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Alkaloids and Ethnobotany of Mexican Peyote Cacti and Related Species[1]

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Some Mexican cacti of the genera Ariocarpus, Mammillaria, Obregonia, Pelecyphora, Solisia *and* Turbinicarpus *have been studied with respect to their alkaloids and ethnobotany. Seven previously known cactus alkaloids were identified. N,N-Dimethyl-4-hydroxy-3-methoxy-phenethylamine was found to occur in* Ariocarpus agavoides. *In* Pelecyphora aselliformis *N,N-dimethyl-3-hydroxy-4,5-dimethoxy-phenethylamine was identified as the major alkaloid. The possible relationship between the vernacular names of these plants and their alkaloid content is discussed.*

In spite of the common occurrence of alkaloids in cacti (1), many alkaloid studies have so far centered on a single plant, the Mexican "peyote," *Lophophora williamsii*. The use of this plant as a psychoactive drug can be attributed to the hallucinogenic alkaloid mescaline, the biosynthesis of which has been extensively studied (cf. 27). Mescaline is also the main alkaloid of the Peruvian cactus "San Pedro," *Trichocereus pachanoi*, which is an ingredient of the hallucinogenic drink "cimora." In a recent screening for cactus alkaloids, several other *Trichocereus* species were found to contain mescaline (3).

Following our earlier studies of hallucinogenic cacti, we now report on the alkaloids and ethnobotany of some Mexican cacti, which for various reasons are considered or suggested to be psychoactive.

Experimental

Plant material. The cacti used in this investigation were collected in Mexico by the authors or obtained from commercial sources. *Ariocarpus agavoides* (Castañeda) E. F. Anderson was collected at Tula, Tamaulipas, *Obregonia denegrii* Frič in the valley of Jaumave, Tamaulipas, and *Pelecyphora aselliformis* Ehrenberg north of San Luis Potosí. *Turbinicarpus pseudomacrochele* (Backeberg) F. Buxb. & Backbg. was found not far from Bernal, Querétaro, and *Solisia pectinata* Britton & Rose was collected at Tecamachalco, Puebla. All plants were collected during 1971 and identified by Dr. Hernando Sánchez-Mejorada, Departamento de Botánica, Instituto de Biología, Universidad Nacional Autónoma de México, Mexico City. *Mammillaria heyderi* Muehl. and *Pelecyphora pseudopectinata* Backeberg were purchased from K. Uhlig, Rommelshausen, DBR. These plants were also obtained from M. Schleipfer, Augsburg, DBR, and checked to confirm with the macromorphological descriptions given by Boke (8), and Anderson & Boke (7). The alkaloid extracts of plants from the above-mentioned two sources were also compared by thin-layer and gas chromatography and displayed no significant differences. Reference cacti have been placed in our greenhouse.

Isolation and identification of alkaloids. Isolation and separation methods for cactus alkaloids have been described earlier (1, 3). The alkaloids were identified by the basic technique outlined by Agurell (1). A preliminary identification of the naturally occurring compounds was achieved by comparison with reference materials, using thin-layer chromatography (tlc) and gas chromatography (glc). For tlc silica gel G plates were chromatographed with chloroform-ethanol-diethylamine (85:5:10) or chloroform-

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[1] Cactaceae Alkaloids XVII. Part XV, Rev. Latinoamer. Quím. 2: 21 (1971). Part XVI, Cact. Suc. Mex. 16: 51 (1971).

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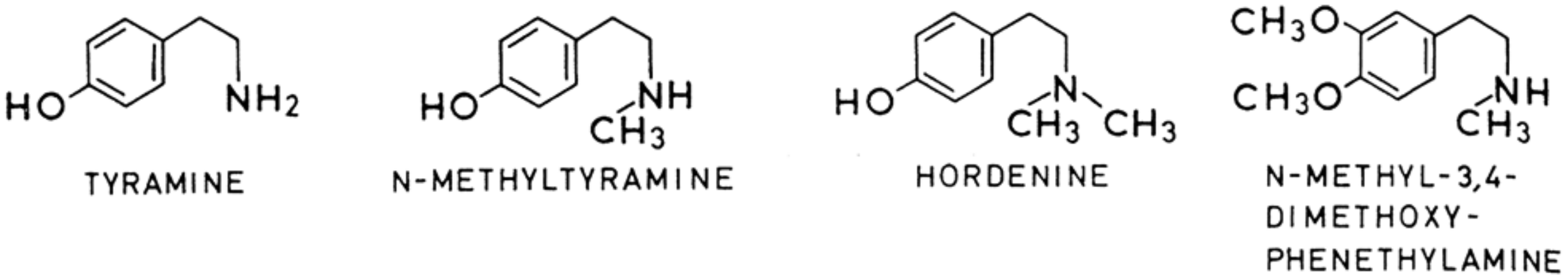

