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ISOLATION AND BIOACTIVITY OF 2-AMINOQUINOLINE FROM *LEUCOPAXILLUS ALBISSIMUS*[1]

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Leucopaxillus albissimus var. *paradoxus* form *albiformis* (Murr.) Sing. & Sm. (Agaricaceae) is a medium to large, white-spored woodland mushroom occurring on the west coast of North America. Other varieties of the species occur elsewhere.

Unlike those of most agarics, carpophores of *L. albissimus* are remarkably resistant to bacterial decay and persist in the environment for long periods of time. It has been speculated that this is at least in part due to the presence of antibiotic substances (1). Because tryptanthrin, an alkaloid with antibacterial properties (2), has been isolated from *Leucopaxillus cerealis* var. *piceina* (3), an investigation of the constituents of *L. albissimus* var. *paradoxus* form *albiformis* seemed to be worthwhile.

Tlc examination of extracts of the mushroom revealed that a compound with a bright blue fluorescence under uv light was present. This compound, which occurred in the tested specimens at the impressive concentration of 2 g/kg fresh wt, was identified as 2-aminoquinoline on the basis of ^{1}H-nmr, ^{13}C-nmr (4), and mass spectra as well as by comparison with an authentic sample.

Although synthetic 2-aminoquinoline has been known since the last century (5), it has heretofore not been reported to occur in nature. This compound possesses an interesting spectrum of biological properties, which include antibacterial (6), protease inhibitory (7), mutagenic (8), and antitumor (9) activity. In our own investigation, 2-aminoquinoline inhibited the growth of the soil microorganisms *Cytophaga johnsonae*, *Streptomyces galilaeus*, and *Penicillium inflatum*. In addition, using the nematode *Nippostrongylus braziliensis*, we were able to demonstrate that 2-aminoquinoline possesses anthelmintic activity.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^{1}H- and ^{13}C-nmr spectra were recorded with a Bruker WM-300 spectrometer at 300 MHz and 75.5 MHz, respectively, with TMS as an internal standard. Mass spectra were obtained with a Finnigan MAT-1125 instrument. Analytical tlc was carried out with Analtech Si gel GF plates.

COLLECTION AND ISOLATION PROCEDURES.—The mushrooms were collected in the Santa Cruz mountains and were identified by David Arora and Bob Sellers of the Fungus Federation of Santa Cruz. A voucher specimen has been deposited in the mycological herbarium of the New York Botanical Garden.

Fresh carpophores of *L. albissimus* var. *paradoxus* form *albiformis* (750 g) were homogenized in a blender with MeOH (2.5 liters) and left at room temperature for 24 h. The slurry was filtered, and the filter cake was washed with MeOH. The filtrate was evaporated to dryness to give 43.4 g of a syrup. An aliquot of this material was partitioned between hexane and 70% aqueous MeOH. Tlc analysis [CH_2Cl_2-MeOH (9:1)] revealed the presence of a bright blue fluorescent compound (R_f 0.4, short wave uv) in both phases. This material was extractable from the hexane layer with 1 N HCl. Accordingly, the total crude extract was distributed between CH_2Cl_2 and 1 N HCl, and the aqueous phase was separated, made basic with K_2CO_3, and extracted with CH_2Cl_2. Evaporation of the dried (K_2CO_3) extract left 1.5 g of crude crystalline 2-aminoquinoline. A small sample was recrystallized from toluene, mp 128–130° [lit. (10) mp 129–130°]; ^{1}H nmr (300 MHz, $CDCl_3$) δ 4.87 (s, NH_2), 6.72 (d, J = 8.8 Hz, H-3), 7.26 (ddd, $J_{5,6}$ = 6.2 Hz, $J_{6,7}$ = 6.9 Hz, $J_{6,8}$ = 1.2 Hz, H-6), 7.55 (ddd, $J_{6,7}$ = 6.9 Hz, $J_{7,8}$ = 7.9 Hz, $J_{5,7}$ = 1.5 Hz, H-7), 7.64 (d, J = 6.2 Hz, H-5), 7.66 (d, J = 7.9 Hz, H-8), 7.87 (d, J = 8.8 Hz, H-4) ppm; ^{13}C nmr ($CDCl_3$) δ 122.6 (C-3), 122.8 (C-6), 123.6 (C-10), 125.9 (C-8), 127.5 (C-5), 129.7 (C-7), 138.1 (C-4),

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147.7 (C-9), 157.2 (C-2) ppm; ms *m/z* $[M]^+$ 144. *Anal.* calcd for $C_9H_8N_2$: C 74.97, H 5.59, N 19.43; found C 75.30, H 5.77, N 19.07.

BIOASSAY.—2-Aminoquinoline was tested at 50 μg/ml against the fourth larval stage of the nematode *N. braziliensis* as previously described (11), resulting in 50% reduction of motility, 74% reduction of viability, and 52% reduction of cast formation (ability to molt to the adult stage). It should be noted that this compound occurs in the mushroom at a concentration 40 times higher than that used for this assay.

The effect of the compound on various soil microorganisms was evaluated in a disk assay. Disks weighing 40 mg each and containing either 100 μg of 2-aminoquinoline in vehicle (H_2O with 1% EtOH) or vehicle alone were applied to agar plates streaked with each microorganism. Zones of inhibition were measured within 1 to 5 days of incubation, at which time good growth was observed on the vehicle control plates. Of the 13 microorganisms tested, *C. johnsonae* (ATCC No. 29589) was strongly inhibited (zone size 16 mm), and *S. galilaeus* (ATCC No. 14969) and *P. inflatum* (ATCC No. 48995) were slightly inhibited (zone size 6 mm). Of these three organisms, the antibiotic agent amphotericin B (100 μg/disk) inhibited only *P. inflatum*.

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