The metabolism in rat of tiflorex, a *m*-trifluoromethylthio-substituted phenylisopropylamine

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The metabolism of the new anorectic agent tiflorex has been studied in the rat using the [^{14}C]-labelled compound, ((±)-1-(*m*-trifluoromethylthiophenyl)-1-[^{14}C]-2-ethylaminopropane hydrochloride) which was given either orally or intravenously (10 mg/kg, 250 μCi/kg).

Table 1 The urinary and faecal excretion of [^{14}C] and metabolites in 0–48 h urine of rats dosed either orally or intravenously with [^{14}C]-tiflorex (10 mg/kg; 250 μCi/kg). The results are expressed as a percentage of the dose ± s.d. and are for six male rats

Compound	*Route of administration* *Intravenous*	*Oral*
Tiflorex	2.0 ± 0.1	0.5 ± 0.0
Tiflorex sulphone	7.0 ± 0.8	6.5 ± 0.8
Tiflorex sulphoxide	7.8 ± 1.2	5.5 ± 0.2
Nortiflorex sulphone	20.1 ± 0.4	20.9 ± 1.0
Nortiflorex sulphoxide	9.7 ± 0.4	10.8 ± 0.4
Total	46.6 ± 0.6	44.2 ± 0.5
Total [^{14}C] in 0–48 h urine	72.9 ± 0.7	70.2 ± 1.0
Total [^{14}C] in 0–48 h faeces	14.9 ± 0.7	11.1 ± 1.9

Urinary excretion of [^{14}C] in the first 48 h by rats dosed either orally or intravenously with [^{14}C]-tiflorex was about 70% of the dose in both cases (Table 1) indicating that the compound is well absorbed by the oral route.

Analysis of the urine by means of solvent extraction, derivatisation and reverse phase thin layer chromatography of the extract followed by autoradiography to locate the radioactive spots indicated that the major metabolites (Table 1) were the sulphones and sulphoxides of tiflorex and nortiflorex, nortiflorex sulphone being the most important. Nortiflorex itself was barely detectable (<1%). The identity of these compounds was confirmed by e.i./c.i. gas-chromatography-mass spectrometry of the urine extracts and comparison with the authentic compounds.

It was shown in plasma analysed in a similar fashion that intravenously administered, tiflorex, nortiflorex sulphone and nortiflorex sulphoxide had elimination half lives of 8.2, 9.3 and 4.8 h respectively.

The predominant route of metabolism in the rat of phenylisopropylamines is by *p*-hydroxylation (Williams, Caldwell & Dring, 1973). However this route is not apparent when the phenyl ring is substituted with the *m*-trifluoromethylthio group where S-oxidation appears to be more important.

Reference

WILLIAMS, R.T., CALDWELL, J. & DRING, L.G. (1973). Comparative metabolism of some amphetamines in various species. In *Frontiers in Catecholamine Research*. ed. S.H. Snyder and E. Usdin, pp. 927–932, Oxford: Pergamon.