Fig. 1. Alkaloids identified in this study.

ethanol-conc. ammonia (85:15:0,4) and sprayed with a iodoplatinate solution to locate alkaloids. For phenolic alkaloids, *o*-dianisidine spray and Gibbs' reagent (0,1% 2,6-dichloroquinone chlorimide in ethanol followed by 10% sodium carbonate in water) were found to be more specific. Gas chromatography was carried out using a Varian model 204 Aerograph (flame ionization detector) and 5% SE-30 and 5% XE-60 columns (100/120 mesh Gas Chrom P).

The preliminary data were verified by comparison with reference compounds using gas chromatography — mass spectrometry (glc-ms) (LKB 9000 instrument), or IR spectrophotometry (Perkin-Elmer 237 IR spectrophotometer). In some cases, the alkaloids were also identified by additional tlc in other systems [e.g. chloroform-cyclohexane-diethylamine (6:3:1) or chloroform-*n*-butanol-conc. ammonia (50:50:2,5)] and by combination of preparative tlc and gas chromatography. Tyramine could be further identified as the main alkaloid of *Obregonia denegrii* by a simple "peak-shift" technique (28). The extract was dissolved in acetone, thus forming the Schiff's base of any primary amine(s), and the retention time of the new major peak was the same as that of reference tyramine dissolved in acetone.

Identification of N,N-dimethyl-4-hydroxy-3-methoxy-phenethylamine. Gas chromatographic data indicated that a minor peak in the phenolic alkaloid fraction of *Ariocarpus agavoides* could be N,N-dimethyl-4-hydroxy-3-methoxyphenethylamine or the isomeric N,N-dimethyl-3-hydroxy-4-methoxyphenethylamine. The mass spectrum supported this preliminary identification, but did not clearly distinguish between the two compounds. Reference N,N-dimethyl-4-hydroxy-3-methoxy-phenethylamine and N,N-dimethyl-3-hydroxy-4-methoxyphenethylamine, prepared as described by Lundström (26, 27), were however well separated by tlc on silica gel G plates with chloroform-ethanol-diethylamine (85:5:10) as solvent (*cf.* 3).

The phenolic alkaloids of *A. agavoides* and the two isomeric compounds were then chromatographed in this system and sprayed with Gibbs' reagent. Reference N,N-dimethyl-4-hydroxy-3-methoxy-phenethylamine (R_F 0.55) and the minor phenolic alkaloid from *A. agavoides* (R_F 0.55) showed a whitish color, while the isomeric N N-dimethyl-3-hydroxy-4-methoxyphenethylamine (R_F 0.44) developed a blue color.

The identification was also confirmed by "on column methylation" (3). When the total phenolic alkaloid fraction was treated with trimethylanilinium hydrox-

ide, a new peak, having the retention time of N,N-dimethyl-3,4-dimethoxyphenethylamine, appeared in the gas chromatogram.

Results and Discussion

One approach in cactus alkaloid studies is the search for additional "peyote" cacti, assuming that cacti so called may be similar to *Lophophora williamsii* in psychoactive and/or alkaloidal properties. The chemical interest in supposedly hallucinogenic cacti has, however, not been equalled by ethnobotanical research on these little known plants, although Schultes (41, 42) has repeatedly suggested that they should be studied by ethnobotanists and chemists, preferably working together (*cf.* 16).

In this paper, we present both ethnobotanical and chemical data for some Mexican cacti, either called "peyote," or related to a known "peyote," or figuring in the same magic context as "peyote." The cacti studied and the alkaloids identified in this study are listed in Table I.

