Cactus Alkaloids. XIX. Crystallization of Mescaline HCl and 3-Methoxytyramine HCl from *Trichocereus pachanoi*

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The large columnar cactus, *Trichocereus pachanoi* Britton and Rose, has been used for centuries in South America as the basis of a hallucinogenic drink (1, 2). This species is known in various regions as aguacolla, giganton, huachuma, or San Pedro and is indigenous to Ecuador and Peru where it is widely cultivated as an ornamental and hedge plant (3). In the United States, the plant is currently being promoted as a "natural and legal" psychedelic, and it is reportedly readily available through certain domestic cactus dealers (4), although some dealers have voluntarily restricted their sales.[1]

In 1960, mescaline was discovered by Turner and Heyman as the plant's major alkaloid, but these workers incorrectly identified the cactus as *Opuntia cylindrica* (5). Poisson is generally credited with the first report of the isolation of mescaline from authentic *T. pachanoi* (6, 7). More recently, Agurell and coworkers have combined gas-liquid chromatography with mass spectrometry (glc-ms) to identify in the plant, in addition to mescaline, traces of tyramine, hordenine, 3-methoxytyramine, 3,4-dimethoxy-β-phenethylamine, 3,4-dimethoxy-4-hydroxy-β-phenethylamine, 3,5-dimethoxy-4-hydroxy-β-phenethylamine, and anhalonidine (7, 8). Biosynthetic studies by Lundström *et al.* have examined the formation of mescaline and 3,4-dimethoxy-β-phenethylamine in the species and have resulted in the detection of small amounts of the additional alkaloid, anhalinine (9). A total of over 25 species of *Trichocereus* have revealed the presence of alkaloids, and many of these additional species also contain mescaline (7–13).

[1]Private communication. C. Glass. 1972.

The present reinvestigation of *T. pachanoi* was initiated to ascertain if the mescaline content of plants available in the United States is sufficent to make the species a serious item of drug abuse. In addition, the crystallization of the trace alkaloids was attempted to confirm their presence since their previous identification had been based only on chromatographic and spectral data.

By utilizing our usual procedures for isolating cactus alkaloids, the equivalent of 0.331% of mescaline base was isolated from freeze-dried plant material. This compares favorably with 0.357% of mescaline base obtained by Turner and Heyman (5). The concentration of mescaline in dried peyote, *Lophophora williamsii* (Lem.) Coult., is variable up to 6% but rarely exceeds 1% in the dried whole plant (13–15). Consequently, the concentration of mescaline in *T. pachanoi* approaches that of peyote, and this finding confirms claims in the lay press regarding the equivalence of doses of peyote and San Pedro (4).

Utilizing preparative thin-layer chromatography (tlc), we were able to isolate and crystallize the major phenolic alkaloid, 3-methoxytyramine HCl. By mp, mmp, and ir spectral comparisons, the previous identification (by glc-ms and ir) of this compound in the plant was confirmed (7). This is apparently the first report of the crystallization of 3-methoxytyramine from the plant kingdom. Although it has been previously found in the urine of patients with various brain disorders and cancers of the nervous system (16, 17), its psychotropic effects are unknown. The small concentration of 3-methoxytyramine (ca. 0.01%) found in the

plant is likely insufficient to cause any effects upon ingestion of preparations made from the plant material.

EXPERIMENTAL[2]

PLANT MATERIAL.—Living sections of *T. pachanoi*, conforming to published descriptions of the plant (3), were purchased, and a reference specimen is being maintained in the Department's greenhouse. The fresh cacti were sliced, frozen, freeze-dried, and reduced to a coarse powder in the Fitzpatrick mill.

ISOLATION OF ALKALOID FRACTIONS.—A 255 g quantity of the dried plant material was defatted, basified, and extracted by percolation with chloroform (18). The viscous syrup remaining after concentration of the 4 liters of percolate was dissolved in 1 N HCl and processed through acid-base partitioning as previously described (19). The resulting alkaloid fraction was dissolved in ethanol and resolved into phenolic and nonphenolic fractions using Amberlite IRA–401 in hydroxide form (20).

ISOLATION OF MESCALINE HCL.—The residue from the nonphenolic alkaloid fraction was dissolved in 0.5 N HCl and again taken through acid-base partitioning (19), and the residue of free base was dissolved in a small amount of absolute ethanol. Addition of 5% (w/w) HCl in absolute ethanol reduced the pH to 2 (moist pH paper). Anhydrous ethyl ether was added to induce crystallization, and after cooling, 963 mg of mescaline HCl was obtained.

The mother liquor from this crystallization was streaked onto five 1 mm-thick preparative tlc plates of $SGPF_{254}$ (19) and developed in ethyl ether–methanol–conc. ammonium hydroxide (17:2:1). Elution of the major band with 5% conc. ammonium hydroxide in absolute ethanol and crystallization of the residue, as described above, yielded 26 mg of additional mescaline HCl. An attempt to crystallize and identify a trace nonphenolic alkaloid, which separated on the preparative plates, was unsuccessful.

Recrystallization of the combined mescaline HCl (989 mg) was carried out with absolute ethanol–ethyl ether (mp 184–185°, mmp 184–185°, reference mp 184–185°). The ir spectra of the isolated and reference mescaline HCl were superimposable.

ISOLATION OF 3-METHOXYTYRAMINE.—Analytical tlc (19) showed that the major alkaloid in the phenolic fraction was 3-methoxytyramine. The phenolic fraction was streaked onto 17 preparative tlc plates and developed in chloroform–acetone–diethylamine (10:5:1). Elution and crystallization of the major band, as described above, resulted in the isolation of 3-methoxytyramine HCl. After one recrystallization, the yield was 26 mg (mp 204–206°, mmp 205–208°, reference mp 210°). The ir spectra of the isolated and reference 3-methoxytyramine HCl were indistinguishable.

[2]Infrared spectra were obtained in KBr pellets with a Beckman IR 33 spectrophotometer. Melting points were determined with a Mel-Temp apparatus and are corrected. Plants of *T. pachanoi* were obtained from Abbey Garden, Reseda, California, and identification was confirmed by Mr. Charles Glass, editor of *Cactus and Succulent Journal*. Reference mescaline HCl was obtained from Sigma Chemical Company and 3-methoxytyramine was obtained from Calbiochem.

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