BENNETT, A. & POSNER, J. (1971). Studies on prostaglandin antagonists. *Br. J. Pharmac.*, **42**, 584–594.

FLESHLER, B. & BENNETT, A. (1969). Responses of human, guinea-pig and rat colonic circular muscle prostaglandins. *J. Lab. Clin. Med.*, **74**, 872.

HAMBERG, M., HEDQVIST, P., STRANDBERG, K., SVENSSON, J. & SAMUELSSON, B. (1975). Prostaglandin endoperoxides IV. Effects on smooth muscle. *Life Sci.*, **16**, 451–462.

MONCADA, S., MUGRIDGE, K.G. & WHITTLE, B.J.R. (1977). The differential response of a novel bioassay tissue, the rabbit transverse stomach-strip, to prostacyclin (PGI_2) and other prostaglandins. *Br. J. Pharmac.*, **61**, 451–452P.

NUGTEREN, D.H. & HAZELHOF, E. (1973). Isolation and properties of intermediates in prostaglandin biosynthesis. *Biochim. Biophys. Acta*, **326**, 448–461.

C.22

A study of receptors activated by analogues of prostaglandin H_2

A. BENNETT, C. JAROSIK & D.E. WILSON

Department of Surgery, King's College Hospital Medical School, London SE5 8RX.

The prostaglandin (PG) endoperoxides PGG_2 and PGH_2 are biologically active intermediates in the formation of PGs and thromboxanes. It is not known whether the endoperoxides and PGs act on the same receptors. We have studied this problem using the PG antagonist SC-19220 (Sanner, 1969).

Rat gastric fundus strips and segments of guinea-pig ileum were suspended under loads of 0.5–1.0 g in Krebs solution at 37°C bubbled with 5% CO_2 in O_2. Isotonic contractions of longitudinal muscle were registered with transducers and pen recorders.

PGE_2 and the PGH_2 analogues, (15S)-hydroxy-9α,11α- and (15S)-hydroxy-11α,9α-(epoxymethano)-prosta-5Z,13E-dienoic acids (U-44069 and U-46619) contracted both tissues. This was shown by cumulative dose-response curves in the rat stomach and by responses to single doses in the guinea-pig ileum.

On the rat stomach the potencies were PGE_2 > U-46619 > U-44069, and the maximum contractions were usually similar. SC-19220 (5 μg/ml) shifted the dose response curve of PGE_2 to the right (Table 1). In contrast, there was no significant effect on the dose-response curves of the analogues ($P > 0.2$). The responses of guinea-pig ileum to the analogues were small and variable. The maximum responses to U-44069 and U-46619 were, respectively, 11 ± 27 (±s.e. mean) and 26 ± 16% of that to PGE_2. Approximate doses required to produce ED_{50} responses were 4 μg/ml for the analogues and 10 ng/ml for PGE_2. SC-19220 2 μg/ml reduced responses to PGE_2 more than those of the analogues. Responses to doses of PGE_2, U-44069 and U-46619 that produced approximately 50% of maximum contractions were reduced by 73 ± 3, 54 ± 6 and 35 ± 9% respectively.

Table 1 ED_{50} concentrations (ng/ml) before (control) and after addition of SC-19220, 5 μg/ml

Drug	*Control*	n	+SC-19220	n
PGE_2	2.7 ± 0.1	23	7.0 ± 1.3*	8
U-44069	15.7 ± 1.6	13	10.6 ± 2.5	5
U-46619	10.5 ± 1.8	13	14.0 ± 4.3	7

Mean ± 1 s.e. mean.
* $P < 0.001$.

We conclude that the potencies of the analogues relative to PGE_2 vary with the tissue, and that at least so far as the rat stomach is concerned, the receptors for PGE_2 and the analogues are different.

Reference

SANNER, J.H. (1969). Antagonism of prostaglandin E_2 by 1-acetyl-2-(8-chloro-10,11-dihydrobenz (b,f) (1,4) oxazepine-10-carbonyl) hydrazine (SC-19220). *Archs. int. Pharmacodyn. Ther.*, **180**, 46–56.