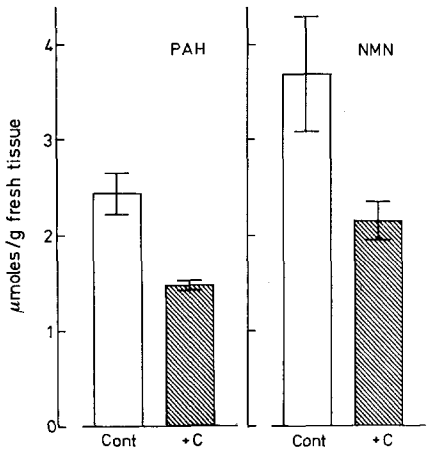

Fig. 3. Effect of (+)-catechin on PAH and NMN uptake by dog renal cortex slices. Tissues were incubated for 1 h in 0.1 m*M* PAH or 0.1 m*M* NMN with or without 3.5 m*M* (+)-catechin. The inhibitory effect of (+)-catechin is significant at the 0.1% level in both cases. Results are the means ± SEM of 6 experiments.

(+)-catechin may act preferentially on this membrane, where the transport mechanisms for NMN and PAH are thought to be located[13–15]. The inhibition of the uptake of both these substrates by (+)-catechin provides further support for the hypothesis of an interaction with the basal membrane.

Ring et al.[4] suggested that (+)-catechin reduces the passive permeability of membranes by interaction with some of the lipophilic membrane components. Such an explanation would agree with the decreased passage of sugars and amino-acids across the peritubular membrane. Equally, a direct effect of (+)-catechin at that locus would affect the accumulation of PAH and NMN across that membrane. It remains to be elucidated why (+)-catechin appears specifically to affect the peritubular membrane, rather than that of the brush-border. It is probable that the different compositions of the two membranes may be responsible for this specificity.

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Histamine Receptors in the Cat Mesenteric Circulation

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Summary. The distribution of histamine receptors was studied in the isolated perfused vascular bed of the cat terminal ileum. The results indicated that the depressor effect of histamine is mediated through the stimulation of metiamide-sensitive H_2-receptors, while the pressor effect of the amine is mediated by the stimulation of mepyramine-sensitive H_1-receptors.

The distribution of histamine receptors in the tissues could easily be studied using classically known H_1 and recently discovered H_2-receptor blockers[2,3]. Both receptors have been shown to be present in different regional vessels. Using H_2-receptor blockers, we have recently shown the presence and the role of H_2-receptors in the vascular bed of the guinea-pig lung[4], rabbit kidney[5], guinea-pig heart[6] and rabbit ear[7].

In continuing these studies, we recently indicated the presence of histamine H_2-receptors in the mesenteric circulation of the cat terminal ileum. The present report contains the data of this investigation.

Material and method. The terminal ileums from adult mongrel cats, anesthetized with sodium pentobarbital (30 mg/kg i.v.), were isolated according to the method described previously[8,9]. The ileal segment was perfused with oxygenated (5% CO_2 in O_2) and warmed (37 °C)

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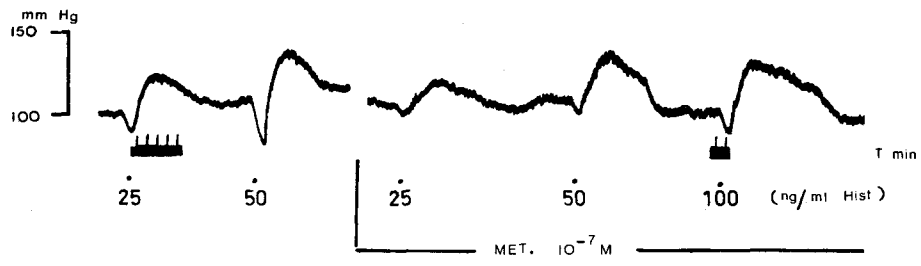

Fig. 1. A recorder tracing fromisolated perfused cat terminal ileum showing the effect of histamine on perfusion pressure before and after addition of metiamide (Met) to the perfusion medium.

