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The absorption and elimination of orally administered [^{14}C]hyoscine *N*-butylbromide (butylscopolamine)

The absorption of quaternary ammonium antiacetylcholine agents from the gastrointestinal tract has been much debated (Möller & Rosén, 1968; Hellström, Rosén & Söderlund, 1970; Beermann, Hellström & Rosén, 1971, 1972) and hyoscine *N*-butylbromide (butylscopolamine) has roused particular interest. While many authors hold that its absorption from the gut is insignificant (Herxheimer & Haefeli, 1966; Guignard, Herxheimer & Greenwood, 1968; Brömster, Carlberger & others, 1969; Hellström & others, 1970), its use clinically, even by mouth, has been found helpful in the treatment of various gastrointestinal disorders (Schmid, Bleichert & others, 1969).

In animal studies with the labelled drug an enterohepatic circulation was proved (Pentikäinen, Penttilä & others, 1973). It has been suggested that after oral administration, though only absorbed slightly, it accumulates in the intestinal wall and the bile, and thus has a local effect (Pomeroy & Rand, 1968). This suggestion is supported by our animal results (Pentikäinen & others, 1973). To throw more light on this question, the labelled drug has been given to two patients and the radioactivities of serum, bile and urine measured.

[^{14}C]Hyoscine butylbromide was synthesized (Pentikäinen & others, 1973). Two volunteer female patients with normal liver function, aged 24 and 46 years and weighing 54 and 60 kg, had a T-drain, kept under a constant suction by a pressure of 50 mm of water (see Kaltiala, Penttilä & others, 1974), inserted into the common bile duct after choledocholithotomy. On the morning after the operation one 10 mg tablet of the drug, containing 17·1 μCi ^{14}C, was taken with a glass of water on an empty stomach.

Blood samples were taken from the cubital vein 20, 40, 60 and 180 minutes later

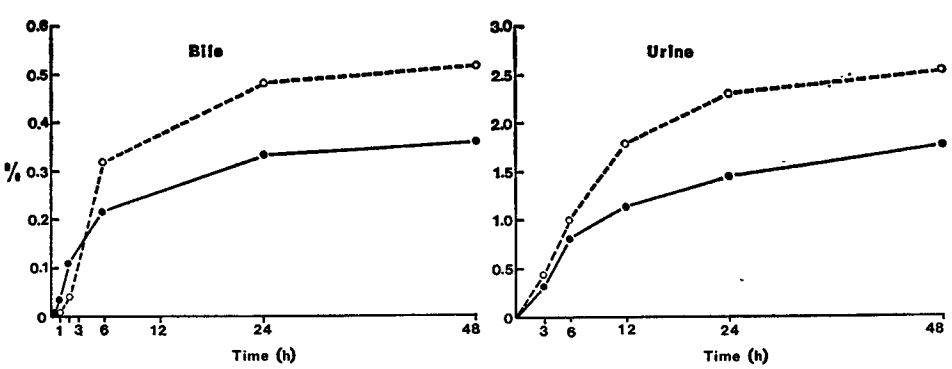

FIG. 1. Cumulative excretion of radioactivity in urine and bile in two volunteers after oral administration of 10 mg of [^{14}C] hyoscine butylbromide.

and the urine was collected over 1–3, 3–6, 6–12, 12–24 and 24–48 h and bile over 0–1/2, 1/2–1, 1–2, 2–6, 6–24 and 24–48 h.

Aliquots of bile, urine and serum were assayed for radioactivity by a liquid scintillation technique (Pentikäinen & others, 1973). The unchanged hyoscine butylbromide was separated from its metabolites by paper chromatography on Whatman No. 1 paper with n-butanol–acetic acid–water (80:20:20). The chromatograms were cut in pieces and the radioactivity of each piece was measured.

The radioactivity of the serum was not significantly greater than background. The cumulative radioactivity of the bile is seen in Fig. 1. Maximal excretion of radioactivity was observed at 2–6 h. The total excretion was only 0·5 and 0·4%, respectively, of the dose. Maximal radioactivity in the urine was recovered at 6–12 h in one patient and at 3–6 h in the other (Fig. 1). In 48 h, 2·5 and 1·8%, respectively, of the radioactive dose was excreted.

Two radioactive spots were found in both bile and urine. In the bile some 80% of the activity was localized in the spot corresponding to unmetabolized hyoscine butylbromide, and in the urine this was about 70%. Radioactivities in urine and bile were similar to earlier findings (Hellström & others, 1970; Beermann & others, 1971, 1972), in which the data on the bile were based on indirect estimations. The present method has the advantage that the excreted bile is collected almost quantitatively.

A possible explanation to the apparent discrepancy between the poor gastrointestinal absorption of hyoscine butylbromide and reasonable clinical results might be that the small part of the dose which is absorbed still suffices for a therapeutic effect. The amounts measured in urine in several investigations (Hellström & others, 1970; Beermann & others, 1971, 1972), as well as in the present work, indicate that 2–8% is absorbed (i.e. up to 1·0 mg of unmetabolized drug) with the usual oral dose of 20 mg. In a clinical study (Kewenter & Kock, 1971), 10 mg of the drug given intravenously after morphine reduced the common bile duct pressure nearly maximally, whereas atropine, 0·5 mg, was ineffective. This suggests that much lower doses than 10 mg of hyoscine butylbromide would have been sufficient to produce the desired effect.

In the light of our previous animal experiments (Pentikäinen & others, 1973) and the present finding that in man most of the radioactivity excreted into the bile is due to unmetabolized hyoscine butylbromide, a local effect in man is a possibility.

Research Laboratories of Medica Ltd,
SF-00510 Helsinki 51,
Central Hospital Kemi, SF-94100 Kemi 10, Finland.

H. VAPAATALO
ANERI PENTTILÄ
E. KALTIALA

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