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A note on the effect of (+)- and (−)-amphetamine on lipid metabolism

Both (+)- and (−)-amphetamine have anorectic properties (Lawlor, Trivedi & Yelnosky, 1969; Mantegazza, Müller & others, 1970). However, while the effect of (+)-amphetamine on plasma free fatty acids (FFA) and triglycerides is well established, data on the effect of the (−)-isomer on lipid metabolism are scanty. We have compared, (+)- and (−)-amphetamine for their effects on plasma FFA and triglycerides, on triglyceride absorption, and on body temperature, intestinal transit and food intake.

Charles River male rats, 200 g, four to a cage, were used. Except where specified, food was available until the experiments began. (+) and (−)-Amphetamine sulphate (obtained by courtesy of Recordati, Milan) were administered intraperitoneally; all doses refer to the salt. Controls received saline. Rectal temperature was recorded before treatment and after 30, 60, 120, 180, 240, 300 and 360 min. Food intake was measured in rats fasted for 18 h. Pellets were made available to the animals just after the treatment. The amount of food consumed during the subsequent 4 h was recorded.

The intestinal motility was measured according to De Feo, Piccinelli & Silvestrini (1971). Photoluminescent pigment and drug were given at the same time, rats were killed 60 min after treatment.

Triglyceride absorption was determined as follows: 2 h after amphetamine, the animals received 20 ml kg^{-1} of olive oil by stomach tube and 2 h later, they were decapitated and plasma triglycerides measured according to Van Handel, Zilversmit & Bowman (1957). Plasma FFA were measured according to Dole (1956).

(+)-Amphetamine, at 5 and 10 mg kg^{-1}, caused hyperthermia, up to 120 min after

Table 1. *Effect of (+)- and (−)-amphetamine on body temperature, food consumption and triglyceride absorption.*

Treatment mg kg^{-1} i.p.	Body temperature °C ± s.e. 30 min	60 min	90 min	Food consumption %	Plasma triglycerides % Controls	Oil loaded
Saline	36·9 ± 0·3	36·6 ± 0·2	36·5 ± 0·2	100	100	100
(+)-Amphetamine 1·25	—	—	—	—	90	60**
,, 2·50	—	—	—	54	84	60**
,, 5·00	37·3 ± 0·2	37·3 ± 0·2	37·4 ± 0·1*	63	82	62**
,, 10·00	38·4 ± 0·3**	38·4 ± 0·5**	38·0 ± 0·5**	49	57	61**
−)-Amphetamine 1·25	—	—	—	—	78	50**†
,, 2·50	—	—	—	87	68	51**†
,, 5·00	36·8 ± 0·1	36·9 ± 0·1	36·9 ± 0·1	75	73	37**‡
,, 10·00	36·9 ± 0·4	37·1 ± 0·3	36·9 ± 0·2	67	75	55**†

Body temperature was measured in aggregated rats.
Food consumption was measured for 4 h in overnight fasted rats. Figures are mean of 4 rats. Animals were allowed food immediately after treatment.
Plasma triglycerides were measured in rats treated with amphetamine 4 h before death. Oil loaded animals received olive oil 20 ml kg^{-1} b.w. by gavage. Absolute triglyceride concentration for untreated rats were 51·2 ± 3·3 mg per 100 ml and for untreated oil loaded 140·2 ± 9·3 mg per 100 ml.

* $P < 0.01$ versus saline; ** $P < 0.05$ versus saline.

† $P < 0.02$ and ‡ $P < 0.05$ versus (+)-amphetamine.

dosage while the (−)-isomer, at similar doses, did not do so at any time even up to 6 h (Table 1).

Both isomers at 2·5 to 10 mg, reduced food intake but the (−)-isomer, particularly at 2.5 and 5 mg kg^{-1}, appeared less active (Table 1). Both isomers, significantly ($P < 0.05$) inhibited the transit of a photoluminiscent pigment through the small intestine: saline 79%; (+)-isomer 67 and 64%, (−)-isomer 66 and 67% at the 2·5 and 5 mg kg^{-1} dose respectively. The isomers in doses having only a mild effect on plasma triglycerides in normal rats, strongly inhibited the rise in plasma triglycerides elicited by olive oil gavage (Table 1). The (−)-isomer proved the more effective (Student's *t*-test).

Both isomers caused a pronounced elevation in plasma FFA. For instance, 60 min after administration of (+)-amphetamine 5 mg kg^{-1} and (−)-amphetamine 10 mg kg^{-1} (i.p.) the level of plasma FFA was increased by 63% and 54% respectively.

These results suggest that the reduced intestinal motility, observed after the administration of amphetamine and amphetamine-like drugs, might be only partially responsible for the inhibition of triglyceride absorption.

The above observations and the fact that (−)-amphetamine is less toxic than (+)-isomer (Moore, 1963) suggest the importance of further investigating the effect of this compound on lipid metabolism.

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