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Note

Detection of carbon disulphide (a Disulfiram metabolite) in expired air by gas chromatography

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A recent paper[1] described a method for the detection of carbon disulphide (a metabolite of the drug Disulfiram, Antabuse) in the breath of patients taking the drug Disulfiram. The method relies on the formation of a copper complex which colours an organic solvent layer yellow. The method is qualitative and is intended to give an indication of possible Antabuse ingestion.

A method for the detection of carbon disulphide in breath which could form the basis of a quantitative procedure would be an obvious asset. Such a method is described.

EXPERIMENTAL

Material and apparatus

All reagents are of "analytical" grade.

A glass bubbler, 30 ml, Drechsel type, was used, supplied by Johns Glass (Toronto, Canada).

For gas chromatography a Varian 1400 gas chromatograph (Varian, Walnut Creek, Calif., U.S.A.), equipped with a flame ionization detector and a 0–1 mV pen recorder and containing a 4-ft. coiled glass column (1/4 in. O.D.) packed with 1.5% FFAP on 80–100 mesh Varoport 30 (Chromatographic Specialities, Brockville, Ontario, Canada), was used. The operating conditions for the results shown in Fig. 1 are as follows: injection port temperature, 200°; column temperature, 125°; detector temperature, 220°; carrier gas (nitrogen) flow-rate, approximately 40 ml/min.

Confirmational gas chromatography was carried out on a 6-ft. glass column (1/4 in. O.D.) packed with 3% SE-30 on 80–100 mesh Varoport 30 at a column temperature of 135° and a nitrogen flow-rate of approximately 40 ml/min.

Analytical procedure

Three millilitres of a 5% solution (v/v) of diethylamine in acetone are placed in a bubbler and expired air is bubbled through the solution. After five exhalations the solution is decanted into a 15-ml centrifuge tube and six drops of methyl iodide are added. The solution is reduced almost to dryness at 50° with a stream of nitrogen; 2 ml of distilled water are added followed by three drops of 3 *N* sulphuric acid and approximately 1 ml *n*-butyl chloride. The mixture is shaken on a vortex mixer for

1 min and then centrifuged. The upper organic layer is pipetted into a 3-ml reacti-vial and the solvent evaporated with a stream of dry nitrogen at 50°. The residue is taken up in 50 μl *n*-butyl chloride and 5 μl are injected into the gas chromatograph.

RESULTS AND DISCUSSION

The basis of the method described is the formation of the methyl ester of diethyldithiocarbamic acid. The reactions involved can be summarised as follows:

$$2\ Et_2NH + CS_2 \rightarrow Et_2NCS_2^- + \overset{+}{N}H_2Et_2$$
$$Et_2NCS_2^- + CH_3I \rightarrow Et_2NCS_2CH_3 + I^-$$

The methyl ester can be detected in sub-microgram quantities by a gas chromatograph equipped with a flame ionization detector.

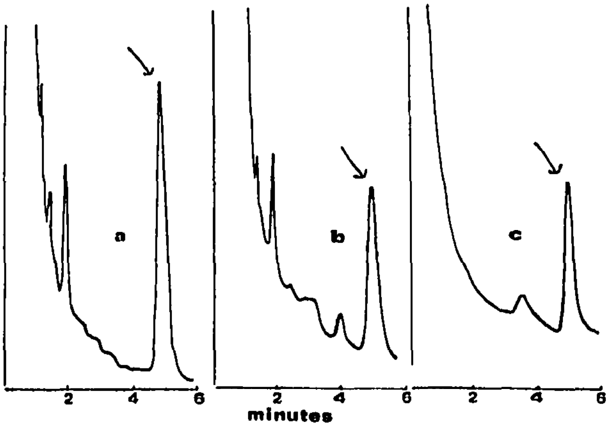

Fig. 1. Gas chromatographic traces of (a) a breath sample from a male patient, (b) a breath sample from a female patient, and (c) the methyl ester of diethyldithiocarbamic acid.

Fig. 1 illustrates the results obtained. Traces a and b represent the gas chromatograms obtained from the breath of two patients on an Antabuse program; trace c corresponds to the standard methyl ester. A limited number of blank determinations were carried out with people not taking Antabuse and no peak corresponding to the methyl ester was detected.

The detection of carbon disulphide in the blood (10 ml) of patients taking Antabuse so far has not been successful. A technique similar to that above was used except that nitrogen was bubbled through an acid solution of the blood (the acid should release carbon disulphide from any thiocarbamates that are present) prior to bubbling through the diethylamine in acetone solution.

The quantitative estimation of carbon disulphide in breath should be possible if fixed volumes of alveolar air can be collected. Devices are available that can deliver known volumes of alveolar air*.

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* Breath Analyser Collection Unit (Stephenson, Red Bank, N.J., U.S.A.) and Vacu-sampler Breath (Cand-Aire, Highland Park, Ill., U.S.A.).

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1 M. Kraml, *CMA Journal*, 6 (1973) 578.