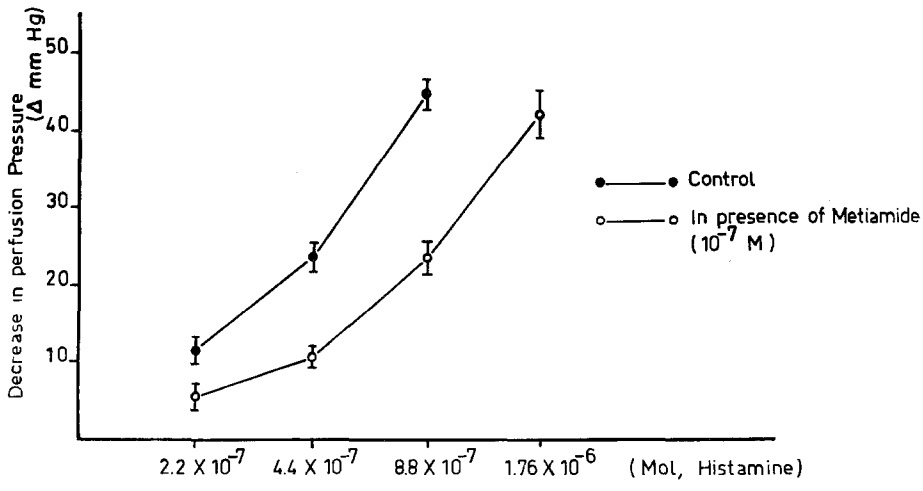

Fig. 2. The log dose-response curve of histamine before and after addition of metiamide to the perfusion medium. Each point shows the mean value of 5 experiments. Vertical bars represent SEM.

Krebs' solution through the ileo-caecal branch of the superior mesenteric artery by a peristaltic pump (Harvard) delivering a constant flow of 15 to 18 ml/min. The perfusion pressure was measured by a pressure transducer (Statham p 23 Dc) and recorded on a Grass polygraph (Model 79 D). In all experiments a tygon tubing was inserted into the intestinal lumen and the intestinal material was discarded throughout the experiments. Histamine was applied by single injections through a rubber tubing segment proximal to the cannulated artery. The perfusion system was regulated in such a manner that the injected histamine could reach the mesenteric vessels in 1 min. So the final concentration of the amine was determined by dividing the injected amount of histamine by the constant inflow per minute. Following control tests, metiamide, a potent antagonist of histamine H_2-receptors[3], and mepyramine, a classically known histamine H_1-receptor blocker, were separately added to the perfusion medium at different concentrations and the effect of the amine was tested again. The results were statistically evaluated using Student's *t*-test.

Results. Injection of histamine through the mesenteric artery induced a biphasic response in perfusion pressure (Figure 1). A sustained increase following a short decrease in perfusion pressure was obtained after injection of the amine. Both responses were found to be dose-dependent. In some experiments ($n = 4$), only depressor effect was observed after injection of histamine. In these experiments, the perfusion pressure was not higher than the others in which a biphasic response was obtained. Addition of metiamide to the perfusion medium, at the concentrations of 1.8 to 5.4×10^{-7} *M*, caused an inhibition in the depressor effect of histamine without significantly altering the pressor effect of the amine (Figure 1). The log dose-response curve of histamine measured in the depressor action of the amine is shown in Figure 2. The pA_2 value[10] of metiamide against histamine was found to be 6.93 ± 0.4 ($n = 9$). Metiamide neither inhibited nor potentiated the effects of angiotensin II, acetylcholine and noradrenaline in this preparation. Addition of mepyramine to the perfusion medium at the concentration of 10^{-9} *M* caused a dose-related decrease in the pressor action of histamine without influencing its depressor effect. The control increase in perfusion pressure induced by histamine (4.4×10^{-7} *M*) was 68.0 ± 8.0 mm Hg ($n = 8$), while it was 12.0 ± 3.0 mm Hg ($n = 8$) after addition of mepyramine to the perfusion medium at the concentration of 10^{-9} *M*.

Discussion. The results of this investigation indicate that two kinds of histamine receptors are present in the vascular bed of mesenteric circulation of the cat terminal ileum. The biphasic response to histamine might be the result of the stimulation of these receptors by the amine. It is apparent that the depressor effect of histamine is mediated through the stimulation of metiamide-sensitive H_2-receptors while the pressor effect of the amine is mediated by the stimulation of mepyramine-sensitive H_1-receptors. In this respect, the present findings are similar to those found in the guinea-pig pulmonary circulation[4], in rabbit renal vasculature[5], in rabbit ear vasculature[7] and in guinea-pig coronary vessels[6]. The antagonism between histamine and metiamide seems to be a competitive one, since the log dose-response curve of the amine shifted to the right and remained parallel to that of control in presence of the antagonist. The antagonistic effect of metiamide was found to be specific against histamine, since it does not alter the effects of angiotensin II, acetylcholine and noradrenaline. On the other hand, antagonistic potency of metiamide in this preparation was found to be equal to that found in the rabbit ear vessels, since the estimated pA_2 values in both preparations were not significantly different[7].

From these results, it was concluded that H_2-receptors are also present in the mesenteric vessels of the cat terminal ileum, as had been observed in the blood vessels previously investigated, and that they are responsible for the depressor effect of the amine.

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