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ASIMILOBINE AND LIRINIDINE, SEROTONERGIC RECEPTOR ANTAGONISTS, FROM *NELUMBO NUCIFERA*

NOBORU SHOJI,* AKEMI UMEYAMA, NOBUAKI SAITO, AKIO IUCHI, TSUNEMATSU TAKEMOTO

Department of Pharmacy, Tokushima-Bunri University, Tokushima-shi, Tokushima 770, Japan

AKIKO KAJIWARA, and YASUSHI OHIZUMI

Mitsubishi-Kasei Institute of Life Sciences, Machida-shi, Tokyo 194, Japan

Various parts of *Nelumbo nucifera* Gaertner (Nymphaeaceae) have been employed medicinally for a variety of indications in Oriental countries (1). Previous phytochemically-directed studies on the species have yielded numerous alkaloids (2-9). As part of our bioassay-directed studies on medicinal plants, we have isolated two serotonin antagonistic alkaloids from leaves of *N. nucifera*. This is the first report of the presence of asimilobine and lirinidine in *N. nucifera*. Both alkaloids inhibited the contraction of rabbit isolated aorta induced by serotonin (10^{-6}M). The pA_2 values of asimilobine and lirinidine are 5.78 and 7.36, respectively. Detailed pharmacological properties will be reported elsewhere.

EXPERIMENTAL

PLANT MATERIAL.—The dried leaves of *N. nucifera* were purchased from Nakaikoshindo, Ltd., Kobe, Japan, and a herbarium specimen of the plant material is being preserved in this laboratory.

EXTRACTION AND ISOLATION.—The leaves (5 kg) were exhaustively extracted with MeOH at room temperature. The concentrated extract was partitioned between H_2O and EtOAc. The aqueous layer was then extracted with *n*-BuOH. The *n*-BuOH extract was concentrated and the residue (404 g) adsorbed onto celite (600 g). After drying the resulting powder, the material was chromatographed over a Si gel (1.5 kg) column packed in $CHCl_3$, eluted with $CHCl_3$/MeOH mixtures of increasing polarity, and fractionated successively. Alkaloids were eluted with $CHCl_3$-MeOH (9:1). The crude alkaloid mixture was repeatedly subjected to column chromatography over Sephadex LH-20 with MeOH as the solvent and Si gel with NH_4OH-saturated $CHCl_3$ to afford asimilobine (75 mg) and lirinidine (110 mg), along with eight known alkaloids already isolated from the same species (nuciferine, nornuciferine, *N*-methylasimilobine, anonaine, roemerine, armepavine, *N*-norarmepavine, and liriodenine).

IDENTIFICATION DATA.—Each of the alkaloids was homogenous on tlc and spectroscopically pure but failed to crystallize. Data to identify asimilobine and lirindinine included $[\alpha]_D$, eims, uv, ir, ^1H nmr, and ^{13}C nmr. The nmr assignments were made on the basis of reported data of analogous compounds (10), together with ^1H-^1H and ^1H-^{13}C 2D correlation spectra. Their physical properties are in agreement with those published in the literature (10). This data is available upon request to the major author.

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FLAVONOL AND COUMARIN GLYCOSIDES FROM *ARTEMISIA INCANESCENS*

J. ALBERTO MARCO,* OSCAR BARBERÁ, and J. SÁNCHEZ-PARAREDA

Departamento de Química Orgánica, Facultad Químicas, Burjasot, Valencia, Spain

In the course of our research on the chemotaxonomy of the genus *Artemisia* (Compositae), we previously reported (1) on the isolation of several 3-methoxyflavones and coumarins from the ether-soluble portion of a MeOH extract of *Artemisia incanescens* Jordan [syn.=*A. alba* Turra, *A. camphorata* Vill., *A. lobelii* All., and *A. suavis* Jordan (2)]. We now report the results of our studies on the more polar fraction of the MeOH extract, which enabled the isolation of four flavonol aglycones, six flavonol glycosides, and two coumarin glycosides. Furthermore, we report the results of our investigation on a root extract, which yielded coniferyl alcohol and the coumarins scopoletin and isofraxidin. Sesquiterpene lactones and coumarin-sesquiterpene ethers (3) were not found.

Within the genus *Artemisia* flavonol derivatives appear to be specially abundant in the sect. *Abrotanum*, whereas the species of the sect. *Absinthium* form predominantly flavones and only a few classes of flavonols (4). The rich variety of flavonols we have isolated from *A. incanescens* (1) would perhaps support its inclusion into the sect. *Abrotanum* rather than *Absinthium*, as proposed by Greger (3) for the synonymous *A. alba*.

PLANT MATERIAL, EXTRACTION, AND ISOLATION.—The plant material and methods have been described previously (1). The EtOAc extract (1) was concentrated to dryness (11 g) and chromatographed on Polyamide MN SC6 (500 g). Elution with H_2O to MeOH gave, after inspection by tlc, two main fractions A (4.3 g) and B (4.1 g). Fraction A was rechromatographed on polyamide (elution with toluene-MeOH-MeCOEt, 3:1:1). This gave successively isorhamnetin (4 mg), 6-methoxykaempferol (3 mg), kaempferol (15 mg), quercetin (20 mg), kaempferol 3-glucoside (13 mg), isorhamnetin 3-glucoside (5 mg), a ca. 1:1 mixture of quercetin 3-glucoside and 3-galactoside (90 mg), kaempferol 3-rutinoside (27 mg), and quercetin 3-rutinoside (78 mg). The crude products were percolated through Sephadex LH-20 (elution with MeOH) and crystallized from MeOH/H_2O mixtures. Fraction B was rechromatographed on Si gel (elution with $CHCl_3$-MeOH, 4:1). In this way scopoletin 7-glucoside (105 mg) and esculetin 6-glucoside (15 mg) were successively eluted. ^{13}C nmr of scopoletin-7-glucoside (DMSO-d_6, 50.32 MHz, 27°): δ 160.58 (C-2), 149.91 (C-7), 148.93 (C-9), 146.02 (C-6), 144.25 (C-4), 113.31 (C-3), 112.30 (C-10), 109.70 (C-5), 103.04 (C-8), 99.65 (C-1′), 77.15, 76.77 (C-3′, C-5′), 73.11 (C-2′), 69.66 (C-4′), 60.71 (C-6′), 56.06 (OMe). For numbering, see Sankar *et al.* (5).