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## Pharmacodynamic Interaction between H<sub>2</sub>-Receptor Antagonists and GABA in Isolated Guinea Pig Ileum

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### AIM

Convulsive activity of H<sub>2</sub>-receptor antagonists has been attributed to their antagonistic action at central  $\gamma$ -aminobutyric acid (GABA)-receptors. The aim of the present study was to investigate whether H<sub>2</sub>-receptor antagonists act at peripheral GABA sites as well.

### MATERIALS AND METHODS

In order to explore this, GABA and the GABA<sub>A</sub>-agonist muscimol were applied in isolated ileal guinea pig preparations in the absence and presence of two H<sub>2</sub>-receptor antagonists, famotidine and cimetidine.

### RESULTS

Responses of the preparations showed that both GABA and muscimol produce a concentration-dependent contractile effect on the guinea pig ileum. Famotidine and cimetidine modify this contractile effect, either by enhancing or by inhib-

iting it, the result depending not only on their concentration, but also on that of GABA or muscimol. In addition, famotidine's action is different from cimetidine's action. Indeed, when tested at the concentration of 10<sup>-5</sup> M, famotidine enhances the contractile response of the ileum to either GABA or muscimol, while cimetidine does not modify it. At the high concentration of 3 x 10<sup>-4</sup> M, both the H<sub>2</sub>-receptor antagonists tested inhibit the contractile effect of either GABA or muscimol. However, the inhibition produced by famotidine is more potent than the one produced by cimetidine.

### CONCLUSIONS

In conclusion, the interaction of H<sub>2</sub>-receptor antagonists with GABA receptors is not limited to the central nervous system, but it is also present in the peripheral nervous system. This interaction mainly concerns GABA<sub>A</sub>-receptors and depends on both the specific H<sub>2</sub>-antagonist and its concentration used.