the background mass spectra in temperature programmed gas chromatography—mass spectrometry will be published shortly.

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Notes

Observations on the gas chromatographic behaviour of some amines used in anorectic formulations

Medicinal amines have been analyzed by gas–liquid chromatography in this laboratory without evidence of decomposition, *e.g.* amphetamine[1], the ephedrines[2], lignocaine[3], and 34 others[4]. In contrast, VAN ZWOL[5] recently reported that the gas chromatographic separation and identification of ten sympathomimetic amines, using large amounts of stationary phase on non-KOH coated supports, was difficult owing to amine decomposition. Chromatographic conditions similar to those used by VAN ZWOL were therefore investigated to clarify the discrepancy and the reported decomposition.

Experimental

Perkin-Elmer F 11 gas chromatographs, with hydrogen-flame ionization detectors, were used together with Leeds and Northrup Type G (0–5 mV) and Hitachi 159 (0–2.5 mV) recorders.

Column packing materials and operating conditions are listed in Table I.

Solutions of the ten amines* studied by VAN ZWOL were obtained by extraction of alkaline aqueous solutions of their corresponding salts with freshly distilled AnalaR diethyl ether. Each solution contained approximately 4 μg base per μl (slightly less for phenylpropanolamine because of water favourable partition characteristics). A solution of all ten amines was prepared by mixing 5 ml of each concentrated ethereal solution.

Results and discussion

Chromatography of 1 μl of the mixture of the ten amines on the 22.5 % Carbo-

* Amphetamine, methylamphetamine, isopropylhexedrine, phenylpropanolamine, diethylpropion, phenmetrazine, phendimetrazine, chlorphentermine, methylphenidate and phentermine.

TABLE I

GAS–LIQUID CHROMATOGRAPHY SYSTEMS

Injection port temperatures 200–250°.
Stream splitters (ratio 1:5) were used with systems C and D.
All columns were conditioned at their operating conditions for 24 h and silanized *in situ* with hexamethyldisilazane before use.

System	*Tubing*	*Liquid phase*	*Solid support*	*Length (m)*	*Column temp. (°C)*	*Gas pressures (lbs. in.$^{-2}$)*		
						N_2	H_2	Air
A	Glass 1/4 in. O.D.	22.5% Carbowax 20 M	Diatoport S DMCS treated 80–100 mesh	1	120	20	24	30
B	Glass 1/4 in. O.D.	10% KOH 22.5% Carbowax 20 M	Diatoport S DMCS treated 80–100 mesh	1	90	10	12	15
					150	20	24	30
C	S.S. 1/8 in. O.D.	5% KOH 5% PEG 6000	Chromosorb G A/W DMCS treated 80–100 mesh	3	160	20	20	25
D	S.S. 1/8 in. O.D.	5% KOH 2% Carbowax 20 M	Chromosorb G A/W DMCS treated 80–100 mesh	1	140	15	15	25

wax 20 M column only gave three peaks, corresponding to those of diethylpropion, phenmetrazine, and phendimetrazine. Furthermore, only small peaks were observed for the other amines when 1 μl aliquots of their concentrated solutions were chromatographed, thus supporting VAN ZWOL's results of decomposition of phenylpropanolamine, chlorphentermine, phentermine, and isopropylhexedrine on the column.

In contrast, almost symmetrical peaks were obtained for all ten amines not only on the columns used routinely in this laboratory[1–4] (see Figs. 1 and 2 combined), but also on the 10% KOH–22.5% Carbowax 20M column (*e.g.* see Fig. 3). Thus the support (Diatoport S, DMCS treated, 80–100 mesh), or the stationary phase on

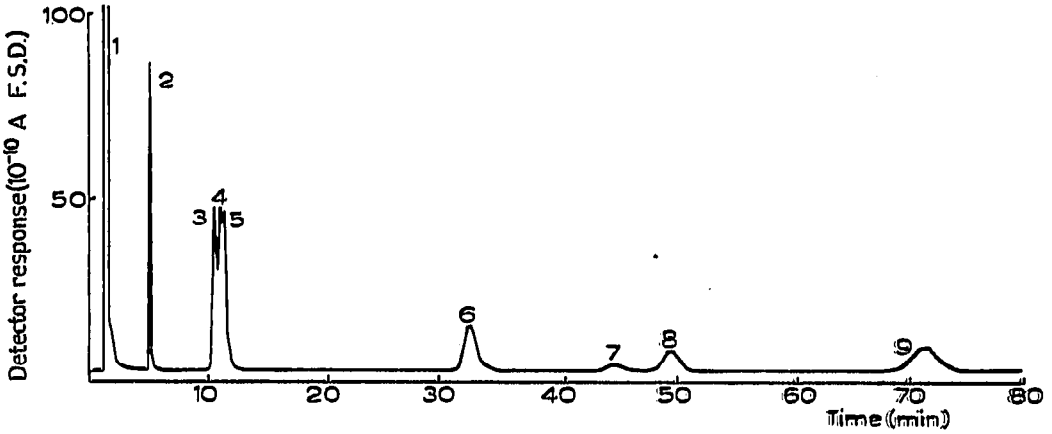

Fig. 1. Gas chromatogram of the mixture of the ten amines on the 5% KOH–5% PEG 6000 column. Column temperature: 160°. 1 = Ether; 2 = isopropylhexedrine; 3 = methylamphetamine; 4 = phentermine; 5 = amphetamine; 6 = chlorphentermine; 7 = diethylpropion; 8 = phendimetrazine; 9 = phenmetrazine.

