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 any effects upon ingestion o tions made from the plant

EXPERIMENTAL[2]

PLANT MATERIAL.—Living sect *pachanoi*, conforming to publish tions of the plant (3), were purch reference specimen is being maint Department's greenhouse. The were sliced, frozen, freeze-dried, a to a coarse powder in the Fitzpat

ISOLATION OF ALKALOID FRA 255 g quantity of the dried pla was defatted, basified, and ex percolation with chloroform (18) cous syrup remaining after conc the 4 liters of percolate was disso HCl and processed through acid tioning as previously described resulting alkaloid fraction was c ethanol and resolved into phenol phenolic fractions using Amberlit in hydroxide form (20).

ISOLATION OF MESCALINE HCL. due from the nonphenolic alkal was dissolved in 0.5 N HCl and through acid-base partitioning (1 residue of free base was dissolve amount of absolute ethanol. 5% (w/w) HCl in absolute etha the pH to 2 (moist pH paper). ethyl ether was added to induce tion, and after cooling, 963 mg o HCl was obtained.

The mother liquor from this cry was streaked onto five 1 mm-thick tlc plates of $SGPF_{254}$ (19) and d ethyl ether–methanol–conc. amm droxide (17:2:1). Elution of the with 5% conc. ammonium hy absolute ethanol and crystalliza residue, as described above, yield additional mescaline HCl. An crystallize and identify a trace alkaloid, which separated on the plates, was unsuccessful.

Recrystallization of the com caline HCl (989 mg) was carrie absolute ethanol–ethyl ether (m mmp 184–185°, reference mp The ir spectra of the isolated a mescaline HCl were superimposa

ISOLATION OF 3-METHOXYTYRA alytical tlc (19) showed that the loid in the phenolic fraction w

[2]Infrared spectra were obtained in with a Beckman IR 33 spectrophotome points were determined with a Mel-Te and are corrected. Plants of *T. pa* obtained from Abbey Garden, Reseda, and identification was confirmed by Glass, editor of *Cactus and Succul* Reference mescaline HCl was obtaine Chemical Company and 3-methoxyt obtained from Calbiochem.

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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LITERATURE CITED

1. SCHULTES, R. E. 1970. The plant kingdom and hallucinogens (part III). *U.N. Bull. Narcotics* 22: 25.
2. EMBODEN, W. A., Jr. 1972. *Narcotic plants*. The Macmillan Co., New York. pp. 55–56.
3. BRITTON, N. L. and J. N. ROSE. 1920. *The Cactaceae, vol. 2*. Carnegie Institution, Washington D.C. pp. 134–135.
4. SUPERWEED, M. J. 1970. *Herbal Highs*. Stone Kingdom Syndicate, San Francisco. pp. 5, 16.
5. TURNER, W. J. and J. J. HEYMAN. 1960. The presence of mescaline in *Opuntia cylindrica*. *J. Org. Chem.* 25: 2250.
6. POISSON, M. J. 1960. Presence de mescaline dans une Cactacee peruvienne. *Ann. Pharm. Fr.* 18: 764.
7. AGURELL, S. 1969. Cactaceae alkaloids. I. *Lloydia* 32: 206.
8. AGURELL, S. 1969. Identification of alkaloid intermediates by gas chromatography-mass spectrometry. I. Potential mescaline precursors in *Trichocereus* species. *Lloydia* 32: 40.
9. LUNDSTRÖM, J. 1970. Biosynthesis of mescaline and 3,4-dimethoxyphenethylamine in *Trichocereus pachanoi* Br. and R. *Acta Pharm. Suecica*. 7: 651.
10. LINDGREN, J. E., S. AGURELL, J. LUNDSTRÖM, and U. SVENSSON. 1971. Detection of biochemical intermediates by mass fragmentography: mescaline and tetrahydroisoquinoline precursors. *FEBS Lett.* 13: 21.
11. CORTES, M., J. A. CARBARINO, and B. K. CASSELS. 1972. Isolation of candicine from *Trichocereus chilensis*. *Phytochemistry* 11: 849.
12. RETI, L. and J. A. CASTRILLON. 1951. Cactus alkaloids I. *Trichocereus terscheckii* (Parmentier) Britton and Rose. *J. Amer. Chem. Soc.* 73: 1767.
13. RETI, L. 1950. Cactus alkaloids and some related compounds. *Fortsch. Chem. Org Naturst.* 6: 242.
14. LUNDSTRÖM, J. 1971. Biosynthetic studies on mescaline and related cactus alkaloids. *Acta Pharm. Suecica* 8: 275.
15. MCLAUGHLIN, J. L. and A. G. PAUL. 1967. The cactus alkaloids. II. Biosynthesis of hordenine and mescaline in *Lophophora williamsii*. *Lloydia* 30: 91.
16. PERRY, T. L., S. HANSEN, L. MACDOUGALL, and C. J. SCHWARZ. 1965. Studies of amines in normal and schizophrenic subjects. *Amines Schizophrenia, Pap. Symp., Atlantic City*. 1965: 31; *Chem. Abstr.* 68: 37621.
17. VON STUDNITZ, W. 1968. Urinary excretion of methoxy catechol amines in neuroblastoma. *Scand. J. Clin. Lab. Invest.* 21: 333; *Chem. Abstr.* 70: 1799.

18. NEAL, J. M., P. T. SATO, C. L. JOHNSON, and J. L. MCLAUGHLIN. 1971. Cactus alkaloids. X. Isolation of hordenine and *N*-methyltyramine from *Ariocarpus kotschoubeyanus*. *J. Pharm. Sci.* **60**: 477.
19. WEST, L. G. and J. L. MCLAUGHLIN. 1973. Cactus alkaloids. XVIII. Phenolic β-phenethylamines from *Mammillaria elongata*. *Lloydia* **36**: 346.
20. MCLAUGHLIN, J. L. and A. G. PAUL. 1966. The cactus alkaloids I. Identification of *N*-methylated tyramine derivatives in *Lophophora williamsii*. *Lloydia* **29**: 315.

Cactus Alkaloids. Oth

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Previous reports concer presence of "toxic" alk *Dolichothele* species (1) a botanical connections of th genus with "peyote" (2, prompted phytochemical tions of members of this genu earlier study reported by I and Paul (4, 5) an unusual alkaloid, dolichotheline (*N*-i histamine), was crystalliz extracts of *Dolichothele s* (Dietr.) Br. and R. The bic of this compound was sub investigated (6, 7), and, foll administration of unnatura sors, this species was found t aberrant alkaloids (8). Re closer examination of this s resulted in the isolation o phenethylamine alkaloids: β ylsynephrine, *N*-methyltyra ephrine, and *N*-methylph mine (9). Since *D. sphae* tained a variety of alkaloic felt that a study of the alk tent of other species in t would be worthwhile in our physiologically active cactu

From chromatographic scr five members [*D. longi* (DC.) Br. and R., *D. ube* (Zucc.) Br. and R., *D. m* (Kar.) Craig, *D. baumii* Werd. and F. Buxb., and *D losa* (Boed.) F. Buxb.] suspected member [*Mam saffordii* (Br. and R.) Brav genus it can be concluded genus *Dolichothele* is rich loids. *D. longimamma uberiformis* were found to large number of unusual co that were unidentified when via tlc with 44 reference cac loids. *D. melaleuca* and *D.*