ARIOCARPUS AGAVOIDES (Castañeda) E. F. Anderson

Ariocarpus is according to Anderson (5) a cactus genus of only six species, some of which are stated in the literature to have been called "peyote" (35, 41). *Ariocarpus fissuratus* has been utilized by the Tarahumara Indians as a narcotic and magic plant (25), and recently *Ariocarpus retusus* was described as a "false peyote" of the Huicholes, having undesirable psychological effects (19). The latter species is also used medicinally for fevers (10). A common feature of the *Ariocarpus* species is the occurrence of extensive mucilage-containing structures (5), and this mucilage is used as a glue (11).

Ariocarpus agavoides is one of the least known species of this genus, described for the first time in 1941 and only known from the type locality near Tula, Tamaulipas (5). At Tula we found that the plants are commonly called "magueyitos," *i.e.* "little agaves."

Because of the relationship of this cactus to established "peyote" cacti we found it of interest to study the alkaloids. Earlier N-methyl-3,4-dimethoxyphenethylamine, hordenine, N-methyl-tyramine and N-methyl-4-methoxyphenethylamine have been identified in various *Ariocarpus* species (31, 43). No alkaloid studies of *Ariocarpus agavoides* have been published, although hordenine seems to have been observed in this plant by paper chromatography (5). This is now verified since the phenolic alkaloid fraction contained hordenine as the major alkaloid. A minor constituent was identified as N,N-dimethyl-4-hydroxy-3-methoxyphenethylamine (see **Experimental**). This alkaloid has earlier been found only in *Lophophora williamsii*, where its occurrence was established using an inverse isotope dilution technique (27).

The non-phenolic fraction contained small amounts of N-methyl-3,4-dimethoxyphenethylamine. This compound was identified for the first time as a natural product in the cactus *Lepidocoryphantha runyonii* (1), and it has also been found in *Echinocereus merkeri* (2), and together with hordenine and N-methyltyramine in other *Ariocarpus* species as well (31, 43).

Besides *Ariocarpus fissuratus*, the Tarahumara Indians of northern Mexico have long used other cacti for their medicinal and psychoactive properties (see 25, 36). The best known species is doubtless *Lophophora williamsii*, but some of these cacti are still unidentified, whereas others seem to have been largely overlooked by botanists and chemists alike.

MAMMILLARIA HEYDERI Muehl.

Mammillaria heyderi is a little discussed species, which has been reported to be used by the Tarahumaras. We first encountered this species in the Tarahumara-English dictionary compiled by the Swedish explorer Ivar Thord-Gray (45). Discussing sorcery and black magic among the Tarahumaras, Thord-Gray reports, that "only the shaman is *umeru-ame* (powerful) enough to locate wizards and witches. To do this he will make medicine from ball-cactus *wichu-ri-ki* (*Mammillaria*

TABLE I

OCCURRENCE OF ALKALOIDS*

Taxon	Presence of Alkaloids†	Amount of Alkaloids‡	Alkaloids
Ariocarpus			
A. agavoides (Castañeda) E. F. Anderson	+	3	Hordenine
		1	N,N-Dimethyl-4-hydroxy--3-methoxyphenethylamine
		tr.	N-Methyl-3,4-dimethoxyphenethylamine
		tr.	Unknowns
Mammillaria			
M. heyderi Muehl.	++	3	N-Methyl-3,4-dimethoxyphenethylamine
		1	Unknown
Obregonia			
O. denegrii Frič	+	3	Tyramine
		1	Hordenine
		tr.	N-Methyltyramine
		tr.	Unknowns

heyderi. Mex. *biznaga*), which is greatly feared for its magical powers. This medicine will clear his vision. It matters not how well the *suku-ru-ame* (wizard, witch) is hidden, the shaman can see him clearly" (45, p. 425).

According to Patoni (in ref. 44), the Mexican name for *Mammillaria heyderi* is "biznaga de chililos," and Ochoterena (34) gives the name "chilito" for the small red fruit, which is edible and used by the Tarahumara Indians (36, 45). Not only is this cactus useful for locating wizards and supplying food, but it is also used as a medicine to cure or relieve headaches (45). "After the spines are removed, the plant is cut up into two or more pieces, roasted for a few minutes, and then part of the stuff is pushed into the ear."