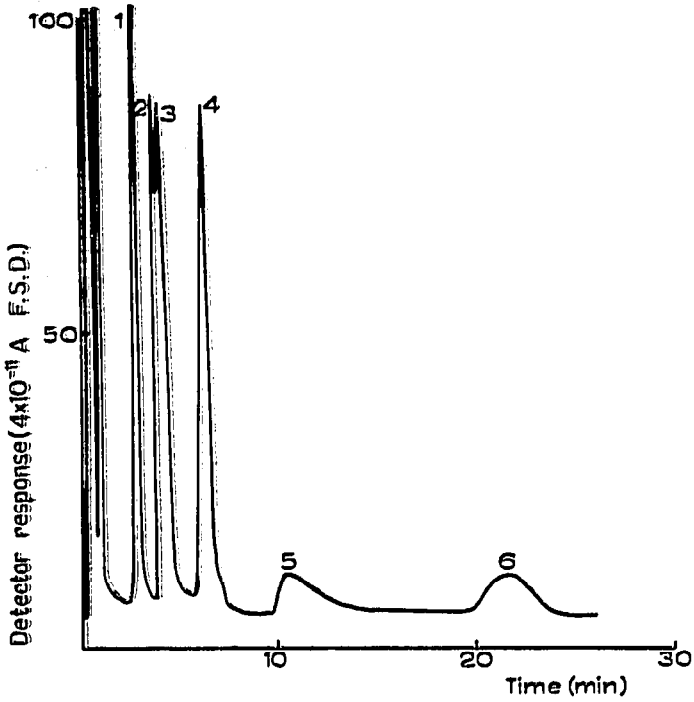

Fig. 2. Gas chromatogram of the mixture of the ten amines on the 5% KOH–2% Carbowax 20M column. Column temperature: 140°. 1 = Chlorphentermine; 2 = diethylpropion; 3 = phendimetrazine; 4 = phenmetrazine; 5 = phenylpropanolamine; 6 = methylphenidate.

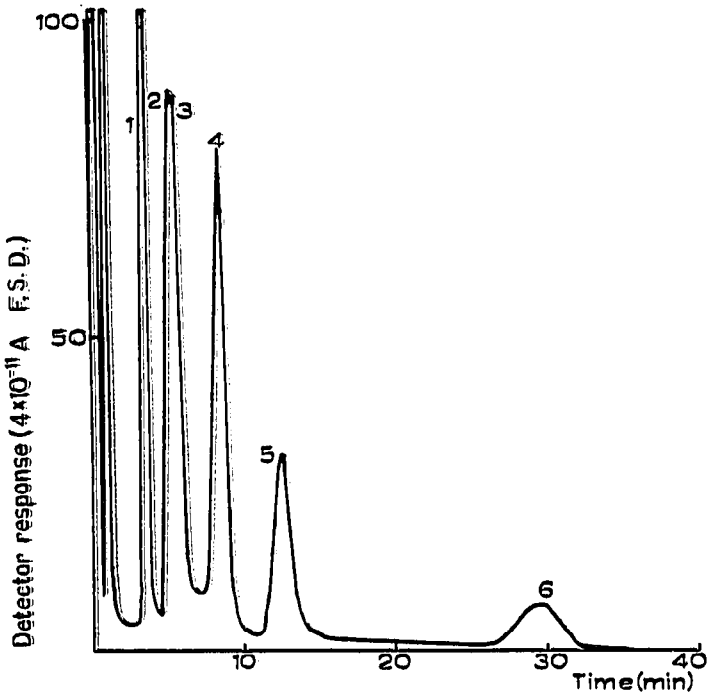

Fig. 3. Gas chromatogram of the mixture of the ten amines on the 10% KOH–22.5% Carbowax 20M column. Column temperature: 150°. 1 = Chlorphentermine; 2 = diethylpropion; 2 = phendimetrazine; 4 = phenmetrazine; 5 = phenylpropanolamine; 6 = methylphenidate.

VAN ZWOL's column, decomposes or adsorbs the amines, while alkaline coating of the support before application of the stationary phase prevents this phenomenon.

VAN ZWOL chromatographed the ten amines on four other columns using different stationary phases and the above support, although peak tailing occurred. The support is therefore unlikely to be responsible for the failure to elute the amines from the 22.5 % Carbowax 20 M column and thus the stationary phase, or its impurities, is implicated.

Using a 5 % KOH–5 % PEG 6000 column we were able to detect quantities of amphetamine as low as 0.01 μg; asymmetry factors[5] of 1.1 were obtained. On the other hand VAN ZWOL, using the best of his five columns, was only able to detect amphetamine to the 0.15 μg level and the peaks had asymmetry factors of 1.3. With the column described by us[1] and utilizing an internal standard (N,N-dimethylaniline), linear calibrations (in the range 0.01–1.0 μg amphetamine base) passing through the origin were obtained whereas VAN ZWOL, using large amounts of stationary phase, could only obtain curves of peak height against concentration over the same range.

Another advantage of using KOH treated columns is that the bleed-off of column material, and subsequent long conditioning times of columns, is markedly reduced (due to the high bleed-off rate, the 22.5 % Carbowax 20 M column took a week at a temperature of 180° before the highest sensitivity ranges of the instrument could be used, whereas the 10 % KOH–22.5 % Carbowax 20 M column could be used at all sensitivity ranges after only 24 h conditioning).

Although, in general, KOH coated supports are advantageous for the chromatography of amines, in certain cases a non-KOH coated support may be preferable, *e.g.* diethylpropion gave relatively smaller peaks on KOH treated columns than on non-treated columns, possibly because of enolisation of the drug molecule followed by decomposition by, or reaction with, the KOH-coated support.

We therefore maintain that GLC using KOH-treated columns and the internal standard technique[1–4] is completely satisfactory for the identification and determination of the majority of sympathomimetic amines used in anorectic formulations.

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