

Prostacyclin (PGI₂): a potential mediator of inflammation

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PGI₂ has been primarily associated with physiological regulatory processes including control of platelet aggregation and blood flow. The role of PGI₂ and its metabolite, 6-oxo-F_{1α}, in inflammatory and other pathological conditions, is also of interest. This is because 6-oxo-F_{1α} is an important end-product of prostaglandin biosynthesis in the mouse macrophage (Humes, Bonney, Pelus, Dahlgren, Sadowski, Kuehl & Davies, 1977) and both PGI₂ and 6-oxo-F_{1α} potentiate vascular permeability changes induced by bradykinin in the rabbit skin (Peck & Williams, 1978).

Oedema formation was induced in the hind paw of female Wistar rats (120–160 g) by the injection of 0.1 ml volumes of either carrageenan (1% w/v), histamine (200 µg/ml), bradykinin (100 µg/ml) or prostaglandins (0.1–10 µg/ml) dissolved or suspended in

Tyrode solution. PGE₁, PGE₂ and PGI₂ (100 ng per rat), but not 6-oxo-F_{1α}, significantly potentiated carrageenan-induced oedema in the rat. The effect with PGI₂, despite its relative instability in aqueous solution, was similar to that observed for PGE₁ and considerably greater than that observed for PGE₂. PGI₂ and PGE₁ also significantly potentiated paw oedemas produced by the injection of histamine and bradykinin (see Table 1).

It is concluded that PGI₂ resembles E series prostaglandins and acts to potentiate the effects of other inflammatory mediators. It must, therefore, be considered as a potential modulator of inflammatory responses.

References

- HUMES, H.L., BONNEY, R.J., PELUS, L., DAHLGREN, M.E., SADOWSKI, S.J., KUEHL, F.A. & DAVIES, P. (1977) Macrophages synthesis and release prostaglandins in response to inflammatory stimuli. *Nature, Lond.*, **269**, 149–150.
- PECK, M.J. & WILLIAMS, T.J. (1978) Prostacyclin (PGI₂) potentiates bradykinin-induced plasma exudation in rabbit skin. *Br. J. Pharmac.*, **62**, 464P–465P.

Table 1 Effects of prostaglandins on carrageenan, histamine and bradykinin-induced oedema

Agent	Dose (µg/0.1 ml)	n	% Increase in paw volume (0.5 h)
Carrageenan alone		33	14.9 ± 1.7
Carrageenan + PGI ₂	0.1	10	70.5 ± 6.1*
Carrageenan + PGE ₁	0.1	5	64.4 ± 4.5*
Carrageenan + PGE ₂	0.1	5	37.3 ± 3.6*
Carrageenan ± 6oxoPGF _{1α}	1	5	21.6 ± 1.9
Tyrode alone		10	−2.3 ± 1.1
PGI ₂	0.1	20	5.7 ± 1.7
Histamine	20	15	5.0 ± 1.7
Histamine ± PGI ₂	20 + 0.1	5	30.3 ± 3.5*
Bradykinin	10	15	20.0 ± 2.7
Bradykinin + PGI ₂	10 + 0.1	5	52.1 ± 2.6*

Results are expressed as % increase in paw volume (mean ± s.e. mean).

* $P < 0.005$ —significant potentiation of either the carrageenan, histamine or bradykinin response by the addition of prostaglandins.