This use of *Mammillaria heyderi* is corroborated by Bennett & Zingg[3], who describe the same manner of roasting the cactus before "the soft center is pushed into the ear in case of ear-ache or deafness" (24).

Thord-Gray also reports that *wichu-ri-ki* is an important medicine that will prolong life, "make the foot light and increase the speed of a runner in a race" (45).

The Tarahumara name for the cactus listed by Bennett & Zingg is *witculíki*. *Witculíki* and *wichu-ri-ki* are possibly related to *wichuwa-ka*, which means "crazy, demented, mad, insane" etc. (45).

Mammillaria heyderi is a latex-containing species and such Mammillarias are popular folk remedies, often sold in drug stalls of Mexican markets (40).

The alkaloid fraction of *Mammillaria heyderi* now tested by us contained one major alkaloid, which was identified through gas chromatographic and mass spectral data as N-methyl-3,4-dimethoxyphenethylamine. Earlier the very closely

[3] In "The Tarahumara, An Indian Tribe of Northern Mexico." Chicago, 1935. Cited from La Barre (24).

TABLE I (*Continued*)

Taxon	Presence of Alkaloids†	Amount of Alkaloids‡	Alkaloids
Pelecyphora			
P. aselliformis Ehrenberg	++	2	Anhalidine
		2	Hordenine
		2	N,N-Dimethyl-3-hydroxy--4,5-dimethoxyphenethyl-amine
		tr.	Pellotine
		tr.	Unknowns§
P. pseudopectinata Backeberg	+++	3	Hordenine
		tr.	Unknowns
Solisia			
S. pectinata Britton & Rose	++	3	Hordenine
		2	N-Methyltyramine
		1	Unknowns
Turbinicarpus			
T. pseudomacrochele (Backeberg) F. Buxb. & Backbg.	+	4	Hordenine

* Quarternary alkaloids or neutral compounds not included.

†Presence of alkaloids: + + + = over 50 mg/100 g; + + = 10-50 mg/100 g; + = 1-10 mg/100 g; tr. = trace, less than 1 mg/100 g fresh plant.

‡Per cent of alkaloid fraction: 4 = only alkaloid present; 3 = over 50%; 2 = 10-50%; 1 = 1-10%; tr. = trace, less than 1% of alkaloid fraction.

§Some alkaloids of *P. aselliformis* have been identified by Neal et al. (33), and are discussed in the text.

related species *Mammillaria meiacantha* was found to give a positive Mayer's test for alkaloids, and gas chromatography indicated one principal compound (13).

In his study of *Mammillaria heyderi*, Boke also discusses *M. applanata*, *M. hemisphaerica* and *M. meiacantha* (8). He concludes that "no evidence was found that the species could readily be segregated. All appear to be referable to *M. heyderi* in this broad sense." He adds: "It is therefore reasonable to treat these mammillarias as a unit regardless of what revisions taxonomists may make in the future."

OBREGONIA DENEGRII Frič

Obregonia denegrii (Fig. 2) has been repeatedly mentioned in reviews of "peyote" cacti (41, *cf.* 32). These reports can be traced to an article by Blas Pablo Reko (39), published in 1934. The group of plants called "peyote" according to Reko includes "fast alle stachellosen Cacteen (Lophophora, Pelecyphora, Astrophytum, Roseocactus, Obregonia, Aztecum)." No further data are given in this paper, but in an earlier survey Reko lists the Mexican plants known to contain alkaloids or glucosides, or *suspected* of containing such substances (38). In this list, *Obregonia denegrii* is included with the only notation that it is similar ("es

Photos by Jan G. Bruhn.

Fig. 2. *Obregonia denegrii* in the valley of Jaumave, Tamaulipas. Length of ruler 15 cm.

semejante") to various *Roseocactus* (*Ariocarpus*) species, which have been called "peyote." No common name is however given for *Obregonia denegrii*, so it seems that Reko only suggested *Obregonia* to be a "peyote," because of its resemblance to the *Ariocarpus* species. *Obregonia* and *Ariocarpus* are similar in many characters, but Anderson, who has performed field studies of *Obregonia* in Mexico, states that no common names are known for this plant (6).

When we collected *Obregonia denegrii* in the valley of Jaumave, our native guide called the plant "obregona," a name that he had apparently learnt from cactus collectors. He also explained very clearly that "peyote" is a different plant and that the "obregonas" are not employed in folk medicine. They are however collected on a large scale by cactus dealers and are now in danger of becoming extinct.

