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## Prostaglandins and the response of rat isolated ileum and duodenum to bradykinin

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An involvement of prostaglandins in the contractile action of bradykinin upon the longitudinal muscle of rat isolated terminal ileum was reported by Crocker & Willavoys (1976). Preliminary data has been presented suggesting that prostaglandins may be involved in the contractile action of bradykinin during mucosal but not serosal perfusion of the rat ileum (Crocker, Walker & Wilson, 1978). We have investigated further this interrelationship of prostaglandins and bradykinin in the contraction of the ileum and extended the study to the involvement of prostaglandins in the relaxation of the duodenum to bradykinin.

The terminal ileum or proximal duodenum was removed from male Wistar rats (180-250 g), placed under a tension (1 g) and perfused through the Lumen at 3 ml/min with Krebs solution at 37°C, bubbled with 5%  $CO_2$  in  $O_2$ . In experiments involving pretreatment, indomethacin (8 mg/kg) was injected subcutaneously 2 h prior to removal of the appropriate tissue. All contractions were recorded isometrically. Bradykinin (0.2 ml) was injected into the Krebs solution prior to perfusion of either the mucosal surface, or the serosal surface after eversion of the ileum or duodenum.

The longitudinal muscle contractions of the ileum, or relaxations of the duodenum, to bradykinin perfused over the serosal surface were unaffected by either indomethacin 2.8  $\mu M$  ( $n = 5$ ) or 28  $\mu M$  ( $n = 5$ ) added to the perfusate, or by pretreatment of the rats with indomethacin. However, during mucosal perfusion of the ileum the log-dose response curve of bradykinin on the longitudinal muscle was displaced

to the right with a reduction in the maximal contraction of  $54 \pm 6\%$  ( $n = 5$ )  $P < 0.001$  and  $80 \pm 5\%$  ( $n = 5$ )  $P < 0.001$  by indomethacin 2.8  $\mu M$  and 28  $\mu M$  respectively when added to the perfusate. Pretreatment of rats with indomethacin also reduced the maximal contraction of the ileum to bradykinin during mucosal perfusion by  $45 \pm 6\%$  ( $n = 5$ )  $P < 0.001$ . Similarly, during mucosal perfusion of the duodenum the maximal relaxation observed was reduced by  $41.5 \pm 6\%$  ( $n = 6$ )  $P < 0.001$  and  $53.4 \pm 5\%$  ( $n = 6$ )  $P < 0.001$  by indomethacin 2.8  $\mu M$  and 28  $\mu M$  respectively when added to the perfusate. Pretreatment of rats with indomethacin also reduced the maximal relaxation observed to bradykinin by  $43.6 \pm 16\%$  ( $n = 7$ )  $P < 0.01$ .

These results provide further support for an involvement of prostaglandins in the response of the rat small intestine to bradykinin during mucosal perfusion but not during serosal perfusion. Thus it appears that the involvement of prostaglandins is not confined to the contractile action of bradykinin since it also occurred during relaxation of the duodenum to bradykinin.

R.W. is an SRC student. We thank Merck Sharp and Dohme for indomethacin.

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