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Monkeys as metabolic models for man – the fate of amphetamine in the vervet and patas monkey

J. CALDWELL*, J. O'GORMAN & R.L. SMITH

Department of Biochemical and Experimental Pharmacology, St. Mary's Hospital Medical School, London W2 1PG

and

O. BASSIR, M.A. FAFUNSO & M.R. FRENCH

Department of Biochemistry, University of Ibadan, Ibadan, Nigeria

If animal investigations are to have relevance to the human situation, the species chosen should resemble man both in response to and disposition of the drug in question. Inter-species variations in drug metabolism frequently emerge as a major factor influencing species differences in drug effect, and it has been shown that non-human primates generally exhibit metabolic patterns closer to man than those of other laboratory animals (Smith & Caldwell, 1976). Only 12 of the 214 primate species have been investigated from the viewpoint of drug metabolism. There are presently difficulties in ensuring adequate supplies of commonly used primates for these purposes, and thus evaluation of other species is desirable. We now report on the fate of the habit forming drug amphetamine in two species of Old World monkey, the vervet, or African green monkey (*Cercopithecus aethiops*) and the patas monkey (*Erythrocebus patas patas*).

The monkeys (2 adult females of each species; vervets, wt. 2.5 kg, patas, wt. 4 kg) were housed in the Primate Colony of the Department of Biochemistry, University of Ibadan, and received (\pm)-[^{14}C]-amphetamine sulphate (5 mg/kg i.m.; 10 $\mu\text{Ci}/\text{animal}$)

dissolved in sterile isotonic saline. They were placed in strong metabolic cages and their urine collected for 24 h into trays containing 5 ml of 2% HgCl_2 as preservative. The urines were frozen and transported by air to London for analysis. The [^{14}C] content of the urines was determined by liquid scintillation spectrometry and urinary metabolites assayed by radiochromatography and reverse isotope dilution as described by Caldwell, Dring & Williams (1972).

The quantitative and qualitative results are shown in Table 1. The recovery of administered [^{14}C] was low (ca. 25% of dose), probably due to difficulties in obtaining a complete urine collection under these conditions. In addition to unchanged amphetamine, the urine of both species contained four metabolites, free and conjugated 4'-hydroxyamphetamine, benzoic acid and hippuric acid. Table 1 also presents data obtained previously in human volunteers and other animal species (Caldwell, 1976; Caldwell, Dring, Franklin, Köster, Smith & Williams, 1977). It is clear that there occur considerable inter-primate variations in metabolism, and it is of interest to examine the vervet and patas monkey as potential metabolic models for man. Both these monkeys produce more 4'-hydroxyamphetamine than does man, and excrete correspondingly less unchanged amphetamine. The metabolic profile of amphetamine in the vervet is similar to that of man, although there is more 4'-hydroxyamphetamine formed, but in the patas monkey the pattern is different with both metabolic routes being more important than elimination of unchanged drug. Table 1 shows clearly that the metabolism of amphetamine in the marmoset, a New World monkey, and the rat has no similarity to the human situation. These studies thus show the importance of considering inter-primate variations in drug metabolism, and neither of the species considered here offers an animal model of human amphetamine metabolism as good as the rhesus monkey.

In certain studies of drug dependence, the use of

non-human primates may be desirable since their behavioural complexity approaches that of man, and they develop psychic and physical dependence to a number of drugs in the same way as does man (Deneau, 1969). When choosing a primate species as a model for man, its metabolic profile should be considered, since this may make one species far more acceptable than another, despite the fact that both may be valid from other viewpoints.

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Table 1 Metabolism of Amphetamine in the Patas Monkey and Vervet, compared with Man, other Primates and the Rat

Administration of drug and analysis of urine as described in the text. Results are the mean of two animals. Data from other species from Caldwell (1976) and Caldwell *et al.* (1977).

	% of urinary [¹⁴ C] excreted as that compound by:					
	<i>Patas monkey</i>	<i>Vervet</i>	<i>Man</i>	<i>Rhesus monkey</i>	<i>Marmoset</i>	<i>Rat</i>
Amphetamine	18	34	55	41	79	16
4'-Hydroxyamphetamine						
free	25	12	} 6	} 15	} 4	} 80
conjugated	18	15				
Benzoic acid	19	27	} 39	} 41	} 13	} 4
Hippuric acid	18	10				
Total [¹⁴ C] in 0–24 h urine (% dose)	21	27	42	52	68	77