Anderson (6) and Domínguez *et al.* (18) found alkaloids to be present in *Obregonia denegrii*, but no attempt was made to isolate and characterize them. The latter workers also tentatively identified β-sitosterol in this plant. The first structural work on the alkaloids was recently published by Neal *et al.* (32), who isolated tyramine, N-methyltyramine and hordenine. Working independently on material collected in Jaumave, we have now identified the same alkaloids. Tyramine was found to be the main alkaloid. This compound has earlier been crystallized from *Cereus forbesii* (1), and is found in several cacti. These phenolic phenethylamines in the cactus might account for the antibiotic activity of extracts of *Obregonia denegrii* (30, cf. 37).

Pelecyphora aselliformis Ehrenberg

Pelecyphora aselliformis (Fig. 3) is a relatively well known Mexican "peyote," reported by several botanists as a medicinal plant (10, 12, 17, 40). It has been variously called "peyote," "peote," "peyotillo," "peotillo" (12), and also "piote" and "peyote meco" (29). In the drug markets of San Luís Potosí it has been sold as a remedy for fevers (40), and when we collected the plant some miles north of this city, a native informant told us that this "peyote" is used for rheumatic pains. Interestingly, the same use is reported for two other peyote cacti, *Lophophora williamsii* and *Ariocarpus fissuratus* (36).

In his peyote studies, Rouhier received in Paris a mixture of *Ariocarpus fissuratus* and *Pelecyphora aselliformis* "comme

Fig. 3. *Pelecyphora aselliformis*, "peyote," in the collection locality north of San Luís Potosí.

étant des véritables Peyotes" (23, p. 41, footnote 4). According to Hobschette (23), pulverized *Pelecyphora aselliformis* has also been sold in Paris as "poudre de Peyote."

Earlier we have reported on the presence of anhalidine and hordenine in *Pelecyphora aselliformis* (3). During the present work, Neal *et al.* (33) described the isolation and identification of N,N-dimethyl-3-hydroxy-4,5-dimethoxyphenethylamine (3-demethyltrichocereine) and pellotine in this cactus. Continuing our studies of the phenolic alkaloid fraction on plant material collected in San Luis Potosí, we have now verified these findings by comparison with reference materials. In contrast to Neal *et al.* (33), we found that in our cactus sample N,N-dimethyl-3-hydroxy-4,5-dimethoxyphenethylamine, and not hordenine, is the major alkaloid. When the phenolic alkaloid fraction was subjected to preparative tlc, these two alkaloids co-chromatographed, but they were well resolved and identified by glc-ms (Fig. 4).

In the non-phenolic alkaloid fraction Neal et al. (33) have also identified trace amounts of mescaline, N-methylmescaline, 3,4-dimethoxy-phenethylamine and N-methyl-3,4-dimethoxy-phenethylamine. The minor amounts of these alkaloids can, however, as discussed by the authors, not be responsible for any physiological effects of the cactus (33). These compounds may be present also in our extract, but can not be clearly detected because of the relatively larger amounts found of other, as yet unidentified, non-phenolic alkaloids. The hordenine present may, as with *Lophophora williamsii* (37), explain the antibiotic activity found in extracts of *Pelecyphora aselliformis* (30).

The co-occurrence of N,N-dimethyl-3-hydroxy-4,5-dimethoxyphenethylamine, anhalidine and pellotine is biosynthetically reasonable since Lundström showed in biosynthetic experiments (26), that pellotine is formed from N-methyl-3-hydroxy-4,5-dimethoxyphenethylamine. This compound is also a likely progenitor of anhalidine and N,N-dimethyl-3-hydroxy-4,5-dimethoxyphenethylamine. All these alkaloids occur in *Lophophora williamsii*, where the N-monomethylated compound, but not the N,N-dimethyl derivative, is an efficient precursor of pellotine (26).

