THE EFFECT OF FENFLURAMINE ON COLLAGEN-INDUCED PLATELET AGGREGATION *IN VITRO*

We have previously shown that fenfluramine inhibits adrenaline-induced platelet aggregation *in vitro* whereas it does not affect ADP-induced aggregation (Barradas *et al.*, 1982). Since fenfluramine and adrenaline are similar in structure, we had originally suggested that the fenfluramine-induced inhibition results from blockade of platelet α -adrenoceptors which mediate the proaggregatory effect of adrenaline (Grant & Scrutton, 1979). Our previous findings require re-interpretation in the light of further experimental work.

We have extended our initial observations by evaluating the effect of fenfluramine on *in vitro* collagen-induced platelet aggregation. The experiments were carried out as previously described (Barradas *et al.*, 1982). Briefly, fenfluramine at various concentrations (Table 1) was incubated for 5 min with platelet rich plasma (PRP) obtained from 10 healthy volunteers. Aggregation was then induced by the addition of collagen (Hormon-Chemie, West Germany). The final concentrations of collagen were 0.5 and 1.0 mg/l. Aggregation was calculated as the percentage fall in optical density 3 min after addition of collagen. These experiments were repeated by adding platelet activating factor (PAF; kindly provided by Roche Products Ltd, U.K.), final concentration 20 μ g/l, to initiate platelet aggregation. PRP from seven subjects was used in this latter experiment. All aggregations re-

ported in the present study included a 'second' phase as judged from the patterns of the aggregation curves.

Collagen-induced aggregation was significantly inhibited by fenfluramine (Table 1). Although strict comparison of platelet aggregation induced by different agonists is difficult, the pattern of inhibition (mainly involving the 'second' phase of aggregation) and the inhibitory concentrations of fenfluramine resemble those previously described by us for adrenaline-induced aggregation (Barradas *et al.*, 1982). PAF-induced aggregation, though inhibited by fenfluramine, was much less sensitive to this drug.

Since it is unlikely that collagen- or PAF-induced aggregation is dependent on ' α -adrenoceptors', our findings suggest that the inhibitory action of fenfluramine may, at least in part, be independent of ' α -adrenoceptor' blockade.

Further work is in progress to identify the mechanisms involved in the responses described.

M.A. BARRADAS, D.P. MIKHAILIDIS & P. DANDONA

Metabolic Unit, Department of Chemical Pathology, Royal Free Hospital & School of Medicine, Pond Street, London NW3 2QG

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Table 1 Median percentage *in vitro* platelet aggregation following incubation with fenfluramine (range of percentage aggregation shown in brackets)

Aggregating agent (final concentration)	Fenfluramine final concentration (mg/l)			
	0	0.2	2	20
Collagen (0.5 mg/l)	60 (42–70)	60 (40–68)	38* (22–63)	14* (0–32)
Collagen (1.0 mg/l)	66 (49–84)	60 (46–78)	52 (23–71)	29* (6–66)
PAF (20 μ g/l)	55 (51–70)	51 (46–65)	46 (43–62)	10* (0–26)

* $P < 0.01$ All values were compared with percentage aggregation in the control samples using paired Wilcoxon rank sum tests.

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