Notes

Gas chromatography of peyote alkaloids. A new peyote alkaloid

It is generally accepted that gas chromatographic procedures for the analysis of drugs and biological amines, when applicable, surpass other methods in specificity and sensitivity. Reports dealing with gas chromatographic methods for the separation, identification and estimation of alkaloids are surprisingly not numerous. However, analysis by gas chromatography of alkaloids with molecular weights up to 400 has been studied by several workers (refs. 1–4 and others).

The main objective of the present study was to develop a gas chromatographic method for the separation and identification of the alkaloids of peyote, *Lophophora williamsii* (Lem. ex SD.) Coult. This cactus, sometimes used as a narcotic, contains some 14 known alkaloids of the phenylethylamine and the tetrahydroisoquinoline groups[5,6].

Experimental

All separations were carried out isothermally with a Varian Aerograph Model 202 (thermal conductivity detector) or Model 204 (flame ionization detector) gas chromatograph. Chromosorb W or Gas Chrom P sieved to 80/100 or 100/120 mesh, acid washed and silanized, was used as solid support. Flash heater and detector temperatures were maintained 30–50° above column temperature. Column dimensions: for the Aerograph 202; 6 ft. × 1/4 in. O.D.; for the Aerograph 204, 6 ft. × 1/8 in. O.D. Other conditions are given in Table I. Alkaloids were extracted and fractionated into phenolic

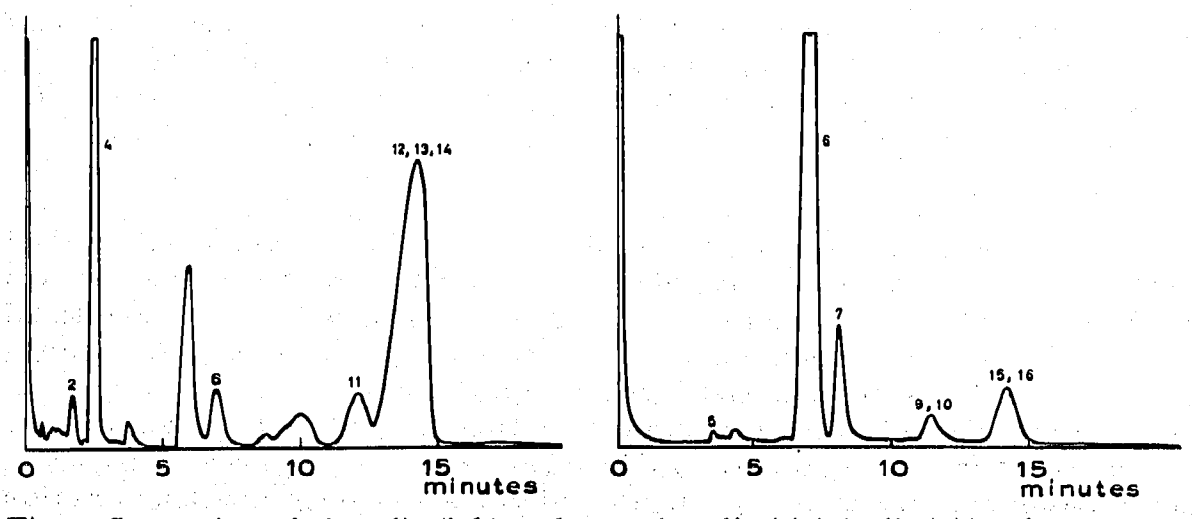

Fig. 1. Separation of phenolic (left) and non-phenolic (right) alkaloids of peyote on a 5% SE-30 column (6 ft. × 1/8 in.), 150°, as described in Table I. Numbers refer to compound numbers in Table I. Compound 5 (3,4-dimethoxyphenylethylamine) has previously not been identified in peyote but was identified in this study by GLC and gas chromatography–mass spectrometry. The peak designated 5 from peyote had a mass spectrum identical with that of reference 3,4-dimethoxyphenylethylamine. Molecular ion at *m/e* 181; other peaks at *m/e* 152, 151, 137, 108, 107, 30 (base peak).

TABLE I

GAS CHROMATOGRAPHIC DATA FOR PEYOTE ALKALOIDS[a] AND RELATED COMPOUNDS

No.	Alkaloid	Mol. wt.	Retention time (min)				
			Aerograph 204 (anal.)			Aerograph 202 (prep.)	
			5% SE-30 Gas Chrom. P, 150°	7% F60-2%Z Gas Chrom. P, 170°	5% XE-60 Chromosorb. W, 150°	5% SE-30 Chromosorb. W, 190°	5% XE-6 Chromoso W, 184°
1	4-Methoxyphenylethylamine[b]	151	1.5	2.1	0.9	1.0	0.7
2+[d]	Tyramine	137	1.8	—[c]	4.6	1.2	3.5
3+	N-Methyltyramine	151	2.2	—	4.4	1.3	3.3
4+	Hordenine = Anhaline	165	2.4	—	3.4	1.4	2.8
5	3,4-Dimethoxyphenylethylamine	181	3.5	5.4	2.8	1.8	2.6
6	Mescaline	211	6.8	11.1	6.6	3.3	5.2
7	N-Methylmescaline	225	8.0	11.3	6.2	3.2	5.0
8	O-Methylanhalidine[b]	237	10.5	11.7	4.8	5.2	4.4
9	Anhalinine	223	11.3	17.5	7.8	5.6	6.8
10	O-Methylanhalonidine	237	11.6	14.5	6.1	5.3	5.5
11+	Anhalidine	223	12.0	—	8.4	5.6	6.9
12+	Anhalamine	209	12.4	—	13.6	5.8	10.5
13+	Anhalonidine	223	13.0	—	10.8	6.1	8.2
14+	Pellotine	237	13.1	—	7.6	6.0	6.5
15	Anhalonine	221	14.2	22.1	9.5	6.8	8.0
16	Lophophorine	235	14.5	18.3	6.7	6.2	6.3
17	Trichocereine[b]	237	8.5	11.7	5.6	4.0	4.0

[a] For formulas, see refs. 5 and 6.
[b] Not identified in peyote.
[c] Used only for non-phenolic compounds.
[d] + signifies phenolic alkaloid.

and non-phenolic alkaloids by Amberlite IRA 400 (OH^-) ion-exchange resin[5]. When properly operated (elution rate 20 ml/h) the resin enriches an alkaloid to at least 98%, in the corresponding fraction. Gas chromatography–mass spectrometry was carried out with an LKB 9000 instrument[7].

