 (system 2). The IR spectrum of **2** exhibited absorption bands for active H (3358-3350  $\text{cm}^{-1}$ ), stretching and deformation vibrations of  $\text{CH}_2-$  and  $\text{CH}-$  at 2885 and 1410, and an ether at 1028. The PMR spectrum of **2** contained signals for methylene protons at 1.0-2.0 ppm as unresolved multiplets of intensity 8H. Base **2** was identified as nortropine, which we prepared by hydrolysis of convolvine. Nortropine was isolated from the plant for the first time.

Thus, the aerial part of *C. subhirsutus* growing in Tashkent district afforded six alkaloids: convolvine, convolamine, phyllalbine, convolidine, a new base that turned out to be phyllalbine N-oxide, and nortropine, which was isolated from the plant for the first time.

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## EXPERIMENTAL

IR spectra were recorded on a Perkin—Elmer model 2000 IR spectrometer (pressed KBr disks); NMR spectra, on a Tesla BS-567 A/100 MHz instrument (CDCl<sub>3</sub> and CD<sub>3</sub>OD solvents, HMDS internal standard,  $\delta$ -scale). Chromatography used Al<sub>2</sub>O<sub>3</sub> (Brockmann activity II) and the solvent systems CHCl<sub>3</sub>:CH<sub>3</sub>OH (9:1, 1) and CHCl<sub>3</sub>:CH<sub>3</sub>OH:NH<sub>4</sub>OH (25%) (4:1:0.1, 2).

**Isolation of Total Alkaloids.** The air-dried aerial part of *C. subhirsutus* (3 kg) was moistened with ammonia solution (10%), placed in a percolator, and after 2 h treated with CHCl<sub>3</sub> (six times). The combined CHCl<sub>3</sub> extracts were condensed to a volume of 2 L and worked up with H<sub>2</sub>SO<sub>4</sub> solution (10%) to extract exhaustively the alkaloids. The combined acidic solutions were washed twice with a small quantity of CHCl<sub>3</sub> and made basic with ammonia solution (25%). The alkaloids were extracted with CHCl<sub>3</sub> to afford total bases (10.7 g).

**Separation of Total Alkaloids.** Total bases (10.7 g) were dissolved in CHCl<sub>3</sub> (2 L) and worked up with KOH solution (4%, 4 × 100 mL). The alkaline extracts were acidified with H<sub>2</sub>SO<sub>4</sub> solution (20%), cooled, and made basic with ammonia solution (25%). Alkaloids were extracted exhaustively with CHCl<sub>3</sub>. The CHCl<sub>3</sub> solution was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Solvent was distilled off to produce phenolic alkaloids (2.5 g). After work up with base, the CHCl<sub>3</sub> solution was washed with distilled water and worked up successively with citrate—phosphate buffer at pH 6.8 and 5.6 to extract completely the alkaloids. The buffer extracts were made basic with cooling using conc. NH<sub>4</sub>OH solution. Alkaloids were extracted with CHCl<sub>3</sub> to afford bases from the fractions with pH 6.8 (5.5 g, convolvine) and 5.6 (2.2 g, convolvamine with an impurity of convolvine).

**Isolation of Phyllalbine and Convalidine.** The phenolic alkaloids (2.5 g) were boiled in acetone (5 × 50 mL). The combined and condensed acetone solution afforded crude phyllalbine (0.5 g). The crystalline mixture that was insoluble in acetone was worked up with CH<sub>3</sub>OH to afford convalidine (0.3 g).

**Base 1, Nortropine.** The basic aqueous solution left after extraction of alkaloids with CHCl<sub>3</sub> was neutralized with HCl (10%) and dried in a porcelain dish on a water bath. The dry solid was chromatographed over a column of Al<sub>2</sub>O<sub>3</sub> with elution by CHCl<sub>3</sub> and CHCl<sub>3</sub>:CH<sub>3</sub>OH. The separate CHCl<sub>3</sub>:CH<sub>3</sub>OH eluents (95:5) isolated base **1** (0.1 g), *R<sub>f</sub>* 0.85 (system 1) (phyllalbine *N*-oxide). The next fractions afforded an amorphous alkaloid (30 mg) with *R<sub>f</sub>* 0.1 (system 2) (nortropine).

**Hydrolysis of Convolvamine.** Convolvine (0.1 g) in methanolic KOH (5 mL, 10%) was boiled on a water bath for 3 h. The CH<sub>3</sub>OH was removed in vacuo. The solid was worked up with CHCl<sub>3</sub>:CH<sub>3</sub>OH (95:5). Solvent was removed by condensing and drying. The dry solid was an amorphous base identified as nortropine.

**Reduction of Base 1.** Base **1** (50 mg) in HCl solution (10 mL, 10%) was treated with zinc dust (0.1 g) and left at room temperature for 3 h. The acidic solution was decanted, made basic with ammonia, and extracted with CHCl<sub>3</sub> (3 × 30 mL). Drying and removal of CHCl<sub>3</sub> afforded crystals with mp 209–210°C (35 mg), which were identical to a sample of phyllalbine.

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