The rat stomach strip was contracted by prostaglandin E_2 (PGE_2) being more potent than PGG_2 and PGH_2 (2-3 x) and TxA_2 (10 x). On rat colon, TxA_2 was inactive (up to 50 ng); $PGF_{2\alpha}$ was 12–15 times more potent than the endoperoxides. On chick rectum PGE_2 was more potent than the endoperoxides (2-3 x) and TxA_2 (4 x). On rabbit aorta, TxA_2 was 30–50 times more potent than the endoperoxides; PGE_2 and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) were inactive (up to 200 ng). Some of these results confirm ratios previously described (Nugteren & Hazelhof, 1973; Willis, Vane, Kuhn, Scott & Petrin, 1974).

The most interesting effects were on coeliac and mesenteric artery. PGE_2 (1–20 ng) relaxed these preparations, as did PGG_2 and PGH_2 at about one fifth of the potency. In some preparations the PGG_2 or PGH_2 induced relaxation preceded by a short-lasting contraction. Thromboxane A_2 contracted both preparations. Coeliac artery recovered from relaxation in 5 min whereas mesenteric artery took considerably longer.

We conclude that (a) the RCS described by Piper & Vane (1969) was predominantly TxA_2 since it contracted strips of rabbit coeliac artery (Palmer *et al.*, 1973) (b) PGG_2, PGH_2 and TxA_2 are much more potent on vascular tissue than on smooth muscle from gastrointestinal tract and (c) the coeliac artery preparation distinguishes between the endoperoxides and TxA_2. It will be interesting to compare these activities with vascular effects of the same substances *in vivo*.

References

GILMORE, N., VANE, J.R. & WYLLIE, H.J. (1968). Prostaglandins released by the spleen. *Nature*, **218**, 1135–1140.

HAMBERG, M., SVENSSON, J. & SAMUELSSON, B. (1975). Thromboxanes: A new group of biologically active compounds derived from prostaglandin endoperoxides. *Proc. Nat. Acad. Sci. U.S.A.*, **72**, 2994–2998.

NUGTEREN, D.H. & HAZELHOF, E. (1973). Isolation and properties of intermediates in prostaglandin biosynthesis. *Biochim. et Biophys. Acta*, **326**, 448.

PALMER, M.A., PIPER, P.J. & VANE, J.R. (1973). Release of rabbit aorta contracting substance (RCS) and prostaglandins induced by chemical or mechanical stimulation of guinea-pig lungs. *Brit. J. Pharmacol.*, **49**, 226.

PIPER, P.J. & VANE, J.R. (1969). The release of additional factors in anaphylaxis and its antagonism by anti-inflammatory drugs. *Nature, Lond.*, **223**, 29–35.

WILLIS, A.L., VANE, F.M., KUHN, D.C., SCOTT, C.G. & PETRIN, M. (1974). An endoperoxide aggregator (LASS) formed in platelets in response to thrombic stimuli. *Prostaglandins*, **8**, 453–506.

VARGAFTIG, B.B. & DAO HAI, N. (1971). Release of vasoactive substances from guinea-pig lungs by slow reacting substance C and arachidonic acid. *Pharmacology*, **6**, 99–108.

Bioassay and thin-layer chromatography of prostaglandins and their pulmonary metabolites

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Piper & Vane (1969) reported that prostaglandins are released from guinea-pig lungs during anaphylaxis. Mathé & Levine (1973) and Leibig, Bernauer & Peskar (1974) have shown that prostaglandin metabolites are also released. We have therefore investigated the effects of the pulmonary metabolites of the prostaglandins on tissues routinely used to assay parent prostaglandins. Earlier results indicate that high doses of the pulmonary metabolites of prostaglandin E_2 (PGE_2) are indistinguishable from lower doses of PGE_2 on the tissues used (Crutchley & Piper, 1975). The present studies were carried out on the pulmonary metabolites of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$).

Prostaglandins and metabolites were assayed on the rat stomach strip, chick rectum, rat colon and oestrogen-primed rat uterus as described (Crutchley & Piper, 1975). Thin-layer chromatography was carried out using the AI, AII and AIII systems (Green & Samuelsson, 1964; Änggard & Samuelsson, 1964).

Results of bioassay on rat stomach strip, chick rectum and rat colon indicated that 13,14-dihydro-$PGF_{2\alpha}$ was the most potent metabolite, having approximately 0.3 times the activity of $PGF_{2\alpha}$. 13,14-dihydro-15-keto-$PGF_{2\alpha}$ and 15-keto-$PGF_{2\alpha}$ had approximately 0.01 times the activity of the parent prostaglandin. However, the order of potency of metabolites was the same on all three assay tissues, making distinction on this basis impossible (Figure 1).