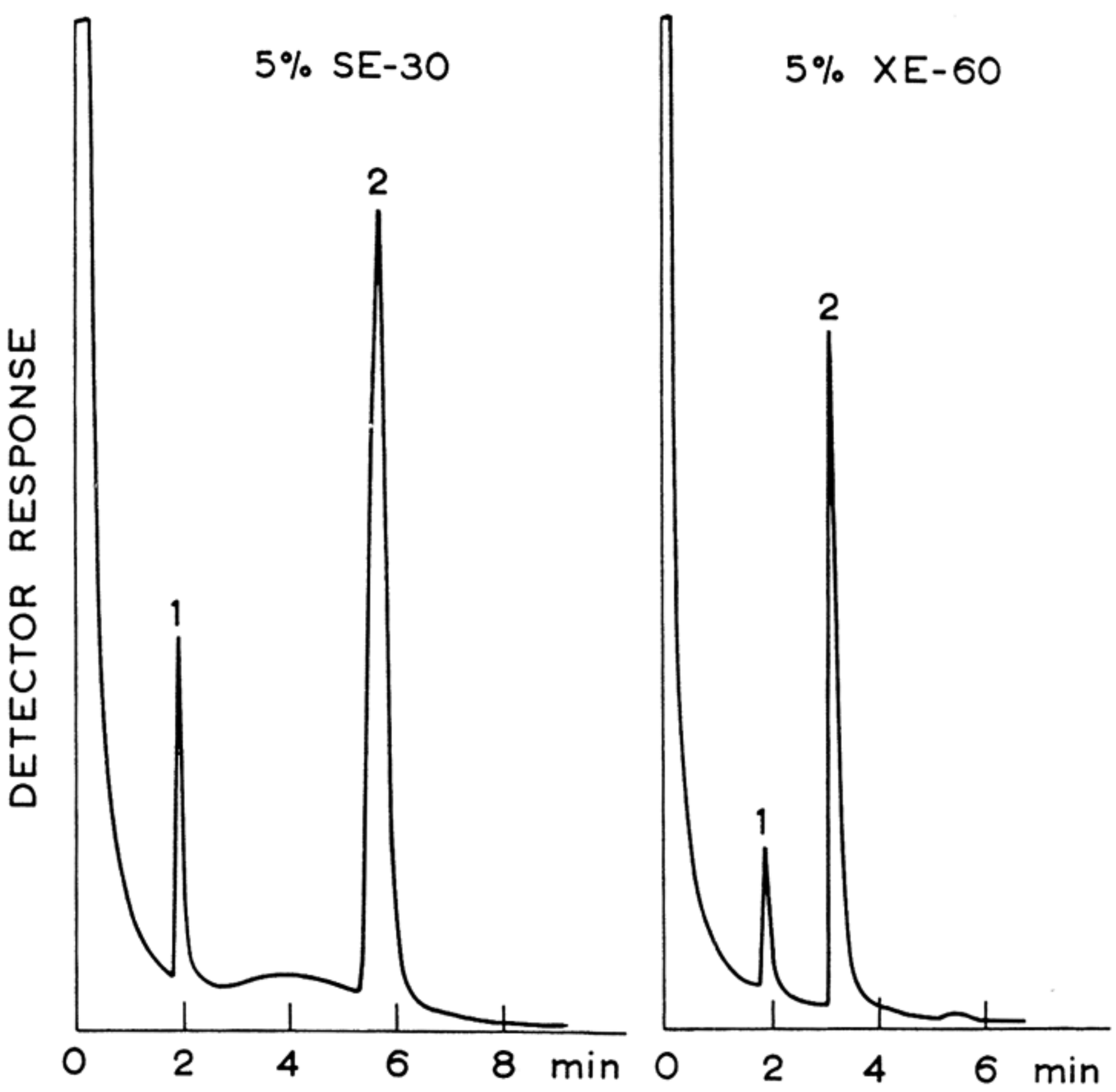

Fig. 4. Gas chromatograms of phenolic alkaloids of *Pelecyphora aselliformis* after preparative tlc in chloroform-ethanol-diethylamine (85:5:10). The fraction corresponding to hordenine (*1*) (above), was found also to contain an unknown compound (*2*), identified through mass spectrum and glc retention times as N,N-dimethyl-3-hydroxy-4,5-dimethoxyphenethylamine. Column temperature: 150° C.

