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SYSTEMATIC APPLICATION OF GAS CHROMATOGRAPHY TO THE ANALYSIS OF PHARMACEUTICAL PREPARATIONS

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SUMMARY

Gas chromatography has been applied to separate mixtures of psychotropic drugs. A number of monoamine oxidase inhibitors and other stimulating psychotropic drugs (imipramine, phenelzine, methylphenidate, tranylcypromine, pipradol, iproniazid, nialamide and isocarboxazide) was studied. Another group consisting of glutethimide, hydroxyzine, carisoprodol, methaqualone and meprobamate was also examined.

The retention times permit a good separation of these drugs.

Gas chromatographic separation and identification of psychotropic drugs has been studied in recent years with the aim of establishing the metabolism of these substances in the human body, or in order to recognize rapidly drugs used for toxicological purposes[1].

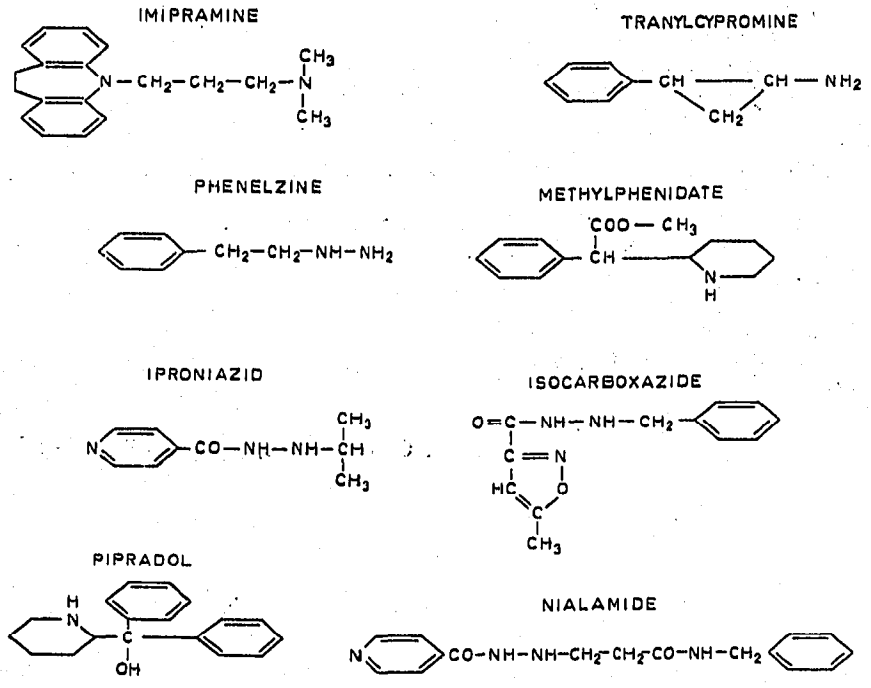

Fig. 1.

The gas chromatographic behaviour of a number of tranquillizers extracted both from phosphate buffer and blood has been studied by this method by NARESH AND KIRK[2], and the relative retention times have been determined.

We have initiated a study of the use of gas chromatography in the analysis of pharmaceutical preparations, both for checking the purity of the substances and for separation and identification of mixtures.

In this preliminary report the separation and identification by gas chromatography of a number of monoamine oxidase inhibitors stimulating psychotropic drugs were studied.

Imipramine, tranylcypromine, phenelzine, methylphenidate, iproniazid, isocarboxazide, pipradol and nialamide were examined. As shown in Fig. 1 all these substances differ in structure but are all characterized by a free amino, hydrazo or hydrazino group.

A good separation of the compounds, with the exception of nialamide, and isocarboxazide, was obtained using the operating conditions given below.

EXPERIMENTAL

Apparatus and materials

Perkin Elmer 801 gas chromatograph, with a differential ionization flame detector.

Glass columns, length 1.80 m and internal diameter 2 mm.

Stationary phase concentration: 2 % GE-SE 30.

Support: Aeropak 30*, 80–100 mesh.

Operating conditions

Glass injector.

Carrier gas flow rate: nitrogen, 50 ml/min.

Operating temperatures: column, programmed 70° to 250° at 10.4°/min; injector 250°; detector 220°.

Method

2.0 μl of a mixture of the above substances in ethereal solution were used. In the mixture the respective concentrations of the substances differed, according to the sensitivity of the material to the conditions used. For quantitative evaluation it was necessary to use a standard chromatogram for all the substances examined.

Under these conditions nialamide and isocarboxazide are decomposed; whereas imipramine, phenelzine, methylphenidate, tranylcypromine, pipradol and iproniazid were separated and detected (Fig. 2).

Another group of psychotropic drugs consisting of glutethimide, hydroxyzine, carisoprodol, methaqualone and meprobamate was examined, although all these substances differ in structure and belong to different chemical groups (Fig. 3).

It was possible to obtain a good separation with the same instrumentation but

* From Varian Aerograph.

with minor variations of the operating conditions (column programmed 100° to 210° at 4.2°/min; injector 200°; detector 230°).

1.0 μl of a 1 % ethereal solution of carisoprodol, glutethimide and methaqualone and 1.0 μl of a 1 % alcoholic solution of hydroxyzine, were injected for this experiment. Meprobamate can be detected, but is partially decomposed.

