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The Absorption, Excretion and Metabolism of Disodium [^{14}C]Cromoglycate in Man

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Disodium cromoglycate, the disodium salt of 1,3-bis-(2-carboxychromon-5-yloxy)-2-hydroxypropane, is used in the treatment of bronchial asthma (Howell & Altounyan, 1967; Kennedy, 1967).

After the oral administration of disodium [^3H]cromoglycate to monkeys, rabbits and rats, 1%, 2% and 4% of the dose was absorbed respectively (G. F. Moss, personal communication). However, intratracheal administration in these three species indicated that disodium cromoglycate was quickly absorbed from the lung (Moss, Jones, Ritchie & Cox, 1970). Intravenous studies (G. F. Moss, personal communication) have shown that this compound is rapidly excreted via the bile and urine in several animal species. Chromatography of bile and urine indicated that all the recovered radioactivity was in unchanged disodium cromoglycate.

The fate of inhaled disodium [^{14}C]cromoglycate has been examined in asthmatic patients. Maximum plasma concentrations (9 ng/ml) were obtained within 15 min of inhaling the disodium cromoglycate (20 mg, 33 μCi), and the half-life in plasma was 81 min. The urinary-excretion findings suggest that drug reaching the lung is rapidly absorbed and excreted. Only 2% of the inhaled dose appeared in the 24 h urine, 84% being recovered in the faeces.

The fate of orally administered disodium [^{14}C]cromoglycate (20 mg, 8 μCi) was examined. The drug was poorly absorbed from the gastrointestinal tract, only 0.4% of the dose appearing in the 24 h urine and 82% being recovered from the faeces. No metabolites were detected chromatographically.

The intravenous administration of disodium [^{14}C]cromoglycate (4 mg, 6 μCi) resulted in approximately equal amounts being excreted in the urine and the faeces. Disodium cromoglycate is highly polar with a molecular weight of 512, and thus satisfies the criteria for biliary excretion (Millburn, Smith & Williams, 1967).

A comparison of our results with the animal data shows that the monkey handles the drug in a similar manner to man.

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The Fate of [^3H]Salbutamol in Man

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The catecholamine isoprenaline is an adrenergic β -receptor stimulant. It affects both bronchial smooth muscle and cardiac muscle. It has been widely used by inhalation in the treatment of asthma, its main disadvantages being its short duration of action and cardiac stimulation. The metabolic fate has been examined in man (Morgan *et al.* 1969).

Salbutamol [2-*tert*.-butylamino-1-(4-hydroxy-3-hydroxymethyl)phenylethanol] is a non-catechol adrenergic β -receptor stimulant. Its advantages over isoprenaline are longer duration of action, selective action on bronchial smooth muscle and the fact that it can be taken orally.

The metabolism and excretion of [^3H]salbutamol has been investigated in rat, rabbit, dog and guinea pig (L. E. Martin, personal communication). In these species between 50 and 80% of the dose was excreted in the urine (0–48 h). The *O*-glucuronide (4-phenyl) of salbutamol was identified as the major metabolite in the urine of rat, rabbit and guinea pig. The dog excreted four unidentified minor metabolites in addition to salbutamol.

The fate of orally administered [^3H]salbutamol (4 mg or 8 mg) has been studied in asthmatic patients. Maximum plasma concentrations (0.23 or 0.43 μM) were obtained 2.5–3 h after dosing. The half-life in plasma was 3.5 h. Analysis of plasma samples indicated that 80% of the radioactivity