PELECYPHORA PSEUDOPECTINATA Backeberg

In our literature search for cactus hallucinogens (*cf.* 14), we have not encountered *Pelecyphora pseudopectinata*, but correspondence with cactus botanists working in Mexico reveals that this species is called "peyote" by the natives of Tamaulipas[4] . The name seems, however, not to be in general use, nor is the plant very familiar as it was only described in 1935 (7). In a recent botanical study, Anderson & Boke concluded that *Pelecyphora pseudopectinata* is not closely related to *Pelecyphora aselliformis* and tentatively transferred the former to *Thelocactus* (7). A new genus, *Normanbokea*, has also been suggested for *P. pseudopectinata* (*cf.* 20). We have now identified hordenine as the main alkaloid in this cactus. Only traces of other alkaloids could be found.

[4] Letters from Charles Glass, Reseda, California, to Jan Bruhn, 1971 and 1972.

SOLISIA PECTINATA Britton & Rose

Solisia pectinata (Fig. 5) was mentioned as a "peyotillo" in the posthumous work of Diguet, "Les Cactacées Utiles du Mexique," which appeared in 1928 (17). The same year Reko (38) reported that this cactus seems to contain a toxic alkaloid, but he didn't give any reason for this, nor did he list any vernacular name. When we collected *Solisia pectinata* outside Tecamachalco, Puebla, we were told that the local name is "cochinito" ("little pig"). However, a field test for alkaloids was negative (15). When a larger amount of plant material was worked up we were able to identify hordenine and N-methyltyramine.

Fig. 5.. *Solisia pectinata* as it occurs at Tecamachalco, Puebla.

Solisia pectinata was first believed to belong to *Pelecyphora*, and this may have led Diguet to include *Solisia* with *Pelecyphora aselliformis* in his list of "peyotillos" (17). As discussed above, *Pelecyphora aselliformis* is a known peyote or peyotillo cactus and is also used in folk medicine. *Solisia* seems to have no recorded history of any aboriginal use, but the species is much liked by cactus collectors and as early as 1937, Bravo reported that it was scarce, due to overcollecting (10). Recent botanical research shows that *Solisia* and *Pelecyphora* are not closely related (7, 9).

TURBINICARPUS PSEUDOMACROCHELE
(Backeberg) F. Buxb. & Backbg.

In Mexico we were informed that *Turbinicarpus pseudomacrochele* might be of interest, since it had been found in a place where native informants said there were "peyotillos"[5]. *Turbinicarpus pseudomacrochele* occurs on limestone hills outside the town of Bernal in the state of Querétaro. Two known peyote cacti, *Lophophora diffusa* and *Strombocactus disciformis*, are also found in Querétaro (21). The possibility that *Turbinicarpus pseudomacrochele* is called peyote or peyotillo is strengthened by Altamirano's statement (4), that there are other peyote cacti in this region beside *Lophophora diffusa*: "Hay también unos *Peyotes falsos* que designan con el nombre de Peyote de imitación." On our short visit to Bernal we were unable to verify this name for *Turbinicarpus pseudomacrochele*, so only further field studies can tell whether this cactus is a "true" peyote. From a botanical point of view it is interesting to note that *Turbinicarpus pseudomacrochele* was first described as a species of *Strombocactus* (10). Hordenine was the only alkaloid detectable in this species.

Conclusions

When the available data are brought together, it becomes evident that some of these "peyote" cacti have had no aboriginal use as hallucinogens, or even as medicinal plants. Nor is there any obvious rela-

[5] Private communication, H. Sánchez-Mejorada, 1971.

tionship between the name "peyote" and the alkaloid content. A possible exception is *Pelecyphora aselliformis*, which comes closest to *Lophophora williamsii* of the peyote cacti now studied. Most of its alkaloids are known from *Lophophora*, as are its medicinal uses against fever and rheumatism.

The presence of hordenine and its N-demethylated relatives N-methyltyramine and tyramine in several "peyote" cacti has led to the suggestion (*cf.* 32) that these amines could be responsible for a stimulating effect of the plants. These amines are weakly sympathomimetic (*cf.* 31), but in a self-experiment as early as 1894, Heffter took 100 mg of hordenine (anhaline) orally and experienced no effects at all (22). The amounts of alkaloids in the plants are also very low, but there may of course be other active plant constituents. Most likely, the name "peyote" has been applied to some of these cacti because they outwardly resemble *Lophophora*.

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