

**Studies in the monkey (*Macaca mulatta*) on the effect of (+)-6-fluorotryptophan and (+)-p-chlorophenylalanine on plasma tryptophan**

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6-Fluorotryptophan (6-FT) and p-chlorophenylalanine (pCPA) deplete cerebral 5-hydroxytryptamine (5-HT) by inhibition of tryptophan hydroxylase (McGeer, Peters & McGeer, 1968; Jequier, Lovenberg & Sjoerdsma, 1967). However, alterations to the ratio of the plasma concentration of tryptophan and other large neutral amino acids (Fernstrom, Hirsch & Faller, 1976), and the proportion of tryptophan bound to plasma albumin (Tagliamonte, Biggio, Vargia & Gessa, 1973) also modify cerebral 5-HT production, and it is in this context that the effects of these inhibitors on free and total plasma tryptophan have been studied.

each peak was observed at 11.00 hours. With pCPA (10 and 100 mg/kg) the mean peak plasma levels of pCPA were 59 and 343 n mole/ml, and peaks were observed at 1100 and 1300 h respectively. It was not possible to measure the plasma levels after ingestion of pCPA (1 mg/kg). The plasma half times for 6-FT and pCPA were about 3.5 and 10.5 hours.

In control studies plasma concentrations of tryptophan increased during the day, and reached their maximum during the afternoon (Table 1). The increases in the plasma concentration at 1300 and 1700 h were highly significant ( $P < 0.01$ ). Oral ingestion of 6-FT (30 and 100 mg/kg) and pCPA (1 and 100 mg/kg) abolished the increase in plasma tryptophan during the day, and total plasma tryptophan concentrations were reduced compared with control levels at the same time of the day. The duration of each effect appeared to be related to the plasma half time of the inhibitor. Free tryptophan was not altered after the ingestion of 6-FT.

It is suggested that the plasma concentrations of the inhibitors, and the reduction in plasma tryptophan concentrations may reduce tryptophan transport across the blood brain barrier and that these effects may also decrease cerebral 5-HT production.

**Table 1** Total plasma tryptophan (n mole/ml) after inhibitors (mg/kg)

	<i>p</i> -Chlorophenylalanine									
	0930	1000	1100	1300	Time of day		1900	2100	0900	1100
Control		48	51	65	60	74	71	60		60
1		48	53	50*	61	51**	50**	61		51
100		42	42	36***	45*	42***	41***	41**		35***
	6-Fluorotryptophan									
	0930	1000	1100	1300	1500	1700	1900	2100	0900	1100
Control	41	45	52	60		51			42	
10	37	42	42	46		38			37	
30	41	50	47	40*		38			40	
100	37	43	39	42*		41			37	

Least Significant differences pCPA \* = 13; \*\* = 18; \*\*\* = 25

6-FT \* = 15; \*\* = 21

Significance levels \* = 5%; \*\* = 1%; \*\*\* = 0.1%

6-FT and pCPA were given orally to six (mean weight 5.3 kg) and five (mean weight 7.5 kg) monkeys respectively maintained on a controlled diet. Plasma amino acid concentrations were estimated using an amino acid analyser, and in the 6-FT studies free tryptophan was determined by equilibrium dialysis (Bender, Boulton & Coulson, 1975). At least 3 weeks separated each ingestion. The drugs were given in marzipan at 0900 h on each occasion. With 10, 30 and 100 mg/kg 6-FT the mean peak plasma levels of 6-FT were 24, 58 and 145 n mole/ml respectively, and

**References**

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