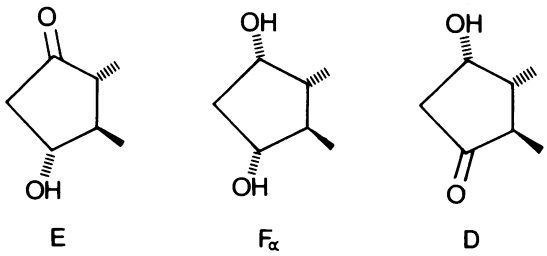

Fig. 1 Structural differences between prostaglandins of the E, F_α and D series.

also pressor, whereas PGE_2 is depressor and $PGF_{2\alpha}$ tends to produce a biphasic response.

On the rabbit oviduct, PGE_2 (0.02 to 0.2 μg/kg) reduces, whereas $PGF_{2\alpha}$ (0.3 to 6 μg/kg), in most experiments, raises intra-luminal pressure (Horton & Main, 1963; 1965), PGD_2 (6 to 13 μg/kg) caused relaxation, sometimes preceded by a contraction. Like PGE_2 and $PGF_{2\alpha}$, PGD_2 contracted the rat fundus and the isolated rabbit jejunum. The equipotent molar ratios for $PGF_{2\alpha}$ and PGD_2 were 3.5 and 47 with respect to PGE_2 (=1.0) on the rat fundus. The ratio of PGD_2 to $PGF_{2\alpha}$ (=1.0) was 7.8 on the rabbit jejunum.

These results establish that PGD_2 has significant pharmacological activity on some smooth muscle preparations. Moreover, its spectrum of activity differs from both PGE_2 and $PGF_{2\alpha}$. Since PGD_2 can be formed enzymatically from the same precursor as PGE_2 and $PGF_{2\alpha}$, its possible biological role merits further study.

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Potentiation by certain amino acids of hypotension induced by arachidonate

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Intravascular injection of arachidonate is followed, after a short latency, by a temporary fall of blood pressure in the hypertensive rat (Cohen, Sztokalo & Hinsch, 1973) and the rabbit (Larsson & Änggård, 1973). As this effect is inhibited by indomethacin it is interpreted as due to a temporary increase in the biosynthesis of prostaglandins from the excess of natural substrate. We have found that in the rabbit and the dog, the hypotension induced by arachidonate is markedly increased by heparin and by tryptophan (Deby and Damas, 1974; Deby, Barac & Bacq, 1974).

We have studied the action of various amino acids on arachidonate-induced hypotension in heparinized rabbits. Well-fed 2.5 kg male rabbits of the same strain were anaesthetized by urethane (80-100 mg/kg). Heparin (20 mg/kg) was injected 1 h before the start of control arachidonate intrajugular injections (arachidonic acid Sigma 99% purity, neutralized to pH 7.6 by NaOH) at doses (50-200 μg/kg) adapted to the sensitivity of each animal. Amino acids (Hoffmann-La Roche or Sigma) 20 mg/kg were injected i.v. in 0.5 ml of 0.15 M sodium phosphate buffer pH 7.6. Injections of arachidonate were repeated after a delay of 10 minutes.

Amino acids fall into three categories: (1) histidine, cysteine, lysine and arginine, like tryptophan, markedly increased the hypotensive effect of arachidonate; (2) leucine and proline were weakly active; (3) glycine, alanine, phenylalanine, tyrosine, glutamic and aspartic acids were inactive.

Our interpretation is that the level of certain amino acids in the blood is one of the factors which controls the synthesis of prostaglandins *in vivo*.

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Actions of prostaglandins A_2, E_1 and $F_{2\alpha}$ on cat skeletal muscle vascular bed

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The effects of prostaglandins (PG) A_2, E_1 and $F_{2\alpha}$ on the consecutive functional sections of the vascular bed of acutely denervated cat calf muscle were investigated. Male cats (n = 57), 2.5-3.2 kg, were anaesthetized with chloralose (46 mg/kg) and urethane (460 mg/kg) intramuscularly. The acutely denervated calf muscle was prepared according to the method described by Mellander (1966). The prostaglandins were given by infusion in doses ranging from 0.007 to 15 $\mu g\ kg^{-1}\ min^{-1}$ intra-arterially.

The results are given in Table 1. All three prostaglandins elicited dose-dependent decreases in peripheral resistance, indicating dilatation of the resistance vessels in the following order of potency: $PGE_1 > PGA_2 > PGF_{2\alpha}$. Whereas dilatation of the capacitance vessels was also observed during the infusion of PGA_2 and PGE_1, a dose-dependent constriction of the capacitance vessels was provoked by the infusion of $PGF_{2\alpha}$. A net increase in interstitial fluid was observed during the infusion of PGA_2 and PGE_1, however, only the effect of PGA_2 was dose-related. $PGF_{2\alpha}$ had no effect on transcapillary fluid filtration.

The effects of PGA_2, PGE_1 and $PGF_{2\alpha}$ on the peripheral vascular bed of cats appeared to be qualitatively similar to those reported for man (Robinson, Collier, Karim & Somers, 1973).

Table 1 Effects of prostaglandins A_2, E_1 and $F_{2\alpha}$ on the acutely denervated vascular bed of cat calf muscle

PG	Dose ($\mu g\ kg^{-1}\ min^{-1}$ i.a.)	n	% Resistance response ± s.e. mean (control = 100%)	Capacitance response ± s.e. mean (ml/100 g tissue)	Transcapillary fluid filtration ± s.e. mean ($ml\ min^{-1}\ 100\ g\ tissue^{-1}$)
A_2	0.062	4	97 ± 7	0.00	+0.03 ± 0.03
	0.187	5	86 ± 8	+0.09 ± 0.05	+0.10 ± 0.01
	0.560	5	77 ± 5	+0.12 ± 0.06	+0.19 ± 0.03
	1.67	4	77 ± 4	+0.23 ± 0.08	+0.19 ± 0.06
E_1	0.007	4	93 ± 1	0.00	+0.09 ± 0.05
	0.021	6	89 ± 2	+0.14 ± 0.03	+0.04 ± 0.03
	0.062	4	88 ± 5	+0.03 ± 0.03	+0.26 ± 0.06
	0.187	4	75 ± 4	+0.39 ± 0.13	+0.05 ± 0.05
	0.560	6	67 ± 3	+0.39 ± 0.12	+0.12 ± 0.05
$F_{2\alpha}$	1.67	6	92 ± 3	−0.17 ± 0.12	0.00
	5.0	4	90 ± 2	−0.32 ± 0.13	−0.05 ± 0.02
	15.0	5	89 ± 3	−0.39 ± 0.2	−0.04 ± 0.04

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