In the AII system, 13,14-dihydro-PGE_2 (R_f 0.80) was almost indistinguishable from PGE_1 (R_f 0.82) and 13,14-dihydro-PGF_2 (R_f 0.50) was similarly indistinguishable from PGE_2 (R_f 0.50). Thin-layer chromatography in the AI and AIII systems also failed to separate these prostaglandins. When tested on rat stomach strip, rat colon and chick rectum

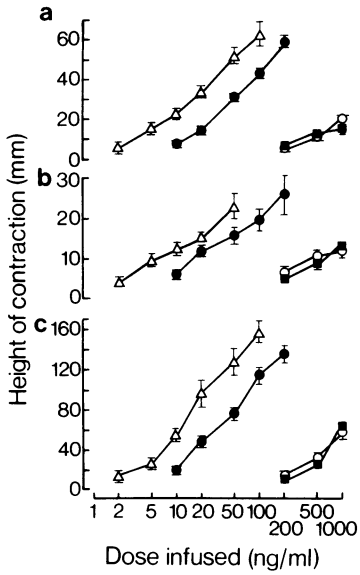

Figure 1 Comparative bioassay of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) (△) and its pulmonary metabolites 13,14-dihydro-PGF (●), 15-keto-$PGF_{2\alpha}$ (○) and 13,14-dihydro-15-keto-$PGF_{2\alpha}$ (■) on (a) rat stomach strip, (b) chick rectum and (c) rat colon. Prostaglandin $F_{2\alpha}$ or metabolites were given as random 2 min infusions into the Krebs solution superfusing the assay tissues. The height of contraction of the assay tissues was plotted against the log dose of agonist. Each point is the mean of 9–11 experiments. Vertical bars show s.e. mean.

PGE_1 and dihydro-PGE_2 did not give parallel bioassay. Similar results were obtained with PGE_2 and 13,14-dihydro-$PGF_{2\alpha}$. However, the differences obtained would not be sufficient to allow distinction between these PGs and metabolites in a biological fluid. 13,14-dihydro-$PGF_{2\alpha}$ was approximately 1.7 times as active as $PGF_{2\alpha}$ and approximately 3.0 times as active as PGE_2 on the oestrous rat uterus.

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References

ÄNGGÅRD, E. & SAMUELSSON, B. (1964). Metabolism of prostaglandin E_1 in guinea-pig lung: the structures of two metabolites. *J. biol. Chem.*, **239**, 4097–4102.

CRUTCHLEY, D.J. & PIPER, P.J. (1975). Comparative bioassay of prostaglandin E_2 and its three pulmonary metabolites. *Br. J. Pharmac.*, **54**, 397–399.

GRÉEN, K. & SAMUELSSON, B. (1964). Thin-layer chromatography of prostaglandins. *J. Lipid Res.*, **5**, 117–120.

LIEBIG, R., BERNAUER, W. & PESKAR, B.A. (1974). Release of prostaglandins, a prostaglandin metabolite, slow-reacting substance and histamine from anaphylactic lungs and its modification by catecholamines. *Naunyn-Schmiedeberg's Arch. Pharmac.*, **284**, 279–293.

MATHÉ, A.A. & LEVINE, L. (1973). Release of prostaglandins and metabolite from guinea-pig lung: inhibition by catecholamines. *Prostaglandins*, **4**, 877–890.

PIPER, P.J. & VANE, J.R. (1969). Release of additional factors in anaphylaxis and its antagonism by anti-inflammatory drugs. *Nature (Lond.)*, **233**, 29–35.

Prostaglandins and tone in isolated strips of mammalian bladder

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It has been demonstrated in a group of patients with paralysed atonic bladders that the intravesical instillation of prostaglandin E_2 (PGE_2) restores a normal pattern of micturition (Bultitude, 1973). The local production of prostaglandins has been implicated in the maintenance of tone and spontaneous activity of smooth muscle of the intestine (Ferreira, Herman & Vane, 1972), uterus (Vane & Williams, 1973) and trachea (Farmer, Farrar & Wilson, 1974). The object of the present investigation was to determine whether prostaglandins have a similar function in the bladder.

Strips of either detrusor or trigone muscle from the bladder of rabbit, rat, cat, dog, sheep, guinea-pig or human were suspended in Tyrode's solution at 37°C, bubbled with O_2 (95%):CO_2 (5%) mixture. A tension of 1 g was applied. Contractions were measured isometrically and displayed on a Servoscribe 1 s potentiometric recorder.

Prostaglandin E_2 (0.2–6.0 μg/ml) and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) (0.2–6.0 μg/ml) caused contractions of the strips, but the log dose-response curve obtained was much less steep than that of carbachol. The tone and spontaneous activity of the strips was reduced by indomethacin (0.5–2 μg/ml), meclofenamic acid