DETERMINATION OF PHENELZINE PLASMA CONCENTRATIONS IN PIGLET AND MAN

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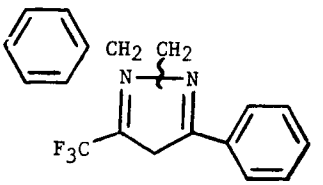
The pharmacokinetics and metabolism of the monoamine oxidase inhibitor, phenelzine remain poorly characterised. Difficulties in the quantitation of trace drug in plasma are exacerbated by its instability (Cooper et al 1978). These workers reported a GLC-electron capture procedure which detected a peak concentration of 2 ng/ml^{-1} at 2 h following a 30 mg dose of sulphate (≡ 17.5 mg base). Caddy et al (1978) described the elimination of phenelzine in urine of patients and found that from day 1 to 13 of dosing there were increases both in apparent half-life, from 0.9 to 4.7 h, and amount recovered, from 1.14 to 4.7% respectively.

A new GLC method for plasma phenelzine is described in which the drug in fresh plasma added to pH 6 citrate buffer is reacted with benzoyltrifluoroacetone to form a phenylethylphenyl trifluoromethylpyrazole (I).



I

This derivative is extracted into heptane, with benzalazine as internal standard, chromatographed at 240^{0} on 10% OV-17 on gas chrom Q in a glass column (2 m X 1.88 mm, i.d.) and detected with an alkaline flame-ionisation detector specific for nitrogen. The drug must be derivatised immediately after plasma collection when the method is quantitative over the range 5 to 1000 ng ml^{-1} with a detection limit of 2 ng ml^{-1}. Hydrazones do not interfere and the procedure may also be adapted for determination of drug in urine.

Phenelzine plasma profiles were followed in 4 piglets (19 to 34 kg) after separate single I.V. and oral solution doses of 2 mg kg^{-1} phenelzine and in a healthy male volunteer following a 50 mg oral solution dose. In piglets a biexponential decay was observed with an initial phase of half-life 0.59 ± 0.06 h (s.e.) and β, 11.05 ± 1.8 h, but the latter was not seen after oral doses. The apparent clearance (I.V.) was 51.5 ± 18 ml min^{-1} kg^{-1} and the ratio of oral/i.v. areas was 16.7 ± 4.8%. In man the peak concentration of 51.2 ng ml^{-1} was observed in 15 min followed by an exponential decay with an initial phase of half-life 2.3 h and β, 6.6 h. The apparent clearance was 67.5 ml min^{-1} kg^{-1} with about 1% of dose recovered in urine.

Caddy, B. et al (1978) Br. J. Clin. Pharmacol. 6: 185-188
Cooper, T.B. et al (1978) Comm. in Psychopharmacol. 2: 505-512

0022-3573/82/120098P-01$02.50/0