A good characterization of meprobamate, and separation from other carbamates

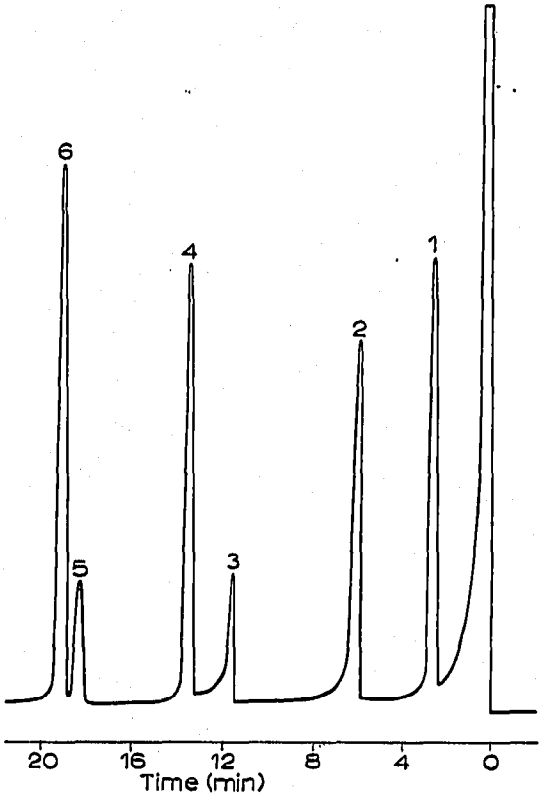

Fig. 2. Separation of a mixture of: (1) phenelzine; (2) tranylcypromine; (3) iproniazid; (4) methylphenidate; (5) pipradol; (6) imipramine.

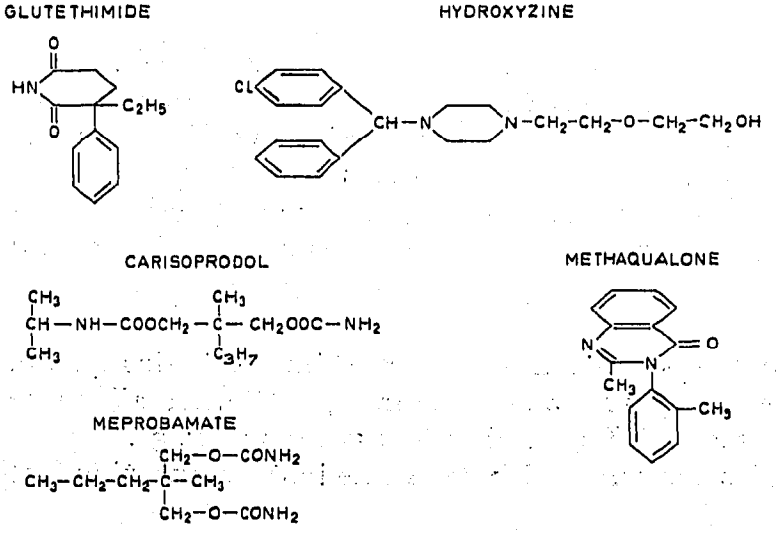

Fig. 3.

such as carisoprodol, mebutamate and tibamate was shown to be possible: the gas chromatographic separation of meprobamate has been studied by DOUGLAS *et al*[3] in plasma and urine, using 1.20 m glass columns containing Diatoport S and 3.8% of methylsilicone VC-W 98; carrier gas flow rate: helium 65 ml/min; detector temperature, 275°; column temperature, 180°.

In our working conditions, the retention times for glutethimide, methaqualone,

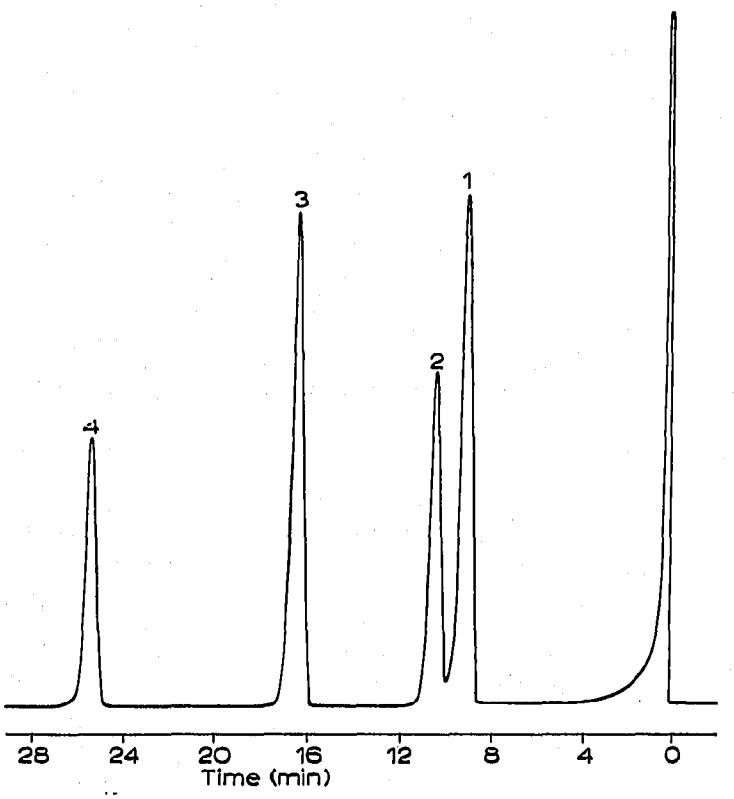

Fig. 4. Separation of a mixture of: (1) glutethimide; (2) methaqualone; (3) carisoprodol; (4) hydroxyzine.

carisoprodol and hydroxyzine permit a good separation of these drugs (Fig. 4). Furthermore, the shape of the peaks also suggests the possibility of quantitative evaluation of these compounds in a mixture.

A limiting factor in the use of GLC is the instability of some drugs to heat, *e.g.* hydrazines, which undergo pyrolysis under the conditions used.

The results obtained indicate that gas chromatographic methods can be used for the evaluation of several psychotropic drugs in mixtures and pharmaceutical preparations.

REFERENCES

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