LETTER TO THE EDITOR

EVIDENCE AGAINST CONVERSION OF HISTAMINE H_1 TO H_2 RECEPTORS IN THE GUINEAPIG ILLEUM AT LOW TEMPERATURES

Sir,

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Interconversion with change in temperature is reported for various receptors subtypes. Buckley and Jorden (1) reported conversion of β-into ∝-adrenoreceptors with reduction in temperature. Kenakin *et al.* (2) reported interconversion of H_1 to H_2 - receptor with reduction in temperaturs from 37°C to 12°C. Bennet and Kamp (3) and Bertaccini and Zappia (4) reported that no such interconversion occurs with change in temperature in adrenoreceptors and histamine receptors, respectively. With availability of specific agonist and antagonist of histamine receptors we reinvestigated if low temperature induces a conversion in histaminergic receptors of guinea-pig ileum.

The terminal ileum of freshly killed guinea-pigs of either sex 350-450 g) was suspended in organbath (30 *ml*) in oxygenated Tyrode solution (mM : NaCl, 137; KCl, 2.7; $NaHCo_3$, 11.9; NaH_2PO_4, 0.4, $MgCl_2$, 1.0 $CaCl_2$, 2.5 and glucose, 5.5, pH 7). Contractions were recorded with a force transducer (initial tension 0.25 g) and displayed on a two-channel recorder (Gemini, UGO BASILE). Complete dose-response curves to histamine, 2-PED, dimaprit and 4-methyl histamine were constructed at 37°C. They were then repeated in the presence of H_1 or H_2-receptors antagonists (contact time, 3 min). Afterwards the bath temperature was gradually lowered in about 2 hours to 20° or to 10°C and the same series of experiments were repeated.

The dose-response curves for histamine and for 2-PED at 37°C, at 20°C and at 10°C are shown in Fig. 1. The maximum response to both agonists was consistently and significantly ($P < 0.05$) higher at 20°C. When the temperature was reduced to 10°C, no such increase in the maximal response was observed. However, contractile response was very slow at 10°C as compared to that at 37°C and 20°C. Almost double the dose of agonist was required at 10°C to produce maximal response than at 37°C. Pretreatment with chlorpheniramine maleate (0.5 *ng/ml*) shifted the dose response curve of both agonist to the right at all the temperatures (Fig. 2). Dimaprit and 4-methyl histamine, specific H_2 -receptors agonists were devoid of any stimulatory effect upto concentration of 100 *μg/ml* at all the three temperatures studied. Cimetidine was unable to modity the dose-response curve to histamine and 2-PED upto the concentration of 30 *μg/ml*.

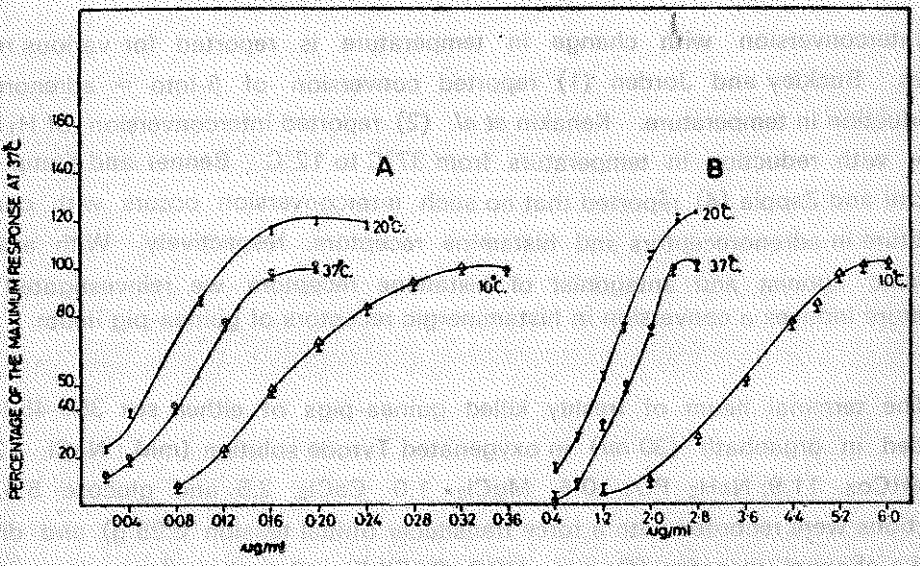

Fig. 1 : Guinea-pig ileum. Dose-response curves to histamine (A) and 2-PED (B) at 37°C (⊙), at 20°C (●) and at 10°C (Δ). Each value represents the mean of the values obtained from 5 to 6 experiments. Vertical bars are standard errors.

The antagonism of histamine and 2-PED by chlorpheniramine maleate suggests that two agonists contracted the puinea-pig ileum through activation of the classical H_1-receptors.

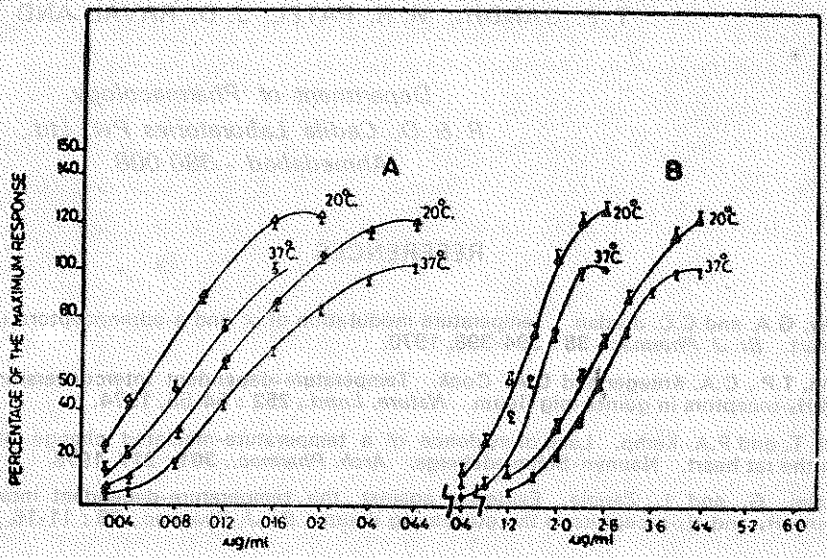

Fig. 2 : [A] Guinea-pig ileum. Dose response curves to histamine (0), histamine + chlorpheniramine chlorpheniramine maleate (●) at 37°C histamine (△), histamine + chlorpheniramine maleate (▲) at 20°C. [B] Dose response curves to 2PED (o), 2PED + Chlorpheniramine maleate (●) at 37°C. 2PED (△), 2PED + chlorpheniramine maleate (▲) at 20°C.

The H_2-receptor agonists were devoid of any effect at all the three temperatures upto a concentration of 100 $\mu g/ml$ Therefore, there was no proof that low temperature converts H_1 receptors into H_2-receptors. Histamine and selective H_1 agonist 2-PED both were more active at 20°C than at 37°C but we observed decrease activity of both the agonists at 10°C. Bertaccini and Zappia (4) have reported increased activity of histamine and selective H_1 agonist 2-amino ethylthiazole at 12°C. This difference might be due to different experimental conditions.

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