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Antihistaminases and gastric secretion stimulated by histamine in cats

by

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It is known that semicarbazide and various other compounds inhibit histaminase (5). MONGAR and SCHILD (4) have shown that semicarbazide potentiates the action of histamine on the isolated guinea-pig's ileum. Several other histaminase inhibitors also potentiated the effects of histamine on the isolated guinea-pig's ileum, tracheal chain and uterus, but they do not increased consistently the depressor effects of histamine on blood

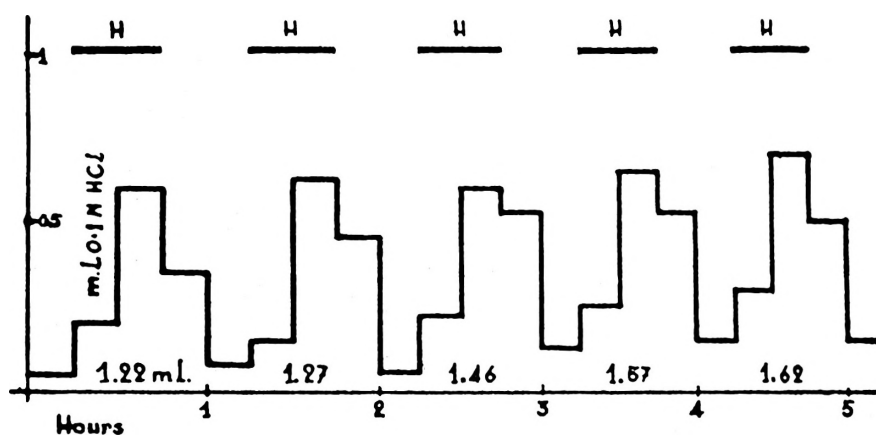


FIG. 1

pressure in cats (1). In the present paper we study the effect of semicarbazide on the acid secretion of the stomach stimulated by histamine.

Methods

Experiments were performed on cats, anaesthetized with intravenous chloralose (60 mg/kg) after induction with ether. A modification of the Howat & Schofield's two-dose histamine technique (3) was used (2): The cardia and pylorus

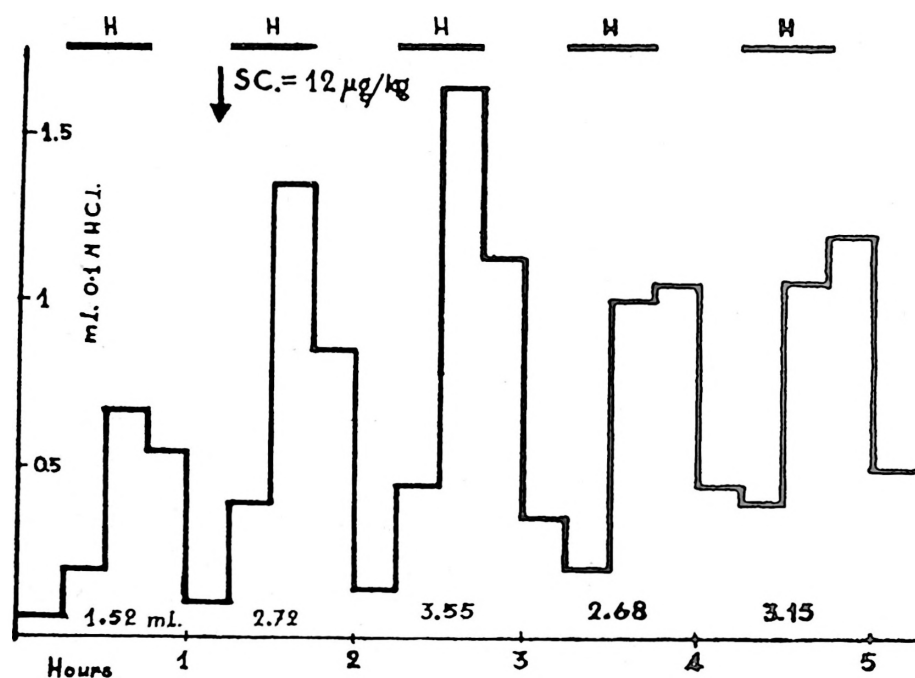


FIG. 2

mine technique (3) was used (2): The cardia and pylorus were occluded with ligatures, care being taken to avoid damage to the blood vessels. A cannula was fixed in an opening made into the stomach, through which washing of the stomach with warmed saline and taking of samples were made with a syringe fitted with a soft rubber tube, every 15 minutes. Gastric acid secretion was stimulated by intravenous infusion of histamine (5 µg/min.) for several periods (4-6) of 30 minutes, by means of a microburette connected to a cannula inserted into the femoral vein. Total acid was estimated by titrating with

0.1 N NaOH and phenolphthalein as indicator. The secretory response of the stomach to a series of infusions of histamine was nearly constant in control experiments (fig. 1).

