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SHORT COMMUNICATION

Urinary excretion of (–)-methylephedrine, (–)-ephedrine and (–)-norephedrine in man

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DESPITE the long and extensive clinical use of ephedrine and related compounds, little is known of their metabolism and excretion in man. It has been reported that the metabolism of (–)-ephedrine in various animals shows considerable species differences (Axelrod, 1953). Thus demethylation to norephedrine is a major route of metabolism in the dog and guinea-pig, but only a minor one in the rat; hydroxylation is of minor importance in the dog but a major pathway in the rat. Williams (1959) suggests that demethylation of ephedrine is likely in man although Richter (1938) claimed that about 100% of the dose was excreted unchanged in 24 hr. It must be noted, however, that the analytical method used by the latter author did not differentiate between ephedrine and norephedrine.

The development of a specific and sensitive gas-liquid chromatographic assay for ephedrine and its congeners in urine, (Beckett & Wilkinson, 1965b), permits detailed investigation into the metabolism and excretion of these compounds. Table 1 shows the results obtained when aqueous solutions of (–)-methylephedrine, (–)-ephedrine, and (–)-norephedrine were administered orally in the form of their hydrochlorides to a male volunteer.

TABLE 1. EXCRETION OF (–)-METHYLEPHEDRINE, (–)-EPHEDRINE AND (–)-NOREPHEDRINE IN MAN (pH OF URINE NOT CONTROLLED)

Drug	Dose, mg base	% Dose excreted in 24 hr		
		Methylephedrine	Ephedrine	Norephedrine
(–)-Methylephedrine	10·0	31·8	8·1	—
(–)-Ephedrine	27·3	—	79·3	4·3
(–)-Norephedrine	25·0	—	—	90·8

The results indicate that demethylation of (–)-methylephedrine and (–)-ephedrine is not a major pathway of metabolism in man and that the pharmacological activity of these drugs probably resides in the parent structure. The rate of excretion of (–)-methylephedrine (pK_a 9·20) and its metabolite, ephedrine (pK_a 9·47) fluctuated with changes in urinary pH. These results are consistent with the concept of reabsorption of the unionised drug moiety in the kidney tubules (Weiner & Mudge, 1964). Thus the excretory behaviour of the ephedrine-type compounds in man shows many similarities with the results already reported for methylamphetamine and its metabolite amphetamine (Beckett & Rowland, 1965) and also with chlorpheniramine (Beckett & Wilkinson, 1965a).

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