Trimethoquinol selectively antagonises longitudinal muscle contractions of rat isolated gastric fundus to thromboxane B_2 and epoxymethano analogues of PGH_2

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Studies with the prostaglandin (PG) antagonist SC-19220 (Sanner, 1969) suggest that in the longitudinal muscle of the rat gastric fundus PGE_2 acts on receptors different from those of PGH_2 (Bennett, Jarosik & Wilson, 1978). We have now included thromboxane (Tx)B_2 in this study and investigated the effects of the PG endoperoxide antagonist trimethoquinol (MacIntyre & Willis, 1978).

Strips of rat gastric fundus cut parallel to the longitudinal muscle were suspended under a load of 1 g in Krebs solution at 37°C bubbled with 5% CO_2 in O_2. Isotonic contractions were measured using transducers and pen recorders, and cumulative dose-response curves were obtained for acetylcholine (ACh), PGE_2, TxB_2 or the analogues of PGH_2, (15S)-hydroxy-11α,9α- and (15S)-hydroxy-9α,11α-(epoxymethano)-prosta-5Z-13E-dienoic acids (U-46619 and U-44069). PGE_2 was about 6 times more potent than U-46619 and U-44069 which were about 80 times more potent than TxB_2 in contracting the tissue.

SC-19220 (5 μg/ml) increased the concentration of PGE_2 or TxB_2 needed to produce a response 50% of maximum (EC_{50}), but only the effect on PGE_2 was significantly greater than that on ACh (Table 1). Trimethoquinol (50 ng/ml) significantly increased the EC_{50} for ACh, PGE_2, TxB_2 and the PGH_2 analogues. However, whereas the block of responses to TxB_2 or the PGH_2 analogues was substantial, the effect on PGE_2 was less and was not significantly different from that on ACh (Table 1).

PGE_2 seems to act on receptors different from those for TxB_2 or the PGH_2 analogues, and responses can be preferentially antagonised by SC-19220 or trimethoquinol respectively.

Trimethoquinol is a β-adrenoceptor stimulant used clinically as a bronchodilator (Yamamura & Kishmoto, 1968), but it is not known whether antagonism of prostanoid action is involved in this effect.

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Table 1 Increase in EC_{50} required after addition of SC-19220 (5 μg/ml) or trimethoquinol (50 ng/ml) (median and semiquartile ranges) compared with ACh (P: Wilcoxon matched pairs test). n = number of preparations

Agonist	*with SC-19220*	*n*	*P*	*with trimethoquinol*	*n*	*P*
ACh	1.4(0.9 – 2)	28		3(2 – 4)	13	
PGE_2	7(4 – 20)	18	<0.0001	4(2 – 7)	6	0.4
TxB_2	2.1(1.5 – 2.2)	6	0.13	26(22 – 75)	6	0.001
U-46619	1.5(1.3 – 2.1)	8	0.44	14(10 – 30)	6	<0.001
U-44069	1.2(0.7 – 2.1)	8	0.51	25(20 – 220)	6	<0.001

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