Results and discussion

Table I summarizes the gas chromatographic data for columns used for analytical and semi-preparative purposes. Also included in Table I are not only the present known *Lophophora* bases, but also some other compounds. These latter have been identified in other cacti[8] which produce the hallucinogenic alkaloid mescaline, or are compounds which are suspected of being present on biogenetic grounds.

It is evident from Table I that a number of these closely related compounds cannot be clearly identified or separated by GLC alone. However, a previous fractionation of the alkaloid mixture into a phenolic and a non-phenolic alkaloid fraction permits the individual alkaloids to be separated, and identified from the data given in Table I.

In agreement with MASSINGILL AND HODGKINS[3], we found that the SE-30 column, separating primarily on the basis of molecular weight, resolved low molecular weight (> 200) phenylethylamines well, whereas the tetrahydroisoquinolines did not

resolve well on this column, as was also found by others[9] (Fig. 1). KAPADIA AND RAO[9] separated a number of peyote alkaloids on a phenyl substituted methylsiloxane column similar to our SE-30 column and the conclusions drawn by them regarding relations between retention time and structure are also, in general, valid for our SE-30 columns. On the other hand the XE-60 column showed separation properties which made it very useful for the identification of tetrahydroisoquinoline alkaloids (Fig. 2).

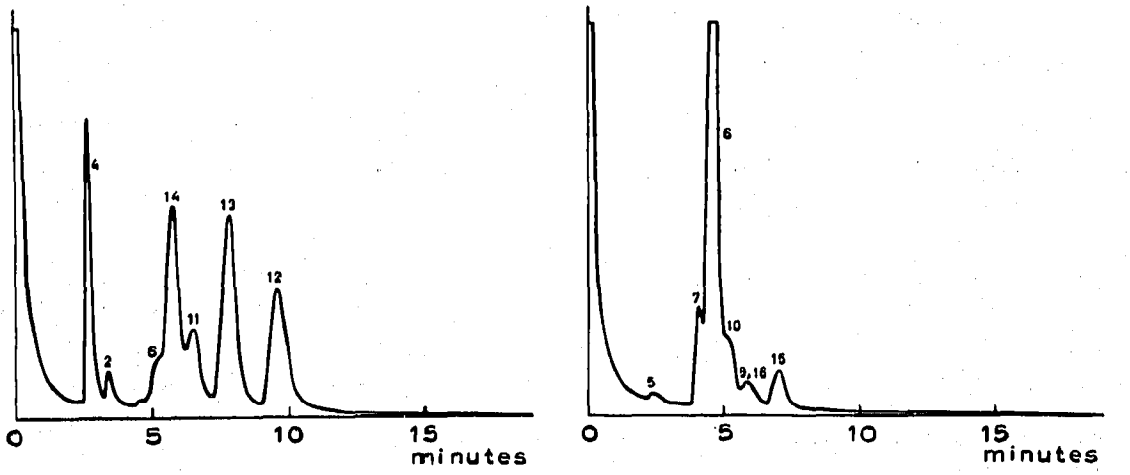

Fig. 2. Separation of phenolic (left) and non-phenolic (right) alkaloids of peyote on a 5% XE-60 column (6 ft. × 1/4 in.), 190°. Other conditions as in Table I.

It may be of interest to note that on the more polar XE-60 column a tertiary amine has shorter retention time than the corresponding N-desmethyl compound (compare compound pairs 4–3, 12–11, 14–13, 16–15, 17–7). In addition the F60/Z column, used by BROOKS AND HORNING[10] for the separation of biological amines, possessed somewhat different separating abilities giving a good resolution of the non-phenolic alkaloids. Gas Chrom P was apparently superior to Chromosorb W as a solid support and generally gave sharp peaks with practically no tailing.

For further identification of a compound, its retention time may be shifted by the formation of simple derivatives using selective reagents. To be of value, this "peak shift technique" must yield derivatives easily and in good yield, and not several products from a single compound. The preparation of the trimethylsilyl ethers[10] of the compounds listed in Table I, in some cases yielded several peaks but the formation[10] of eneamines from primary amines and acetone was found useful. The condensation products of the primary amines in Table I with acetone were found to have close to twice the retention time of the original amine on SE-30.

The present chromatographic procedure was designed to identify (also by the combination of gas chromatography with mass spectrometry) the known alkaloids of peyote and to detect new compounds in peyote and in other cacti. Using this technique (Fig. 1), 3,4-dimethoxyphenylethylamine was detected as a new trace alkaloid in peyote. The separation of peyote alkaloids on an analytical column is shown in Fig. 1. However, the procedure was also designed to permit small scale preparative separation as well as preparative thin-layer chromatography[11] and isolation. Therefore data on the separation of alkaloids on semi-preparative columns are also included

in Table I for comparison. As would be expected the resolution of alkaloid mixtures was superior on the analytical columns.

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