Results

When given intravenously before the second period of histamine infusion, semicarbazide hydrochloride (Doesder) in doses of 10-12 $\mu\text{g}/\text{kg}$ caused potentiation of acid secretion of the stomach for the following two or more periods. The potentiating effect recorded in the fig. 2 was maximum after two periods and reached a degree of potentiation of 2.3 times (The mean % diff. was + 133).

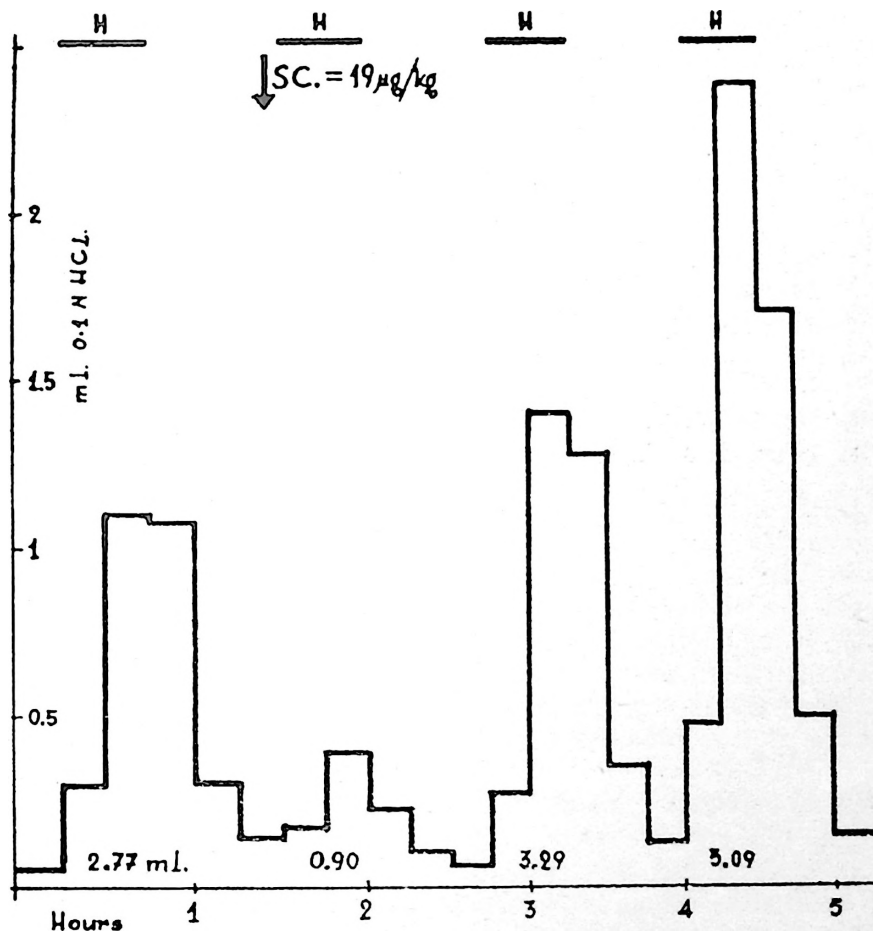


FIG 3

Doses of 18-20 $\mu\text{g/kg}$ of semicarbazide hydrochloride caused an immediate reduction of the flow of histamine-stimulated gastric juice, followed by an striking increase of the acid secretion after 3 or more hours, as the successive periods of histamine infusion took place (fig. 3).

It is interesting to note that after semicarbazide administration there was, sometimes, a change in the shape of the secretory responses, the maximum acidity of the samples being recorded after the 30 minutes period of histamine infusion (see fig. 2, 4th and 5th responses). Basal acidity was also increased.

Doses of semicarbazide producing potentiation would be 2.5×10^{-7} if the volume of distribution was the plasma volume and, similarly, inhibitory doses would be 5×10^{-7} . Corresponding values for isolated guinea-pig's intestine were 10^{-6} and 10^{-4} . Experiments are being carried out to determine whether semicarbazide is concentrated for the gastric mucosa, and to study the effects of semicarbazide on carbonic anhydrase and other enzymatic systems.

References

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